



## Clinical trial results:

**A phase II, open, controlled, multi-center study to evaluate the long-term antibody persistence at 1 year, 3 years and 5 years after the administration of one dose of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y-tetanus toxoid conjugate (MenACWY-TT) vaccine versus one dose of sanofi-pasteur's meningococcal serogroups A, C, W-135 and Y-diphtheria toxoid conjugate vaccine (Menactra®) in healthy adolescents/adults aged 10-25 years and to evaluate the safety and immunogenicity of a booster response to MenACWY-TT vaccine administered at 5 years post-primary vaccination with MenACWY-TT or Menactra® and of a primary vaccination of MenACWY-TT in a newly enrolled group aged 15-<31 years.**

## Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2012-002718-38    |
| Trial protocol           | Outside EU/EEA    |
| Global end of trial date | 20 September 2013 |

## Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 11 May 2016  |
| First version publication date | 18 July 2015 |

## Trial information

### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 111670 |
|-----------------------|--------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00715910 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

## Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
|--|----|

|  |     |
|--|-----|
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 15 April 2014     |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 26 April 2013     |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 20 September 2013 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the long-term persistence of the immunogen-icity induced by MenACWY-TT vaccine as compared to Menactra at 11-25 years of age in terms of the percentage of subjects with N. meningitidis serogroup A (MenA), N. meningitidis serogroup C (MenC), N. meningitidis serogroup W-135 (MenW-135), and N. meningitidis serogroup Y (MenY) titers  $\geq 1:8$  as measured by a serum bactericidal assay using human complement (hSBA).

Protection of trial subjects:

The vaccines were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of a rare anaphylactoid/anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 22 July 2008     |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy, Safety |
| Long term follow-up duration                              | 5 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 648 |
| Worldwide total number of subjects   | 648                |
| EEA total number of subjects         | 0                  |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| Newborns (0-27 days)                     | 0   |
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 68  |
| Adults (18-64 years)                     | 580 |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

|                              |                          |
|------------------------------|--------------------------|
| Period 1 title               | Persistence Phase Year 1 |
| Is this the baseline period? | Yes                      |
| Allocation method            | Randomised - controlled  |
| Blinding used                | Not blinded              |

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Nimenrix 1 Group |

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Nimenrix™                                     |
| Investigational medicinal product code |   |
| Other name                             | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

One dose, as intramuscular injection.

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

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

|  |  |
|--|--|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | Menactra®  |
| Investigational medicinal product code | MenACWY-DT   |
| Other name                             | Sanofi Pasteur's meningococcal serogroups A, C, W-135 and Y diphtheria toxoid conjugate vaccine. |
| Pharmaceutical forms                   | Powder and solvent for solution for injection  |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

One dose, as intramuscular injection.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Nimenrix 2 Group |
|------------------|------------------|

Arm description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

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

|   |   |
|---|---|
| Investigational medicinal product name                                      | Nimenrix™                                     |
| Investigational medicinal product code                                      |   |
| Other name  | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms  | Powder and solvent for solution for injection |
| Routes of administration  | Intramuscular use                             |
| Dosage and administration details:<br>One dose, as intramuscular injection. |   |

| Number of subjects in period 1 | Nimenrix 1 Group | Menactra Group | Nimenrix 2 Group |
|--------------------------------|------------------|----------------|------------------|
| Started                        | 433              | 147            | 68               |
| Completed                      | 433              | 147            | 68               |

## Period 2

|                              |                          |
|------------------------------|--------------------------|
| Period 2 title               | Persistence Phase Year 3 |
| Is this the baseline period? | No                       |
| Allocation method            | Randomised - controlled  |
| Blinding used                | Not blinded              |

## Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Nimenrix 1 Group |

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Nimenrix™                                     |
| Investigational medicinal product code |   |
| Other name                             | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:  
One dose, as intramuscular injection.

