



## Clinical trial results:

### **A Phase 3, Randomized, Observer-blind, Controlled, Multi-Center Study to Evaluate the Lot to Lot Consistency of Investigational Meningococcal ACWY Conjugate Vaccine when One Dose is Administered to Healthy Adolescents 11-18 Years of Age and to Compare the Safety and Immunogenicity of Investigational Meningococcal ACWY Conjugate Vaccine with that of Licensed Meningococcal ACWY Conjugate Vaccine (Menactra™) when One Dose is Administered to Healthy Subjects 11-55 Years of Age**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-003504-79  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 16 January 2008 |

## Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 12 June 2016  |
| First version publication date | 03 January 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>Correction of full data set</li></ul> The occurrence rates were incorrectly entered, they need to be changed. |

## Trial information

### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | V59P13 |
|-----------------------|--------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00450437 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novartis Vaccines & Diagnostics, Inc.  |
| Sponsor organisation address | 350 Massachusetts Ave, Cambridge, MA, United States, 02139                     |
| Public contact               | Posting Director, Novartis Vaccines,<br>RegistryContactVaccinesUS@novartis.com |
| Scientific contact           | Posting Director, Novartis Vaccines,<br>RegistryContactVaccinesUS@novartis.com |

Notes:

## Paediatric regulatory details

|  |     |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
|--|-----|

|  |                     |
|--|---------------------|
| EMA paediatric investigation plan number(s)                          | EMA-000032-PIP01-07 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 04 April 2008 |
| Is this the analysis of the primary completion data? | No            |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 16 January 2008 |
| Was the trial ended prematurely? | No              |

Notes:

## General information about the trial

Main objective of the trial:

This study will evaluate the lot to lot consistency, safety and immune response of the Investigational Meningococcal ACWY conjugate vaccine in healthy US adolescents and adults.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements(s) for the country in which the study is conducted, and applicable standard operating procedures (SOPs). Specifically, this trial was based on adequately performed laboratory and animal experimentation; it was conducted under a protocol reviewed and approved by the Institutional Review Board (IRB) and by scientifically and medically qualified persons; the benefits of the study were in proportion to the risks; the rights and welfare of the subjects were respected; the physicians conducting the trial did not find the hazards to outweigh the potential benefits; each subject, or where applicable, each subject's legally acceptable representative(s) gave his or her written informed consent before any protocol-driven tests or evaluations were performed. Copies of the ICH GCP guidelines and of the Declaration of Helsinki were included in the investigator's study file.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 March 2007 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 3539 |
| Worldwide total number of subjects   | 3539                |
| EEA total number of subjects         | 0                   |

Notes:

| <b>Subjects enrolled per age group</b>    |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 349  |
| Adolescents (12-17 years)                 | 1669 |
| Adults (18-64 years)                      | 1521 |
| From 65 to 84 years                       | 0    |
| 85 years and over                         | 0    |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited from 44 centers.

### Pre-assignment

Screening details:

All enrolled subjects were randomized 1:1:1:1 to Menveo Lot 1, Menveo Lot 2, Menveo Lot 3, or Menactra, and stratified by age group.

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Investigational MenACWY Vaccine (11 to 18 Years) |

Arm description:

One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | MenACWY  |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solution for solution for injection |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

1 dose of 0.5 mL

|                  |   |
|------------------|---|
| <b>Arm title</b> | Licensed Meningococcal Vaccine (11 to 18 Years) |
|------------------|---|

Arm description:

One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | MenACWY                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

1 dose of 0.5 mL

|                  |  |
|------------------|--|
| <b>Arm title</b> | Investigational MenACWY Vaccine (19 to 55 Years) |
|------------------|--|

Arm description:

One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |   |
|--|---|
| Investigational medicinal product name                 | MenACWY   |
| Investigational medicinal product code                 |   |
| Other name   |   |
| Pharmaceutical forms                                   | Powder and solution for solution for injection  |
| Routes of administration                               | Intramuscular use                               |
| Dosage and administration details:<br>1 dose of 0.5 mL |   |
| <b>Arm title</b>                                       | Licensed Meningococcal Vaccine (19 to 55 Years) |

Arm description:

One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | MenACWY                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

1 dose of 0.5 mL

| <b>Number of subjects in period 1</b> | Investigational<br>MenACWY Vaccine<br>(11 to 18 Years) | Licensed<br>Meningococcal<br>Vaccine (11 to 18<br>Years) | Investigational<br>MenACWY Vaccine<br>(19 to 55 Years) |
|---------------------------------------|--|--|--|
| Started                               | 1640   | 540  | 1023   |
| Completed                             | 1594   | 524  | 999  |
| Not completed                         | 46   | 16   | 24   |
| Consent withdrawn by subject          | 10   | 2  | -  |
| Inappropriate enrollment              | 4  | 1  | 3  |
| Protocol deviation                    | -  | 1  | -  |
| Unable to classify                    | 1  | -  | 1  |
| Lost to follow-up                     | 31   | 12   | 19   |
| Administrative reason                 | -  | -  | 1  |
| Protocol deviation                    | -  | -  | -  |

| <b>Number of subjects in period 1</b> | Licensed<br>Meningococcal<br>Vaccine (19 to 55<br>Years) |
|---------------------------------------|--|
| Started                               | 336  |
| Completed                             | 325  |
| Not completed                         | 11   |
| Consent withdrawn by subject          | 1  |
| Inappropriate enrollment              | -  |
| Protocol deviation                    | -  |
| Unable to classify                    | -  |

|                       |   |
|-----------------------|---|
| Lost to follow-up     | 9 |
| Administrative reason | - |
| Protocol deviation    | 1 |

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Investigational MenACWY Vaccine (11 to 18 Years) |
| Reporting group description:<br>One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly. |  |
| Reporting group title   | Licensed Meningococcal Vaccine (11 to 18 Years)  |
| Reporting group description:<br>One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.                                   |  |
| Reporting group title   | Investigational MenACWY Vaccine (19 to 55 Years) |
| Reporting group description:<br>One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly. |  |
| Reporting group title   | Licensed Meningococcal Vaccine (19 to 55 Years)  |
| Reporting group description:<br>One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.                                   |  |

| Reporting group values             | Investigational MenACWY Vaccine (11 to 18 Years) | Licensed Meningococcal Vaccine (11 to 18 Years) | Investigational MenACWY Vaccine (19 to 55 Years) |
|------------------------------------|--|---|--|
| Number of subjects                 | 1640   | 540   | 1023   |
| Age categorical<br>Units: Subjects |  |   |  |

|   |               |               |             |
|---|---------------|---------------|-------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 14.2<br>± 2.2 | 14.1<br>± 2.2 | 39<br>± 9.6 |
| Gender categorical<br>Units: Subjects                                   |               |               |             |
| Female  | 769           | 251           | 774         |
| Male  | 871           | 289           | 249         |

| Reporting group values             | Licensed Meningococcal Vaccine (19 to 55 Years) | Total |  |
|------------------------------------|---|-------|--|
| Number of subjects                 | 336   | 3539  |  |
| Age categorical<br>Units: Subjects |   |       |  |

|   |               |      |  |
|---|---------------|------|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 38.7<br>± 9.9 | -    |  |
| Gender categorical<br>Units: Subjects                                   |               |      |  |
| Female  | 252           | 2046 |  |

|      |    |      |  |
|------|----|------|--|
| Male | 84 | 1493 |  |
|------|----|------|--|