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

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

|  |  |
|--|--|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | Menactra®  |
| Investigational medicinal product code | MenACWY-DT   |
| Other name                             | Sanofi Pasteur's meningococcal serogroups A, C, W-135 and Y diphtheria toxoid conjugate vaccine. |
| Pharmaceutical forms                   | Powder and solvent for solution for injection  |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:  
One dose, as intramuscular injection.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Nimenrix 2 Group |
|------------------|------------------|

Arm description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Nimenrix™                                     |
| Investigational medicinal product code |   |
| Other name                             | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:  
One dose, as intramuscular injection.

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Nimenrix 1 Group | Menactra Group | Nimenrix 2 Group |
|---|------------------|----------------|------------------|
| Started   | 345              | 86             | 56               |
| Completed   | 345              | 86             | 56               |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

### Period 3

|                              |                          |
|------------------------------|--------------------------|
| Period 3 title               | Persistence Phase Year 5 |
| Is this the baseline period? | No                       |
| Allocation method            | Randomised - controlled  |
| Blinding used                | Not blinded              |

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Nimenrix 1 Group |

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Nimenrix™                                     |
| Investigational medicinal product code |   |
| Other name                             | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:  
One dose, as intramuscular injection.

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

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

|  |  |
|--|--|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | Menactra®  |
| Investigational medicinal product code | MenACWY-DT   |
| Other name                             | Sanofi Pasteur's meningococcal serogroups A, C, W-135 and Y diphtheria toxoid conjugate vaccine. |
| Pharmaceutical forms                   | Powder and solvent for solution for injection  |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

One dose, as intramuscular injection.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Nimenrix 2 Group |
|------------------|------------------|

Arm description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Nimenrix™                                     |
| Investigational medicinal product code |   |
| Other name                             | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

One dose, as intramuscular injection.

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Nimenrix 1 Group | Menactra Group | Nimenrix 2 Group |
|---|------------------|----------------|------------------|
| Started   | 218              | 56             | 38               |
| Completed   | 218              | 56             | 38               |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

#### **Period 4**

|                              |                         |
|------------------------------|-------------------------|
| Period 4 title               | Booster Phase           |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

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## Arms

|   |   |
|---|---|
| <b>Arm title</b>  | Menactra Booster Group                        |
| Arm description:<br>Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and will receive 1 dose of Nimenrix vaccine in this current study. |   |
| Arm type  | Active comparator                             |
| Investigational medicinal product name  | Nimenrix™                                     |
| Investigational medicinal product code  |   |
| Other name  | Meningococcal vaccine GSK134612 (MenACWY-TT)  |
| Pharmaceutical forms  | Powder and solvent for solution for injection |
| Routes of administration  | Intramuscular use                             |

Dosage and administration details:

One dose, as intramuscular injection.

| <b>Number of subjects in period 4<sup>[3]</sup></b> | Menactra Booster Group |
|---|------------------------|
| Started   | 38                     |
| Completed   | 37                     |
| Not completed                                       | 1                      |
| Lost to follow-up                                   | 1                      |

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Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

## Baseline characteristics

### Reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | Nimenrix 1 Group |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.  |                  |
| Reporting group title   | Menactra Group   |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination. |                  |
| Reporting group title   | Nimenrix 2 Group |
| Reporting group description:<br>Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.  |                  |

| Reporting group values  | Nimenrix 1 Group | Menactra Group | Nimenrix 2 Group |
|---|------------------|----------------|------------------|
| Number of subjects  | 433              | 147            | 68               |
| Age categorical<br>Units: Subjects  |                  |                |                  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                  |                |                  |
| Age continuous<br>Units: years  |                  |                |                  |
| arithmetic mean   | 15.9             | 16             | 11.2             |
| standard deviation  | ± 2.79           | ± 2.83         | ± 0.42           |
| Gender categorical<br>Units: Subjects   |                  |                |                  |
| Female  | 213              | 78             | 41               |
| Male  | 220              | 69             | 27               |

| Reporting group values  | Total                 |  |  |
|---|-----------------------|--|--|
| Number of subjects  | 648                   |  |  |
| Age categorical<br>Units: Subjects  |                       |  |  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years) | 0<br>0<br>0<br>0<br>0 |  |  |

|                           |     |  |  |
|---------------------------|-----|--|--|
| Adolescents (12-17 years) | 0   |  |  |
| Adults (18-64 years)      | 0   |  |  |
| From 65-84 years          | 0   |  |  |
| 85 years and over         | 0   |  |  |
| Age continuous            |     |  |  |
| Units: years              |     |  |  |
| arithmetic mean           |     |  |  |
| standard deviation        | -   |  |  |
| Gender categorical        |     |  |  |
| Units: Subjects           |     |  |  |
| Female                    | 332 |  |  |
| Male                      | 316 |  |  |

## End points

### End points reporting groups

|  |                        |
|--|------------------------|
| Reporting group title  | Nimenrix 1 Group       |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Menactra Group         |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.  |                        |
| Reporting group title  | Nimenrix 2 Group       |
| Reporting group description:<br>Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Nimenrix 1 Group       |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Menactra Group         |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.  |                        |
| Reporting group title  | Nimenrix 2 Group       |
| Reporting group description:<br>Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Nimenrix 1 Group       |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Menactra Group         |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.  |                        |
| Reporting group title  | Nimenrix 2 Group       |
| Reporting group description:<br>Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Nimenrix 1 Group       |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Menactra Group         |
| Reporting group description:<br>Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.  |                        |
| Reporting group title  | Nimenrix 2 Group       |
| Reporting group description:<br>Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.   |                        |
| Reporting group title  | Menactra Booster Group |
| Reporting group description:<br>Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and will receive 1 dose of Nimenrix vaccine in this current study.  |                        |
| Subject analysis set title   | Nimenrix Pooled Group  |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:<br>Pooled group of subjects 10-25 years of age from Nimenrix 1 and Nimenrix 2 groups in the primary study (NCT00454909) who had received 1 dose of Nimenrix vaccine in that study and will receive a booster dose in this current study. |                        |
| Subject analysis set title   | Nimenrix Naïve Group   |
| Subject analysis set type  | Intention-to-treat     |
| Subject analysis set description:<br>Subjects 15 to <31 years of age at the time of primary vaccination with 1 dose of Nimenrix vaccine at year 5 of the current study.  |                        |

**Primary: Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values. <sup>[1]</sup> |
|-----------------|--|

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

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

End point timeframe:

At year 1 persistence.

Notes:

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

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values             | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|------------------------------|------------------|-----------------|------------------|--|
| Subject group type           | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed  | 356              | 112             | 58               |  |
| Units: Subjects              |                  |                 |                  |  |
| hSBA-MenA [N=350;111;57]     | 102              | 35              | 15               |  |
| hSBA-MenC [N=336;105;56]     | 319              | 77              | 55               |  |
| hSBA-MenW-135 [N=327;107;54] | 322              | 81              | 53               |  |
| hSBA-MenY [N=356;112;58]     | 348              | 97              | 58               |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Number of subjects with hSBA titers equal to or above the cut-off values.**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with hSBA titers equal to or above the cut-off values. <sup>[2]</sup> |
|-----------------|--|

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

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

End point timeframe:

At year 3 persistence.

Notes:

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

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 321              | 80              | 53               |  |
| Units: Subjects             |                  |                 |                  |  |
| hSBA-MenA [N=314;78;51]     | 117              | 37              | 22               |  |
| hSBA-MenC [N=317;80;53]     | 295              | 65              | 51               |  |

|                             |     |    |    |  |
|-----------------------------|-----|----|----|--|
| hSBA-MenW-135 [N=321;79;53] | 306 | 67 | 51 |  |
| hSBA-MenY [N=319;79;51]     | 306 | 70 | 49 |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with hSBA titers equal to or above the cut-off values.

|                 |  |
|-----------------|--|
| End point title | Number of subjects with hSBA titers equal to or above the cut-off values. <sup>[3]</sup> |
|-----------------|--|

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

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

End point timeframe:

At year 5 persistence.