### Subject analysis sets

|                            |  |
|----------------------------|--|
| Subject analysis set title | Investigational MenACWY (11 to 55 Years) |
| Subject analysis set type  | Per protocol                             |

Subject analysis set description:

One dose of the investigational meningococcal ACWY (three lots combined) conjugate vaccine was administered intramuscularly.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Licensed MenACWY (11 to 55 Years) |
| Subject analysis set type  | Per protocol                      |

Subject analysis set description:

One vaccination of the licensed meningococcal ACWY conjugate vaccine was administered intramuscularly.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Investigational MenACWY Lot 1 (11 to 18 years) |
| Subject analysis set type  | Per protocol                                   |

Subject analysis set description:

One dose of the investigational meningococcal ACWY conjugate Lot 1 vaccine was administered intramuscularly.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Investigational MenACWY Lot 2 (11 to 18 years) |
| Subject analysis set type  | Per protocol                                   |

Subject analysis set description:

One dose of the investigational meningococcal ACWY Lot 2 vaccine was administered intramuscularly.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Investigational MenACWY Lot 3 (11 to 18 years) |
| Subject analysis set type  | Per protocol                                   |

Subject analysis set description:

One dose of the investigational meningococcal ACWY Lot 3 vaccine was administered intramuscularly.

| Reporting group values             | Investigational MenACWY (11 to 55 Years) | Licensed MenACWY (11 to 55 Years) | Investigational MenACWY Lot 1 (11 to 18 years) |
|------------------------------------|--|-----------------------------------|--|
| Number of subjects                 | 2663                                     | 876                               | 548  |
| Age categorical<br>Units: Subjects |  |                                   |  |

|   |                |                |             |
|---|----------------|----------------|-------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 23.7<br>± 13.6 | 23.5<br>± 13.6 | 14<br>± 2.2 |
| Gender categorical<br>Units: Subjects                                   |                |                |             |
| Female  | 1543           | 373            | 254         |
| Male  | 1120           | 503            | 294         |

| Reporting group values             | Investigational MenACWY Lot 2 (11 to 18 years) | Investigational MenACWY Lot 3 (11 to 18 years) |  |
|------------------------------------|--|--|--|
| Number of subjects                 | 548  | 544  |  |
| Age categorical<br>Units: Subjects |  |  |  |



|                    |           |           |  |
|--------------------|-----------|-----------|--|
| Age continuous     |           |           |  |
| Units: years       |           |           |  |
| arithmetic mean    | 14.2      | 14.3      |  |
| standard deviation | $\pm 2.2$ | $\pm 2.3$ |  |
| Gender categorical |           |           |  |
| Units: Subjects    |           |           |  |
| Female             | 259       | 256       |  |
| Male               | 289       | 288       |  |

## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Investigational MenACWY Vaccine (11 to 18 Years) |
| Reporting group description:<br>One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly. |  |
| Reporting group title   | Licensed Meningococcal Vaccine (11 to 18 Years)  |
| Reporting group description:<br>One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.                                   |  |
| Reporting group title   | Investigational MenACWY Vaccine (19 to 55 Years) |
| Reporting group description:<br>One dose of the investigational meningococcal ACWY conjugate vaccine (obtained by extemporaneous mixing of components before injection) was administered intramuscularly. |  |
| Reporting group title   | Licensed Meningococcal Vaccine (19 to 55 Years)  |
| Reporting group description:<br>One dose of the licensed meningococcal ACWY conjugate vaccine (supplied as a single 0.5 mL injection) was administered intramuscularly.                                   |  |
| Subject analysis set title  | Investigational MenACWY (11 to 55 Years)         |
| Subject analysis set type   | Per protocol                                     |
| Subject analysis set description:<br>One dose of the investigational meningococcal ACWY (three lots combined) conjugate vaccine was administered intramuscularly.   |  |
| Subject analysis set title  | Licensed MenACWY (11 to 55 Years)                |
| Subject analysis set type   | Per protocol                                     |
| Subject analysis set description:<br>One vaccination of the licensed meningococcal ACWY conjugate vaccine was administered intramuscularly.   |  |
| Subject analysis set title  | Investigational MenACWY Lot 1 (11 to 18 years)   |
| Subject analysis set type   | Per protocol                                     |
| Subject analysis set description:<br>One dose of the investigational meningococcal ACWY conjugate Lot 1 vaccine was administered intramuscularly.   |  |
| Subject analysis set title  | Investigational MenACWY Lot 2 (11 to 18 years)   |
| Subject analysis set type   | Per protocol                                     |
| Subject analysis set description:<br>One dose of the investigational meningococcal ACWY Lot 2 vaccine was administered intramuscularly.   |  |
| Subject analysis set title  | Investigational MenACWY Lot 3 (11 to 18 years)   |
| Subject analysis set type   | Per protocol                                     |
| Subject analysis set description:<br>One dose of the investigational meningococcal ACWY Lot 3 vaccine was administered intramuscularly.   |  |

### Primary: Lot to Lot Consistency of MenACWY as Measured by hSBA GMT Vaccine Group Ratios, Ages 11 to 18 Years

|  |   |
|--|---|
| End point title  | Lot to Lot Consistency of MenACWY as Measured by hSBA GMT Vaccine Group Ratios, Ages 11 to 18 Years |
| End point description:<br>The consistency of immune response for the three lots of Meningococcal ACWY (MenACWY), as measured by human serum bactericidal activity (hSBA) geometric mean titer (GMT) response using human complement (hSBA GMTs) directed against <i>Neisseria meningitidis</i> serogroups A, C, W, and Y (healthy subjects 11 to 18 years of age). |   |
| End point type   | Primary   |

End point timeframe:  
28 days after vaccination

| End point values                            | Investigational<br>MenACWY Lot<br>1 (11 to 18<br>years) | Investigational<br>MenACWY Lot<br>2 (11 to 18<br>years) | Investigational<br>MenACWY Lot<br>3 (11 to 18<br>years) |  |
|---|---|---|---|--|
| Subject group type                          | Subject analysis set                                    | Subject analysis set                                    | Subject analysis set                                    |  |
| Number of subjects analysed                 | 359 <sup>[1]</sup>                                      | 357 <sup>[2]</sup>                                      | 359 <sup>[3]</sup>                                      |  |
| Units: Titer                                |   |   |   |  |
| geometric mean (confidence interval<br>95%) |   |   |   |  |
| Serogroup A                                 | 29 (23 to 38)   | 33 (25 to 42)   | 31 (24 to 40)   |  |
| Serogroup C                                 | 77 (58 to 102)  | 58 (43 to 77)   | 64 (48 to 86)   |  |
| Serogroup W                                 | 87 (70 to 108)  | 111 (89 to<br>138)                                      | 82 (66 to 102)  |  |
| Serogroup Y                                 | 48 (37 to 62)   | 61 (47 to 79)   | 53 (41 to 69)   |  |

Notes:

[1] - N serogroup C: 499  
N serogroup W: 340  
N serogroup Y: 345  
[2] - N serogroup C: 493  
N serogroup W: 341  
N serogroup Y: 345  
[3] - N serogroup C: 491  
N serogroup W: 343  
N serogroup Y: 346

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Equivalence Lot 1 and Lot 2 MenA   |
| Statistical analysis description:   |  |
| The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0). |  |
| Comparison groups   | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis   | 716  |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence <sup>[4]</sup>   |
| Method  | ANOVA  |
| Parameter estimate  | hSBA GMT ratios  |
| Point estimate  | 0.89   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 0.68   |
| upper limit   | 1.16   |

Notes:

[4] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Equivalence Lot 1 and Lot 3 MenA   |
| Statistical analysis description:   |  |
| The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0). |  |
| Comparison groups   | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis   | 718  |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence <sup>[5]</sup>   |
| Method  | ANOVA  |
| Parameter estimate  | hSBA GMT ratios  |
| Point estimate  | 0.95   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 0.73   |
| upper limit   | 1.23   |

Notes:

[5] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Equivalence Lot 2 and Lot 3 MenA   |
| Statistical analysis description:   |  |
| The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0). |  |
| Comparison groups   | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis   | 716  |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence <sup>[6]</sup>   |
| Method  | ANOVA  |
| Parameter estimate  | hSBA GMT ratios  |
| Point estimate  | 1.06   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 0.81   |
| upper limit   | 1.38   |

Notes:

[6] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|   |                                  |
|---|----------------------------------|
| <b>Statistical analysis title</b>   | Equivalence Lot 1 and Lot 3 MenC |
| Statistical analysis description:   |                                  |
| The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0). |                                  |
| The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 990  |                                  |

(instead of 718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[7]</sup>   |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 1.2  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.9  |
| upper limit                             | 1.6  |

Notes:

[7] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 992 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[8]</sup>   |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 1.33   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 1  |
| upper limit                             | 1.77   |

Notes:

[8] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 984 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 716                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[9]</sup> |
| Method                                  | ANOVA                      |
| Parameter estimate                      | hSBA GMT ratios            |
| Point estimate                          | 0.9                        |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.68                       |
| upper limit                             | 1.2                        |

Notes:

[9] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 681 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[10]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 0.79   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.63   |
| upper limit                             | 0.97   |

Notes:

[10] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 683 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[11]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | hSBA GMT ratios             |
| Point estimate                          | 1.06                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.86                        |
| upper limit                             | 1.13                        |

Notes:

[11] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 684 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[12]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 1.35   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 1.09   |
| upper limit                             | 1.67   |

Notes:

[12] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 690 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[13]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | hSBA GMT ratios             |
| Point estimate                          | 0.79                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.61                        |
| upper limit                             | 1.02                        |

Notes:

[13] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[14]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 0.91   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.7  |
| upper limit                             | 1.18   |

Notes:

[14] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y at 1 month after vaccination was contained within the equivalence interval (0.5, 2.0).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|



|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[15]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | hSBA GMT ratios             |
| Point estimate                          | 1.16                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.89                        |
| upper limit                             | 1.5                         |

Notes:

[15] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

### Primary: Number of Participants With at Least One Severe Systemic Reaction, Ages 11 to 55 Years

|                 |  |
|-----------------|--|
| End point title | Number of Participants With at Least One Severe Systemic Reaction, Ages 11 to 55 Years |
|-----------------|--|

End point description:

Safety of Investigational Meningococcal ACWY and of a licensed meningococcal ACWY conjugate vaccine as measured by the number of participants presenting at least one severe systemic reaction during the first 7 days (Days 1-7) following a single vaccination.

Note: severe adverse events: unable to perform normal daily activity

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

End point timeframe:

6 days after vaccination

| End point values                                   | Investigational MenACWY (11 to 55 Years) | Licensed MenACWY (11 to 55 Years) |  |  |
|--|--|-----------------------------------|--|--|
| Subject group type                                 | Subject analysis set                     | Subject analysis set              |  |  |
| Number of subjects analysed                        | 2649                                     | 875                               |  |  |
| Units: Number of subjects                          |  |                                   |  |  |
| number (not applicable)                            |  |                                   |  |  |
| Number of Participants With at Least One Severe Sy | 94                                       | 24                                |  |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Vaccine group difference Inv. Vac., Lic. Vac. sft. |
|----------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine; sft, safety

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
|-------------------|--|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 3524                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[16]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Vaccine group difference        |
| Point estimate                          | 1                               |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | -1                              |
| upper limit                             | 2                               |

Notes:

[16] - MenACWY was considered noninferior to Menactra if the upper limit of the two-sided 95% CI of the difference in the percentage of subjects experiencing at least one severe systemic reaction [MenACWY minus Menactra] was less than 6%.

### Primary: Percentage of Seroresponders, Ages 11 to 18 Years

|  |   |
|--|---|
| End point title  | Percentage of Seroresponders, Ages 11 to 18 Years <sup>[17]</sup> |
| End point description:   |   |
| Immunogenicity of a single injection of Meningococcal ACWY (3 lots pooled) to that of a licensed meningococcal ACWY conjugate vaccine, defined as the percentage of subjects with seroresponse directed against <i>Neisseria meningitidis</i> serogroups A, C, W, and Y (healthy adolescents 11 to 18 years of age). |   |
| Seroresponse to MenACWY: For a subject with hSBA titer <1:4 at baseline, seroresponse is defined as a postvaccination hSBA titer ≥ 1:8; for a subject with hSBA titer ≥ 1:4 at baseline, seroresponse is defined as a postvaccination hSBA titer of at least 4 times the baseline.                                   |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| 28 days after 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: there is no statistical analysis presented for this endpoint.

| End point values                 | Investigational MenACWY Vaccine (11 to 18 Years) | Licensed Meningococcal Vaccine (11 to 18 Years) |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                  | Reporting group                                 |  |  |
| Number of subjects analysed      | 1075 <sup>[18]</sup>                             | 359 <sup>[19]</sup>                             |  |  |
| Units: Percentage of subjects    |  |   |  |  |
| number (confidence interval 95%) |  |   |  |  |
| Serogroup A                      | 75 (72 to 77)                                    | 66 (61 to 71)                                   |  |  |
| Serogroup C                      | 75 (73 to 77)                                    | 73 (69 to 77)                                   |  |  |
| Serogroup W                      | 75 (72 to 77)                                    | 63 (57 to 68)                                   |  |  |
| Serogroup Y                      | 68 (65 to 71)                                    | 41 (35 to 47)                                   |  |  |

Notes:

[18] - N serogroup C: 1483

N serogroup W: 1024

N serogroup Y: 1036

[19] - N serogroup C: 501

N serogroup W: 288

N serogroup Y: 294

### Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenA   |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. |  |
| Comparison groups  | Investigational MenACWY Vaccine (11 to 18 Years) v Licensed Meningococcal Vaccine (11 to 18 Years) |
| Number of subjects included in analysis  | 1434   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[20]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 8  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | 3  |
| upper limit  | 14   |

Notes:

[20] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenC   |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.   |  |
| The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 1894 (instead of 1434, which refers to MenA). |  |
| Comparison groups  | Investigational MenACWY Vaccine (11 to 18 Years) v Licensed Meningococcal Vaccine (11 to 18 Years) |
| Number of subjects included in analysis  | 1434   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[21]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 2  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | -2   |
| upper limit  | 7  |

Notes:

[21] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenW   |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.   |  |
| The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 1312 (instead of 1434, which refers to MenA). |  |
| Comparison groups  | Investigational MenACWY Vaccine (11 to 18 Years) v Licensed Meningococcal Vaccine (11 to 18 Years) |

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 1434                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[22]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Vaccine group difference        |
| Point estimate                          | 12                              |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 6                               |
| upper limit                             | 18                              |

Notes:

[22] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenY |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 1330 (instead of 1434, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Vaccine (11 to 18 Years) v Licensed Meningococcal Vaccine (11 to 18 Years) |
| Number of subjects included in analysis | 1434   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[23]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 27   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 20   |
| upper limit                             | 33   |

Notes:

[23] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

### Primary: Percentage of Seroresponders, Ages 19 to 55 Years

|                 |   |
|-----------------|---|
| End point title | Percentage of Seroresponders, Ages 19 to 55 Years <sup>[24]</sup> |
|-----------------|---|

End point description:

Immunogenicity of a single injection of Meningococcal ACWY (3 lots pooled) to that of a licensed meningococcal ACWY conjugate vaccine, defined as the percentage of subjects with seroresponse directed against *Neisseria meningitidis* serogroups A, C, W, and Y (healthy subjects 19 to 55 years of Age).