Notes:

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

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 142              | 45              | 26               |  |
| Units: Subjects             |                  |                 |                  |  |
| hSBA-MenA [N=141;45;24]     | 69               | 20              | 9                |  |
| hSBA-MenC [N=140;44;26]     | 130              | 35              | 22               |  |
| hSBA-MenW-135 [N=138;44;26] | 120              | 37              | 24               |  |
| hSBA-MenY [N=142;44;26]     | 134              | 40              | 24               |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with hSBA titers equal to or above the cut-off values. |
|-----------------|---|

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

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

End point timeframe:

At year 1 persistence

| <b>End point values</b>      | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|------------------------------|------------------|-----------------|------------------|--|
| Subject group type           | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed  | 356              | 112             | 58               |  |
| Units: Subjects              |                  |                 |                  |  |
| hSBA-MenA [N=350;111;57]     | 106              | 35              | 17               |  |
| hSBA-MenC [N=336;105;56]     | 319              | 77              | 55               |  |
| hSBA-MenW-135 [N=327;107;54] | 322              | 81              | 54               |  |
| hSBA-MenY [N=356;112;58]     | 348              | 97              | 58               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with hSBA titers equal to or above the cut-off values. |
|-----------------|---|

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

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

End point timeframe:

At year 3 persistence.

| <b>End point values</b>     | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 321              | 80              | 53               |  |
| Units: Subjects             |                  |                 |                  |  |
| hSBA-MenA [N=314;78;51]     | 123              | 37              | 23               |  |
| hSBA-MenC [N=317;80;53]     | 295              | 68              | 51               |  |
| hSBA-MenW-135 [N=321;79;53] | 307              | 67              | 52               |  |
| hSBA-MenY [N=319;79;51]     | 306              | 70              | 49               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

|                 |  |
|-----------------|--|
| End point title | Number of subjects with hSBA titers equal to or above the cut- |
|-----------------|--|

off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type Secondary

End point timeframe:

At year 5 persistence.

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 142              | 45              | 26               |  |
| Units: Subjects             |                  |                 |                  |  |
| hSBA-MenA [N=141;45;24]     | 74               | 20              | 9                |  |
| hSBA-MenC [N=140;44;26]     | 134              | 39              | 24               |  |
| hSBA-MenW-135 [N=138;44;26] | 122              | 37              | 24               |  |
| hSBA-MenY [N=142;44;26]     | 134              | 40              | 24               |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA antibody titers.

End point title hSBA antibody titers.

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

End point type Secondary

End point timeframe:

At year 1 persistence.

| End point values                         | Nimenrix 1 Group       | Menactra Group        | Nimenrix 2 Group       |  |
|--|------------------------|-----------------------|------------------------|--|
| Subject group type                       | Reporting group        | Reporting group       | Reporting group        |  |
| Number of subjects analysed              | 356                    | 112                   | 58                     |  |
| Units: Titers                            |                        |                       |                        |  |
| geometric mean (confidence interval 95%) |                        |                       |                        |  |
| hSBA-MenA titers [N=350;111;57]          | 5.4 (4.5 to 6.4)       | 6 (4.3 to 8.5)        | 5.2 (3.4 to 7.9)       |  |
| hSBA-MenC titers [N=336;105;56]          | 172 (142.5 to 207.4)   | 46.7 (30.2 to 72.1)   | 238.3 (154 to 368.9)   |  |
| hSBA-MenW-135 titers [N=327;107;54]      | 197.5 (173 to 225.5)   | 48.9 (32.5 to 73.8)   | 231.2 (174.5 to 306.2) |  |
| hSBA-MenY titers [N=356;112;58]          | 271.8 (237.5 to 311.2) | 100.8 (69.6 to 146.2) | 266.8 (205.1 to 347)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA antibody titers.

|                 |                       |
|-----------------|-----------------------|
| End point title | hSBA antibody titers. |
|-----------------|-----------------------|

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

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

End point timeframe:

At year 3 persistence.

| End point values                         | Nimenrix 1 Group       | Menactra Group      | Nimenrix 2 Group       |  |
|--|------------------------|---------------------|------------------------|--|
| Subject group type                       | Reporting group        | Reporting group     | Reporting group        |  |
| Number of subjects analysed              | 321                    | 80                  | 53                     |  |
| Units: Titers                            |                        |                     |                        |  |
| geometric mean (confidence interval 95%) |                        |                     |                        |  |
| hSBA-MenA titers [N=314;78;51]           | 6.2 (5.2 to 7.3)       | 9.3 (6.2 to 14)     | 8.8 (5.3 to 14.9)      |  |
| hSBA-MenC titers [N=317;80;53]           | 117.9 (94.3 to 147.4)  | 54.8 (33.9 to 88.9) | 131.2 (79.8 to 215.7)  |  |
| hSBA-MenW-135 titers [N=321;79;53]       | 141.6 (122.8 to 163.4) | 75.5 (48.7 to 117)  | 137.6 (98.2 to 192.9)  |  |
| hSBA-MenY titers [N=319;79;51]           | 206.6 (177.9 to 239.8) | 139 (93.8 to 206.2) | 186.6 (130.7 to 266.6) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: hSBA antibody titers.

|                 |                       |
|-----------------|-----------------------|
| End point title | hSBA antibody titers. |
|-----------------|-----------------------|

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

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

End point timeframe:

At year 5 persistence.

| End point values                         | Nimenrix 1 Group      | Menactra Group        | Nimenrix 2 Group      |  |
|--|-----------------------|-----------------------|-----------------------|--|
| Subject group type                       | Reporting group       | Reporting group       | Reporting group       |  |
| Number of subjects analysed              | 142                   | 45                    | 26                    |  |
| Units: Titers                            |                       |                       |                       |  |
| geometric mean (confidence interval 95%) |                       |                       |                       |  |
| hSBA-MenA titers [N=141;45;24]           | 8.9 (6.8 to 11.8)     | 7.9 (4.8 to 13.2)     | 6.3 (3.2 to 12.2)     |  |
| hSBA-MenC titers [N=140;44;26]           | 94.6 (65.9 to 135.9)  | 30.6 (17.3 to 54.4)   | 92.9 (39.6 to 217.6)  |  |
| hSBA-MenW-135 titers [N=138;44;26]       | 103.5 (76.3 to 140.5) | 70.4 (37.2 to 133.1)  | 92.4 (50.5 to 168.8)  |  |
| hSBA-MenY titers [N=142;44;26]           | 224.6 (173.9 to 290)  | 129.3 (77.4 to 215.9) | 113.7 (58.4 to 221.3) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 concentrations equal to or above the cut-off values.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 concentrations equal to or above the cut-off values. |
|-----------------|---|

End point description:

The cut-off values were defined as a concentration  $\geq 0.3$  microgram per milliliter ( $\mu\text{g/mL}$ ) and  $\geq 2.0$   $\mu\text{g/mL}$ .

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

End point timeframe:

At year 1 persistence.

| End point values  | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|---|------------------|-----------------|------------------|--|
| Subject group type                                      | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed                             | 366              | 112             | 59               |  |
| Units: Subjects   |                  |                 |                  |  |
| Anti-PSA $\geq 0.3$ $\mu\text{g/mL}$ [N=355;112;56]     | 340              | 101             | 55               |  |
| Anti-PSA $\geq 2.0$ $\mu\text{g/mL}$ [N=355;112;56]     | 260              | 66              | 38               |  |
| Anti-PSC $\geq 0.3$ $\mu\text{g/mL}$ [N=366;112;58]     | 302              | 56              | 51               |  |
| Anti-PSC $\geq 2.0$ $\mu\text{g/mL}$ [N=366;112;58]     | 162              | 31              | 28               |  |
| Anti-PSW-135 $\geq 0.3$ $\mu\text{g/mL}$ [N=354;104;56] | 319              | 65              | 54               |  |
| Anti-PSW-135 $\geq 2.0$ $\mu\text{g/mL}$ [N=354;104;56] | 178              | 27              | 28               |  |
| Anti-PSY $\geq 0.3$ $\mu\text{g/mL}$ [N=358;112;59]     | 342              | 78              | 55               |  |
| Anti-PSY $\geq 2.0$ $\mu\text{g/mL}$ [N=358;112;59]     | 240              | 38              | 37               |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 antibody concentrations.