Seroresponse to MenACWY: For a subject with hSBA titer <1:4 at baseline, seroresponse is defined as a postvaccination hSBA titer ≥ 1:8; for a subject with hSBA titer ≥ 1:4 at baseline, seroresponse is defined as a postvaccination hSBA titer of at least 4 times the baseline.

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

End point timeframe:

28 days after 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: there is no statistical analysis presented for this endpoint.

| End point values                 | Investigational MenACWY Vaccine (19 to 55 Years) | Licensed Meningococcal Vaccine (19 to 55 Years) |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                  | Reporting group                                 |  |  |
| Number of subjects analysed      | 963 <sup>[25]</sup>                              | 321 <sup>[26]</sup>                             |  |  |
| Units: Percentage of subjects    |  |   |  |  |
| number (confidence interval 95%) |  |   |  |  |
| Serogroup A                      | 67 (64 to 70)                                    | 68 (63 to 73)                                   |  |  |
| Serogroup C                      | 67 (64 to 70)                                    | 58 (53 to 64)                                   |  |  |
| Serogroup W                      | 50 (46 to 55)                                    | 41 (35 to 47)                                   |  |  |
| Serogroup Y                      | 56 (51 to 60)                                    | 40 (34 to 46)                                   |  |  |

Notes:

[25] - N serogroup C: 961

N serogroup W: 484

N serogroup Y: 503

[26] - N serogroup C: 318

N serogroup W: 292

N serogroup Y: 306

## Statistical analyses

| Statistical analysis title   | Vaccine group difference Inv. Vac., Lic. Vac. MenA   |
|--|--|
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. |  |
| Comparison groups  | Investigational MenACWY Vaccine (19 to 55 Years) v Licensed Meningococcal Vaccine (19 to 55 Years) |
| Number of subjects included in analysis  | 1284   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[27]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | -1   |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | -7   |
| upper limit  | 5  |

Notes:

[27] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

| Statistical analysis title   | Vaccine group difference Inv. Vac., Lic. Vac. MenC   |
|--|--|
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.<br>The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 1279 (instead of 1284, which refers to MenA). |  |
| Comparison groups  | Investigational MenACWY Vaccine (19 to 55 Years) v Licensed Meningococcal Vaccine (19 to 55 Years) |

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 1284                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[28]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Vaccine group difference        |
| Point estimate                          | 9                               |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 3                               |
| upper limit                             | 15                              |

Notes:

[28] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenW |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 776 (instead of 1284, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Vaccine (19 to 55 Years) v Licensed Meningococcal Vaccine (19 to 55 Years) |
| Number of subjects included in analysis | 1284   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[29]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 9  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 2  |
| upper limit                             | 17   |

Notes:

[29] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is > -10%.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenY |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 809 (instead of 1284, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Vaccine (19 to 55 Years) v Licensed Meningococcal Vaccine (19 to 55 Years) |
| Number of subjects included in analysis | 1284   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[30]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 16   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 9       |
| upper limit         | 23      |

Notes:

[30] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for the between group difference (investigational vaccine minus licensed vaccine) in percentage of seroresponders one month after vaccination is  $> -10\%$ .

**Secondary: Lot to Lot Consistency for the Percentage of Subjects With Seroreponse, Human Serum Bactericidal Activity (hSBA) Titer  $\geq 1:8$ , and  $\geq 1:4$ , Ages 11 to 18 Years**

|                 |  |
|-----------------|--|
| End point title | Lot to Lot Consistency for the Percentage of Subjects With Seroreponse, Human Serum Bactericidal Activity (hSBA) Titer $\geq 1:8$ , and $\geq 1:4$ , Ages 11 to 18 Years |
|-----------------|--|

End point description:

The consistency of the immune response for three lots of Meningococcal ACWY, as measured by the percentage of subjects with seroreponse, hSBA titer  $\geq 1:4$  and  $\geq 1:8$ , directed against N meningitidis serogroups A, C, W, and Y (healthy adolescents 11 to 18 years of age).

Seroreponse to MenACWY: For a subject with hSBA titer  $<1:4$  at baseline, seroreponse is defined as a postvaccination hSBA titer  $\geq 1:8$ ; for a subject with hSBA titer  $\geq 1:4$  at baseline, seroreponse is defined as a postvaccination hSBA titer of at least 4 times the baseline.

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

End point timeframe:

28 days after vaccination

| End point values                     | Investigational MenACWY Lot 1 (11 to 18 years) | Investigational MenACWY Lot 2 (11 to 18 years) | Investigational MenACWY Lot 3 (11 to 18 years) |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Subject analysis set                           | Subject analysis set                           | Subject analysis set                           |  |
| Number of subjects analysed          | 359 <sup>[31]</sup>                            | 357 <sup>[32]</sup>                            | 359 <sup>[33]</sup>                            |  |
| Units: Percentage of subjects        |  |  |  |  |
| number (confidence interval 95%)     |  |  |  |  |
| Seroreponse in serogroup A           | 71 (66 to 76)                                  | 75 (70 to 79)                                  | 77 (73 to 82)                                  |  |
| Seroreponse in serogroup C           | 78 (74 to 82)                                  | 73 (69 to 77)                                  | 74 (70 to 78)                                  |  |
| Seroreponse in serogroup W           | 74 (69 to 78)                                  | 80 (75 to 84)                                  | 70 (65 to 75)                                  |  |
| Seroreponse in serogroup Y           | 66 (61 to 71)                                  | 72 (67 to 77)                                  | 65 (60 to 70)                                  |  |
| hSBA Titer $\geq 1:8$ in serogroup A | 72 (67 to 77)                                  | 76 (71 to 80)                                  | 78 (74 to 82)                                  |  |
| hSBA Titer $\geq 1:8$ in serogroup C | 86 (82 to 89)                                  | 84 (81 to 87)                                  | 83 (79 to 86)                                  |  |
| hSBA Titer $\geq 1:8$ in serogroup W | 95 (92 to 97)                                  | 97 (95 to 99)                                  | 96 (93 to 98)                                  |  |
| hSBA Titer $\geq 1:8$ in serogroup Y | 86 (82 to 89)                                  | 89 (85 to 92)                                  | 88 (85 to 92)                                  |  |
| hSBA Titer $\geq 1:4$ in serogroup A | 76 (72 to 81)                                  | 79 (74 to 83)                                  | 81 (77 to 85)                                  |  |
| hSBA Titer $\geq 1:4$ in serogroup C | 89 (86 to 91)                                  | 88 (85 to 91)                                  | 88 (85 to 91)                                  |  |
| hSBA Titer $\geq 1:4$ in serogroup W | 95 (92 to 97)                                  | 97 (95 to 99)                                  | 97 (94 to 98)                                  |  |
| hSBA Titer $\geq 1:4$ in serogroup Y | 89 (85 to 92)                                  | 92 (89 to 95)                                  | 93 (90 to 96)                                  |  |

Notes:

[31] - N serogroup C: 499

N serogroup W: 340

N serogroup Y: 345

[32] - N serogroup C: 493

N serogroup W: 341  
 N serogroup Y: 345  
 [33] - N serogroup C: 491  
 N serogroup W: 343  
 N serogroup Y: 346

## Statistical analyses

| Statistical analysis title | Equivalence Lot 1 and Lot 2 MenA |
|----------------------------|----------------------------------|
|----------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[34]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -10  |
| upper limit                             | 3  |

Notes:

[34] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

| Statistical analysis title | Equivalence Lot 1 and Lot 3 MenA |
|----------------------------|----------------------------------|
|----------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[35]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -6   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -12  |
| upper limit                             | 0  |



Notes:

[35] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[36]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -9   |
| upper limit                             | 4  |

Notes:

[36] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 992 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[37]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 5  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0  |
| upper limit                             | 10   |

Notes:

[37] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Equivalence Lot 1 and Lot 3 MenC   |
| Statistical analysis description:   |  |
| Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).<br>The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 990 (instead of 718, which refers to MenA). |  |
| Comparison groups   | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis   | 718  |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence <sup>[38]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine group difference   |
| Point estimate  | 4  |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | -1   |
| upper limit   | 10   |

Notes:

[38] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Equivalence Lot 2 and Lot 3 MenC   |
| Statistical analysis description:   |  |
| Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).<br>The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 984 (instead of 716, which refers to MenA). |  |
| Comparison groups   | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis   | 716  |
| Analysis specification  | Pre-specified  |
| Analysis type   | equivalence <sup>[39]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine group difference   |
| Point estimate  | -1   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | -6   |
| upper limit   | 5  |

Notes:

[39] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the

percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 681 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[40]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -6   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -13  |
| upper limit                             | 0  |

Notes:

[40] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 683 (instead of 718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[41]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 4  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -3   |
| upper limit                             | 11   |

Notes:

[41] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 684

(instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[42]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 10   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 4  |
| upper limit                             | 17   |

Notes:

[42] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 690 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[43]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -6   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -13  |
| upper limit                             | 1  |

Notes:

[43] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[44]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | 1                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -6                          |
| upper limit                             | 8                           |

Notes:

[44] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with seroresponse comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[45]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 7  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0  |
| upper limit                             | 14   |

Notes:

[45] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for percentage of subjects with seroresponse at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[46]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -3                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -10                         |
| upper limit                             | 3                           |

Notes:

[46] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[47]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -6   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -12  |
| upper limit                             | 0  |

Notes:

[47] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[48]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -3                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -9                          |
| upper limit                             | 4                           |

Notes:

[48] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 992 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[49]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 2  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -3   |
| upper limit                             | 6  |

Notes:

[49] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 990 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[50]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | 3                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2                          |
| upper limit                             | 7                           |

Notes:

[50] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 984 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[51]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 1  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -3   |
| upper limit                             | 6  |

Notes:

[51] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 681 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
|-------------------|--|



|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[52]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -2                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -5                          |
| upper limit                             | 1                           |

Notes:

[52] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 683 (instead of 718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[53]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -1   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -4   |
| upper limit                             | 2  |

Notes:

[53] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 684 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[54]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | 1                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2                          |
| upper limit                             | 4                           |

Notes:

[54] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 690 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[55]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -8   |
| upper limit                             | 2  |

Notes:

[55] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[56]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -3                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -8                          |
| upper limit                             | 2                           |

Notes:

[56] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:8$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[57]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 0  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -5   |
| upper limit                             | 5  |

Notes:

[57] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:8$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[58]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -2                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -9                          |
| upper limit                             | 4                           |

Notes:

[58] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[59]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -5   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -11  |
| upper limit                             | 1  |

Notes:

[59] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenA |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain A were contained within the equivalence interval (-10%, 10%).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[60]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -2                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -8                          |
| upper limit                             | 4                           |

Notes:

[60] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain A with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 992 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[61]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 1  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -3   |
| upper limit                             | 5  |

Notes:

[61] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 990 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[62]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | 0                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -4                          |
| upper limit                             | 4                           |

Notes:

[62] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenC |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain C were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 984 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[63]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 0  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -4   |
| upper limit                             | 4  |

Notes:

[63] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain C with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 681 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[64]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -2                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -5                          |
| upper limit                             | 1                           |

Notes:

[64] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 683 (instead of 718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
| Number of subjects included in analysis | 718  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[65]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -1   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -4   |
| upper limit                             | 2  |

Notes:

[65] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenW |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain W were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 684 (instead of 716, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
|-------------------|--|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 716                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[66]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | 1                           |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2                          |
| upper limit                             | 3                           |

Notes:

[66] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain W with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 2 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 2 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 690 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 2 (11 to 18 years) v<br>Investigational MenACWY Lot 1 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[67]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -8   |
| upper limit                             | 1  |

Notes:

[67] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval for all pairs of vaccine lots, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 2 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 1 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 1 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY Lot 1 (11 to 18 years) v<br>Investigational MenACWY Lot 3 (11 to 18 years) |
|-------------------|--|



|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 718                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | equivalence <sup>[68]</sup> |
| Method                                  | ANOVA                       |
| Parameter estimate                      | Vaccine group difference    |
| Point estimate                          | -4                          |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -9                          |
| upper limit                             | 0                           |

Notes:

[68] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 1 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Equivalence Lot 2 and Lot 3 MenY |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Lot-to-lot consistency would be concluded if the two-sided 95% confidence intervals (CIs) for the percentage of subjects with hSBA titer  $\geq 1:4$  comparing Investigational vaccine MenACWY Lot 2 to Investigational vaccine MenACWY Lot 3 for Neisseria Meningitidis strain Y were contained within the equivalence interval (-10%, 10%).

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 691 (instead of 716, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY Lot 3 (11 to 18 years) v<br>Investigational MenACWY Lot 2 (11 to 18 years) |
| Number of subjects included in analysis | 716  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence <sup>[69]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | -1   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -5   |
| upper limit                             | 3  |

Notes:

[69] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs for the percentage of subjects with hSBA titer  $\geq 1:4$  at one month following vaccination was within this equivalence interval, Investigational vaccine MenACWY Lot 2 and Investigational vaccine MenACWY Lot 3 would be equivalent for Neisseria Meningitidis strain Y with respect to the immune response to the vaccine lot.

### **Secondary: Percentage of Subjects With Seroresponse, Human Serum Bactericidal Activity (hSBA) Titer $\geq 1:8$ , and hSBA Titer $\geq 1:4$ , Ages 11 to 55 Years**

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Seroresponse, Human Serum Bactericidal Activity (hSBA) Titer $\geq 1:8$ , and hSBA Titer $\geq 1:4$ , Ages 11 to 55 Years |
|-----------------|---|

End point description:

Immunogenicity of a single injection of MenACWY (3 lots combined) to that of a licensed meningococcal ACWY conjugate vaccine, defined as the percentage of subjects with seroresponse directed against N meningitidis serogroups A, C, W, and Y (healthy subjects 11 to 55 years of age).

Seroresponse to MenACWY: For a subject with hSBA titer  $< 1:4$  at baseline, seroresponse is defined as a postvaccination hSBA titer  $\geq 1:8$ ; for a subject with hSBA titer  $\geq 1:4$  at baseline, seroresponse is defined as a postvaccination hSBA titer of at least 4 times the baseline.