|                        |  |
|------------------------|--|
| End point title        | Anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 antibody concentrations.    |
| End point description: | Antibody concentrations were given as geometric mean concentrations (GMCs) and expressed in µg/mL. |
| End point type         | Secondary  |
| End point timeframe:   | At year 1 persistence.   |

| End point values                         | Nimenrix 1 Group | Menactra Group   | Nimenrix 2 Group |  |
|--|------------------|------------------|------------------|--|
| Subject group type                       | Reporting group  | Reporting group  | Reporting group  |  |
| Number of subjects analysed              | 366              | 112              | 59               |  |
| Units: µg/mL                             |                  |                  |                  |  |
| geometric mean (confidence interval 95%) |                  |                  |                  |  |
| Anti-PSA [N=355;112;56]                  | 5 (4.2 to 5.9)   | 3.7 (2.6 to 5.3) | 4.2 (2.9 to 6.1) |  |
| Anti-PSC [N=366;112;58]                  | 1.8 (1.5 to 2.1) | 0.6 (0.5 to 0.9) | 2.1 (1.4 to 3.1) |  |
| Anti-PSW-135 [N=354;104;56]              | 2 (1.7 to 2.3)   | 0.8 (0.6 to 1.1) | 2 (1.5 to 2.6)   |  |
| Anti-PSY [N=358;112;59]                  | 3.4 (3 to 4)     | 1 (0.7 to 1.3)   | 2.5 (1.8 to 3.4) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with serious adverse events (SAEs) related to a concurrent GSK medication.

|                        |   |
|------------------------|---|
| End point title        | Number of subjects with serious adverse events (SAEs) related to a concurrent GSK medication.   |
| End point description: | SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. |
| End point type         | Secondary   |
| End point timeframe:   | From 6 months up to 1 year following primary vaccination.   |

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 433              | 147             | 68               |  |
| Units: Subjects             |                  |                 |                  |  |
| Any SAE(s)                  | 0                | 0               | 0                |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with SAEs related to study participation or to a concurrent GSK medication.

|                 |  |
|-----------------|--|
| End point title | Number of subjects with SAEs related to study participation or to a concurrent GSK medication. |
|-----------------|--|

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

From 6 months up to 3 years following primary vaccination.

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 345              | 86              | 56               |  |
| Units: Subjects             |                  |                 |                  |  |
| Any SAE(s)                  | 0                | 0               | 0                |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with SAEs related to study participation or to a concurrent GSK medication.

|                 |  |
|-----------------|--|
| End point title | Number of subjects with SAEs related to study participation or to a concurrent GSK medication. |
|-----------------|--|

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

From 6 months up to 5 years following primary vaccination.

| End point values            | Nimenrix 1 Group | Menactra Group  | Nimenrix 2 Group |  |
|-----------------------------|------------------|-----------------|------------------|--|
| Subject group type          | Reporting group  | Reporting group | Reporting group  |  |
| Number of subjects analysed | 218              | 56              | 38               |  |
| Units: Subjects             |                  |                 |                  |  |
| Any SAE(s)                  | 0                | 0               | 0                |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers equal to or above the cut-off values.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers equal to or above the cut-off values. |
|-----------------|---|

End point description:

The cut-off values were defined as hSBA antibody titers  $\geq 1:4$  and  $\geq 1:8$ .