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

End point timeframe:  
28 days after vaccination

| End point values                 | Investigational MenACWY (11 to 55 Years) | Licensed MenACWY (11 to 55 Years) |  |  |
|----------------------------------|--|-----------------------------------|--|--|
| Subject group type               | Subject analysis set                     | Subject analysis set              |  |  |
| Number of subjects analysed      | 2038 <sup>[70]</sup>                     | 680 <sup>[71]</sup>               |  |  |
| Units: Percentage of subjects    |  |                                   |  |  |
| number (confidence interval 95%) |  |                                   |  |  |
| Seroresponse in serogroup A      | 71 (69 to 73)                            | 67 (63 to 71)                     |  |  |
| Seroresponse in serogroup C      | 72 (70 to 74)                            | 67 (64 to 70)                     |  |  |
| Seroresponse in serogroup W      | 67 (64 to 69)                            | 52 (47 to 56)                     |  |  |
| Seroresponse in serogroup Y      | 64 (61 to 66)                            | 41 (37 to 45)                     |  |  |
| hSBA $\geq$ 1:8 in serogroup A   | 72 (70 to 74)                            | 69 (65 to 72)                     |  |  |
| hSBA $\geq$ 1:8 in serogroup C   | 83 (81 to 84)                            | 79 (76 to 82)                     |  |  |
| hSBA $\geq$ 1:8 in serogroup W   | 95 (94 to 96)                            | 89 (86 to 91)                     |  |  |
| hSBA $\geq$ 1:8 in serogroup Y   | 85 (83 to 87)                            | 70 (66 to 73)                     |  |  |
| hSBA $\geq$ 1:4 in serogroup A   | 75 (74 to 77)                            | 73 (69 to 76)                     |  |  |
| hSBA $\geq$ 1:4 in serogroup C   | 87 (86 to 88)                            | 85 (83 to 88)                     |  |  |
| hSBA $\geq$ 1:4 in serogroup W   | 96 (95 to 97)                            | 91 (88 to 93)                     |  |  |
| hSBA $\geq$ 1:4 in serogroup Y   | 90 (88 to 91)                            | 77 (74 to 81)                     |  |  |

Notes:

[70] - N serogroup C: 2444  
N serogroup W: 1508  
N serogroup Y: 1539  
[71] - N serogroup C: 819  
N serogroup W: 580  
N serogroup Y: 600

## Statistical analyses

| Statistical analysis title   | Vaccine group difference Inv. Vac., Lic. Vac. MenA                           |
|--|--|
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. |  |
| Comparison groups  | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis  | 2718   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[72]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 4  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | 0  |
| upper limit  | 8  |

Notes:

[72] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with seroresponse one month after vaccination is  $> -10\%$ .

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Vaccine group difference Inv. Vac., Lic. Vac. MenC                           |
| Statistical analysis description:<br>Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.<br>The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 3263 (instead of 2718, which refers to MenA). |  |
| Comparison groups   | Licensed MenACWY (11 to 55 Years) v Investigational MenACWY (11 to 55 Years) |
| Number of subjects included in analysis   | 2718   |
| Analysis specification  | Pre-specified  |
| Analysis type   | non-inferiority <sup>[73]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine group difference   |
| Point estimate  | 5  |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 1  |
| upper limit   | 9  |

Notes:

[73] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with seroresponse one month after vaccination is > -10%.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Vaccine group difference Inv. Vac., Lic. Vac. MenW                           |
| Statistical analysis description:<br>Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.<br>The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 2088 (instead of 2718, which refers to MenA). |  |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis   | 2718   |
| Analysis specification  | Pre-specified  |
| Analysis type   | non-inferiority <sup>[74]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine group difference   |
| Point estimate  | 15   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 11   |
| upper limit   | 20   |

Notes:

[74] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with seroresponse one month after vaccination is > -10%.

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Vaccine group difference Inv. Vac., Lic. Vac. MenY  |
| Statistical analysis description:<br>Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.<br>The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 2139 (instead of 2718, which refers to MenA). |   |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed |

|   |                                 |
|---|---------------------------------|
|   | MenACWY (11 to 55 Years)        |
| Number of subjects included in analysis | 2718                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[75]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Vaccine group difference        |
| Point estimate                          | 23                              |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 19                              |
| upper limit                             | 28                              |

Notes:

[75] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with seroresponse one month after vaccination is > -10%.

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenA                           |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. |  |
| Comparison groups  | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis  | 2718   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[76]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 4  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | 0  |
| upper limit  | 8  |

Notes:

[76] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:8 one month after vaccination is > -10%.

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenC                           |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine.   |  |
| The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 3263 (instead of 2718, which refers to MenA). |  |
| Comparison groups  | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis  | 2718   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[77]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 3  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0       |
| upper limit         | 7       |

Notes:

[77] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:8 one month after vaccination is  $>$  -10%.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenW |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 2088 (instead of 2718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis | 2718   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[78]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 6  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 4  |
| upper limit                             | 9  |

Notes:

[78] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:8 one month after vaccination is  $>$  -10%.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenY |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 2139 (instead of 2718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis | 2718   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[79]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 15   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 12   |
| upper limit                             | 20   |

Notes:

[79] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:8 one month after vaccination is  $>$  -10%.

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Vaccine group difference Inv. Vac., Lic. Vac. MenA                           |
| Statistical analysis description:  |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. |  |
| Comparison groups  | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis  | 2718   |
| Analysis specification   | Pre-specified  |
| Analysis type  | non-inferiority <sup>[80]</sup>  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine group difference   |
| Point estimate   | 3  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | -1   |
| upper limit  | 7  |

Notes:

[80] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:4 one month after vaccination is  $>$  -10%.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Vaccine group difference Inv. Vac., Lic. Vac. MenC                           |
| Statistical analysis description:   |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 3263 (instead of 2718, which refers to MenA). |  |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis   | 2718   |
| Analysis specification  | Pre-specified  |
| Analysis type   | non-inferiority <sup>[81]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine group difference   |
| Point estimate  | 1  |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | -1   |
| upper limit   | 4  |

Notes:

[81] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:4 one month after vaccination is  $>$  -10%.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Vaccine group difference Inv. Vac., Lic. Vac. MenW                           |
| Statistical analysis description:   |  |
| Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 2088 (instead of 2718, which refers to MenA). |  |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 2718                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[82]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Vaccine group difference        |
| Point estimate                          | 6                               |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 3                               |
| upper limit                             | 8                               |

Notes:

[82] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:4 one month after vaccination is  $> -10\%$ .

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Vaccine group difference Inv. Vac., Lic. Vac. MenY |
|-----------------------------------|--|

Statistical analysis description:

Abbreviations: Inv. Vac., Investigational MenACWY vaccine; Lic. Vac. Licensed MenaCWY vaccine. The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 2139 (instead of 2718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis | 2718   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[83]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | Vaccine group difference   |
| Point estimate                          | 12   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 9  |
| upper limit                             | 16   |

Notes:

[83] - Immunogenicity of the Investigational MenACWY vaccine would be considered non-inferior to that of the Licensed MenACWY vaccine if the lower limit of the two-sided CI for percentage of subjects with hSBA  $\geq$  1:4 one month after vaccination is  $> -10\%$ .

## **Secondary: Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers, Ages 11 to 55 Years**

|                 |   |
|-----------------|---|
| End point title | Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers, Ages 11 to 55 Years |
|-----------------|---|

End point description:

Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers, Ages 11 to 55 Years  
Immunogenicity of a single injection of MenACWY (3 lots combined) to that of a single injection of a licensed meningococcal ACWY conjugate vaccine, as measured by hSBA GMTs directed against N meningitidis serogroups A, C, W, and Y (healthy subjects 11 to 55 years of age).

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

End point timeframe:

28 days after vaccination

| End point values                         | Investigational MenACWY (11 to 55 Years) | Licensed MenACWY (11 to 55 Years) |  |  |
|--|--|-----------------------------------|--|--|
| Subject group type                       | Subject analysis set                     | Subject analysis set              |  |  |
| Number of subjects analysed              | 2038 <sup>[84]</sup>                     | 680 <sup>[85]</sup>               |  |  |
| Units: Titer                             |  |                                   |  |  |
| geometric mean (confidence interval 95%) |  |                                   |  |  |
| Titers in serogroup A                    | 29 (26 to 32)                            | 22 (19 to 26)                     |  |  |
| Titers in serogroup C                    | 55 (49 to 62)                            | 39 (33 to 47)                     |  |  |
| Titers in serogroup W                    | 100 (90 to 112)                          | 57 (49 to 66)                     |  |  |
| Titers in serogroup Y                    | 53 (47 to 60)                            | 21 (18 to 25)                     |  |  |

Notes:

[84] - N serogroup C: 2444

N serogroup W: 1508

N serogroup Y: 1539

[85] - N serogroup C: 819

N serogroup W: 580

N serogroup Y: 600

## Statistical analyses

| Statistical analysis title  | Non-inferiority of Inv.vac., Lic.vac. MenA                                   |
|---|--|
| Statistical analysis description:   |  |
| The study would be considered a success if the lower limit of the two-sided 95% CIs for the hSBA GMT ratios comparing Investigational MenACWY vaccine to Licensed MenACWY vaccine for Neisseria Meningitidis strain A at 1 month after vaccination was to be above 0.5. |  |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis   | 2718   |
| Analysis specification  | Pre-specified  |
| Analysis type   | non-inferiority <sup>[86]</sup>  |
| Method  | ANOVA  |
| Parameter estimate  | hSBA GMT ratios  |
| Point estimate  | 1.32   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided  |
| lower limit   | 1.12   |
| upper limit   | 1.56   |

Notes:

[86] - The equivalence lower limit was 0.5. If the lower limit of two sided 95% CIs for the ratio of the hSBA GMT (GMT for investigational vaccine / GMT for licensed vaccine) at one month following vaccination was above this limit, Investigational MenACWY vaccine would be non-inferior to Licensed MenACWY vaccine for Neisseria Meningitidis strain A with respect to the immune response.

| Statistical analysis title  | Non-inferiority of Inv.vac., Lic.vac. MenC                                   |
|---|--|
| Statistical analysis description:   |  |
| The study would be considered a success if the lower limit of the two-sided 95% CIs for the hSBA GMT ratios comparing Investigational MenACWY vaccine to Licensed MenACWY vaccine for Neisseria Meningitidis strain C at 1 month after vaccination was to be above 0.5. |  |
| The no. of subjects analyzed varied by serogroup. For MenC, the no. of subjects analyzed was 3263 (instead of 2718, which refers to MenA).  |  |
| Comparison groups   | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |



|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 2718                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[87]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | hSBA GMT ratios                 |
| Point estimate                          | 1.4                             |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 1.17                            |
| upper limit                             | 1.67                            |

Notes:

[87] - The equivalence lower limit was 0.5. If the lower limit of two sided 95% CIs for the ratio of the hSBA GMT (GMT for investigational vaccine / GMT for licensed vaccine) at one month following vaccination was above this limit, Investigational MenACWY vaccine would be non-inferior to Licensed MenACWY vaccine for Neisseria Meningitidis strain C with respect to the immune response.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Non-inferiority of Inv.vac., Lic.vac. MenW |
|-----------------------------------|--|

Statistical analysis description:

The study would be considered a success if the lower limit of the two-sided 95% CIs for the hSBA GMT ratios comparing Investigational MenACWY vaccine to Licensed MenACWY vaccine for Neisseria Meningitidis strain W at 1 month after vaccination was to be above 0.5.

The no. of subjects analyzed varied by serogroup. For MenW, the no. of subjects analyzed was 2088 (instead of 2718, which refers to MenA).

|   |  |
|---|--|
| Comparison groups                       | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
| Number of subjects included in analysis | 2718   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority <sup>[88]</sup>  |
| Method                                  | ANOVA  |
| Parameter estimate                      | hSBA GMT ratios  |
| Point estimate                          | 1.76   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 1.51   |
| upper limit                             | 2.05   |

Notes:

[88] - The equivalence lower limit was 0.5. If the lower limit of two sided 95% CIs for the ratio of the hSBA GMT (GMT for investigational vaccine / GMT for licensed vaccine) at one month following vaccination was above this limit, Investigational MenACWY vaccine would be non-inferior to Licensed MenACWY vaccine for Neisseria Meningitidis strain W with respect to the immune response.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Non-inferiority of Inv.vac., Lic.vac. MenY |
|-----------------------------------|--|

Statistical analysis description:

The study would be considered a success if the lower limit of the two-sided 95% CIs for the hSBA GMT ratios comparing Investigational MenACWY vaccine to Licensed MenACWY vaccine for Neisseria Meningitidis strain Y at 1 month after vaccination was to be above 0.5.

The no. of subjects analyzed varied by serogroup. For MenY, the no. of subjects analyzed was 2139 (instead of 2718, which refers to MenA).

|                   |  |
|-------------------|--|
| Comparison groups | Investigational MenACWY (11 to 55 Years) v Licensed MenACWY (11 to 55 Years) |
|-------------------|--|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 2718                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[89]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | hSBA GMT ratios                 |
| Point estimate                          | 2.49                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 2.11                            |
| upper limit                             | 2.95                            |

Notes:

[89] - The equivalence lower limit was 0.5. If the lower limit of two sided 95% CIs for the ratio of the hSBA GMT (GMT for investigational vaccine / GMT for licensed vaccine) at one month following vaccination was above this limit, Investigational MenACWY vaccine would be non-inferior to Licensed MenACWY vaccine for Neisseria Meningitidis strain Y with respect to the immune response.

### Secondary: Number of Subjects With Local and Systemic Reactions, Ages 11 to 55 Years

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Local and Systemic Reactions, Ages 11 to 55 Years |
|-----------------|---|

End point description:

Safety profile following a single injection of MenACWY (3 lots combined) or a single injection of a licensed meningococcal ACWY conjugate vaccine administered to healthy adolescents or adults (11 to 55 years of age).

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

End point timeframe:

Days 1 to 7

| End point values                      | Investigational MenACWY (11 to 55 Years) | Licensed MenACWY (11 to 55 Years) |  |  |
|---------------------------------------|--|-----------------------------------|--|--|
| Subject group type                    | Subject analysis set                     | Subject analysis set              |  |  |
| Number of subjects analysed           | 2649                                     | 875                               |  |  |
| Units: Number of participants         |  |                                   |  |  |
| number (not applicable)               |  |                                   |  |  |
| Pain                                  | 1105                                     | 424                               |  |  |
| Erythema                              | 414                                      | 126                               |  |  |
| Induration                            | 324                                      | 88                                |  |  |
| Chills                                | 168                                      | 50                                |  |  |
| Nausea                                | 260                                      | 65                                |  |  |
| Malaise                               | 279                                      | 99                                |  |  |
| Myalgia                               | 452                                      | 149                               |  |  |
| Arthralgia                            | 197                                      | 54                                |  |  |
| Headache                              | 731                                      | 237                               |  |  |
| Rash                                  | 69                                       | 20                                |  |  |
| Fever ≥38°C                           | 32                                       | 6                                 |  |  |
| Any Other Reaction                    | 555                                      | 183                               |  |  |
| Analgesic/Antipyretic Medication Used | 533                                      | 178                               |  |  |
| Stayed Home                           | 69                                       | 17                                |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were collected from study day 1 to 180.

Adverse event reporting additional description:

A total of 3539 subjects were enrolled in the study; 3524 were vaccinated to receive MenACWY (2649 subjects) or Menactra (875). Overall, 15 subjects were not vaccinated and were excluded from the safety analysis.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 10.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Licensed Meningococcal Vaccine (11 to 55 years) |
|-----------------------|---|

Reporting group description:

One vaccination of the licensed meningococcal ACWY polysaccharide-protein conjugate vaccine was administered intramuscularly.

|                       |  |
|-----------------------|--|
| Reporting group title | Investigational MenACWY Vaccine (11 to 55 years) |
|-----------------------|--|

Reporting group description:

One dose of the investigational meningococcal ACWY (three lots combined) conjugate vaccine was administered intramuscularly.

| Serious adverse events                            | Licensed Meningococcal Vaccine (11 to 55 years) | Investigational MenACWY Vaccine (11 to 55 years) |  |
|---|---|--|--|
| Total subjects affected by serious adverse events |   |  |  |
| subjects affected / exposed                       | 5 / 875 (0.57%)                                 | 23 / 2649 (0.87%)                                |  |
| number of deaths (all causes)                     | 0   | 0  |  |
| number of deaths resulting from adverse events    | 0   | 0  |  |
| Injury, poisoning and procedural complications    |   |  |  |
| Accidental Overdose                               |   |  |  |
| subjects affected / exposed                       | 0 / 875 (0.00%)                                 | 1 / 2649 (0.04%)                                 |  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 1  |  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0  |  |
| Burns Second Degree                               |   |  |  |
| subjects affected / exposed                       | 1 / 875 (0.11%)                                 | 0 / 2649 (0.00%)                                 |  |
| occurrences causally related to treatment / all   | 0 / 1   | 0 / 0  |  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0  |  |
| Clavicle Fracture                                 |   |  |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Craniocerebral Injury</b>                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Dislocation Of Sternum</b>                   |                 |                  |  |
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Fall</b>                                     |                 |                  |  |
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Intentional Overdose</b>                     |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 2 / 2649 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Ligament Rupture</b>                         |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Overdose</b>                                 |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Road Traffic Accident</b>                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 3 / 2649 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| <b>Toxicity To Various Agents</b>               |                 |                  |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Spinal compression fracture                     |                 |                  |  |
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                 |                  |  |
| Vitello-Intestinal Duct Remnant                 |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Vascular disorders                              |                 |                  |  |
| Circulatory Collapse                            |                 |                  |  |
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Nervous system disorders                        |                 |                  |  |
| Dystonia  |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Epilepsy  |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Hypoaesthesia                                   |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Myoclonic Epilepsy                              |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |

|  |                 |                  |  |
|--|-----------------|------------------|--|
| Simple Partial Seizures                              |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Syncope  |                 |                  |  |
| subjects affected / exposed                          | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| General disorders and administration site conditions |                 |                  |  |
| Chest Pain   |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                  |  |
| Pulmonary Embolism                                   |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Respiratory Failure                                  |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Psychiatric disorders                                |                 |                  |  |
| Depression Suicidal                                  |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Suicide Attempt                                      |                 |                  |  |
| subjects affected / exposed                          | 0 / 875 (0.00%) | 2 / 2649 (0.08%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 4            |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders      |                 |                  |  |
| Epiphysiolysis                                       |                 |                  |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Intervertebral Disc Protrusion                  |                 |                  |  |
| subjects affected / exposed                     | 1 / 875 (0.11%) | 0 / 2649 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Infections and infestations                     |                 |                  |  |
| Appendicitis                                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Meningitis Viral                                |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Pneumonia                                       |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Staphylococcal Infection                        |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Tonsillitis                                     |                 |                  |  |
| subjects affected / exposed                     | 0 / 875 (0.00%) | 1 / 2649 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |

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



| <b>Non-serious adverse events</b>                        | Licensed<br>Meningococcal<br>Vaccine (11 to 55<br>years) | Investigational<br>MenACWY Vaccine<br>(11 to 55 years) |  |
|--|--|--|--|
| Total subjects affected by non-serious<br>adverse events |  |  |  |
| subjects affected / exposed                              | 572 / 875 (65.37%)                                       | 1613 / 2649<br>(60.89%)                                |  |
| Nervous system disorders                                 |  |  |  |
| Headache   |  |  |  |
| subjects affected / exposed                              | 240 / 875 (27.43%)                                       | 740 / 2649<br>(27.94%)                                 |  |
| occurrences (all)  | 308  | 969  |  |
| General disorders and administration<br>site conditions  |  |  |  |
| Chills   |  |  |  |
| subjects affected / exposed                              | 50 / 875 (5.71%)   | 169 / 2649 (6.38%)                                     |  |
| occurrences (all)  | 56   | 210  |  |
| Injection site induration                                |  |  |  |
| subjects affected / exposed                              | 88 / 875 (10.06%)  | 324 / 2649<br>(12.23%)                                 |  |
| occurrences (all)  | 91   | 348  |  |
| Injection site erythema                                  |  |  |  |
| subjects affected / exposed                              | 126 / 875 (14.40%)                                       | 414 / 2649<br>(15.63%)                                 |  |
| occurrences (all)  | 133  | 449  |  |
| Malaise  |  |  |  |
| subjects affected / exposed                              | 100 / 875 (11.43%)                                       | 280 / 2649<br>(10.57%)                                 |  |
| occurrences (all)  | 111  | 323  |  |
| Injection site pain                                      |  |  |  |
| subjects affected / exposed                              | 424 / 875 (48.46%)                                       | 1106 / 2649<br>(41.75%)                                |  |
| occurrences (all)  | 471  | 1234   |  |
| Gastrointestinal disorders                               |  |  |  |
| Nausea   |  |  |  |
| subjects affected / exposed                              | 66 / 875 (7.54%)   | 265 / 2649<br>(10.00%)                                 |  |
| occurrences (all)  | 78   | 320  |  |
| Musculoskeletal and connective tissue<br>disorders       |  |  |  |
| Myalgia  |  |  |  |
| subjects affected / exposed                              | 150 / 875 (17.14%)                                       | 453 / 2649<br>(17.10%)                                 |  |
| occurrences (all)  | 169  | 514  |  |
| Arthralgia   |  |  |  |

|                             |                  |                    |  |
|-----------------------------|------------------|--------------------|--|
| subjects affected / exposed | 59 / 875 (6.74%) | 211 / 2649 (7.97%) |  |
| occurrences (all)           | 67               | 250                |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 21 May 2007      | Amendment 1 issues dealt with<br>1) Changing two former immunogenicity secondary objectives to primary objectives, as well as changing immunogenicity endpoint from 4-fold rise in hSBA titer to seroresponse (defined as either an hSBA titer $\geq$ 1:8 or 4-fold rise in titer depending on the subject's baseline titer level). Changes were made to the endpoints to harmonize endpoint definitions across different regulatory agency input.<br>2) Increasing the number of adults aged 35 -55 years in each of the vaccine group, for a total of 400 more adults aged 35 -55 years. |
| 20 December 2007 | Amendment 2 issues dealt with modifying the calculations of power to demonstrate non-inferiority.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/19812260>

<http://www.ncbi.nlm.nih.gov/pubmed/19476428>