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

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

| End point values                       | Menactra Booster Group | Nimenrix Pooled Group | Nimenrix Naïve Group |  |
|--|------------------------|-----------------------|----------------------|--|
| Subject group type                     | Reporting group        | Subject analysis set  | Subject analysis set |  |
| Number of subjects analysed            | 29                     | 109                   | 84                   |  |
| Units: Subjects                        |                        |                       |                      |  |
| hSBA-MenA $\geq 1:4$ [N=28;106;79]     | 28                     | 105                   | 61                   |  |
| hSBA-MenA $\geq 1:8$ [N=28;106;79]     | 28                     | 105                   | 61                   |  |
| hSBA-MenC $\geq 1:4$ [N=29;109;81]     | 29                     | 108                   | 78                   |  |
| hSBA-MenC $\geq 1:8$ [N=29;109;81]     | 29                     | 108                   | 77                   |  |
| hSBA-MenW-135 $\geq 1:4$ [N=29;109;80] | 29                     | 109                   | 74                   |  |
| hSBA-MenW-135 $\geq 1:8$ [N=29;109;80] | 29                     | 109                   | 74                   |  |
| hSBA-MenY $\geq 1:4$ [N=29;109;84]     | 29                     | 109                   | 82                   |  |
| hSBA-MenY $\geq 1:8$ [N=29;109;84]     | 29                     | 109                   | 82                   |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: hSBA antibody titers.**

|                 |                       |
|-----------------|-----------------------|
| End point title | hSBA antibody titers. |
|-----------------|-----------------------|

End point description:

Titers are given as GMTs for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

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

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

| End point values                         | Menactra<br>Booster Group  | Nimenrix<br>Pooled Group  | Nimenrix Naïve<br>Group |  |
|--|----------------------------|---------------------------|-------------------------|--|
| Subject group type                       | Reporting group            | Subject analysis set      | Subject analysis set    |  |
| Number of subjects analysed              | 29                         | 109                       | 84                      |  |
| Units: Titers                            |                            |                           |                         |  |
| geometric mean (confidence interval 95%) |                            |                           |                         |  |
| hSBA-MenA [N=28;106;79]                  | 952 (600.9 to 1508.2)      | 783.8 (601.7 to 1020.9)   | 79.7 (46.3 to 137.4)    |  |
| hSBA-MenC [N=29;109;81]                  | 6722.1 (3950.9 to 11437.2) | 5020.4 (3995.4 to 6308.4) | 534.7 (308 to 928.1)    |  |
| hSBA-MenW-135 [N=29;109;80]              | 3729 (2415.4 to 5757.1)    | 5517.6 (4573.6 to 6656.4) | 237.7 (150.4 to 375.8)  |  |
| hSBA-MenY [N=29;109;84]                  | 6546.4 (4312.3 to 9938)    | 5664.3 (4590 to 6990.1)   | 755.1 (522.4 to 1091.4) |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with vaccine response for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibodies.**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with vaccine response for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibodies. |
|-----------------|--|

End point description:

Vaccine response was defined as: For initially seronegative subjects: antibody titre  $\geq 1:8$  at one month after vaccination For initially seropositive subjects: antibody titre at one month after vaccination  $\geq 4$  fold the titres before vaccination.

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

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

| End point values            | Menactra<br>Booster Group | Nimenrix<br>Pooled Group | Nimenrix Naïve<br>Group |  |
|-----------------------------|---------------------------|--------------------------|-------------------------|--|
| Subject group type          | Reporting group           | Subject analysis set     | Subject analysis set    |  |
| Number of subjects analysed | 29                        | 106                      | 78                      |  |
| Units: Subjects             |                           |                          |                         |  |
| hSBA-MenA [N=28;101;75]     | 24                        | 98                       | 51                      |  |
| hSBA-MenC [N=28;106;68]     | 27                        | 97                       | 47                      |  |
| hSBA-MenW-135 [N=28;105;76] | 24                        | 101                      | 51                      |  |
| hSBA-MenY [N=29;106;78]     | 27                        | 97                       | 53                      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited local symptoms.

|  |   |
|--|---|
| End point title  | Number of subjects with solicited local symptoms. |
| End point description:   |   |
| Solicited local symptoms assessed were pain, redness and swelling. Any was defined as occurrence of any solicited local symptom reported irrespective of intensity grade. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 50 millimeter (mm). |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| During the 4-day (Days 0-3) post primary (naïve control group) and booster vaccination.  |   |

| End point values            | Menactra<br>Booster Group |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 37                        |  |  |  |
| Units: Subjects             |                           |  |  |  |
| Any Pain                    | 20                        |  |  |  |
| Grade 3 Pain                | 0                         |  |  |  |
| Any Redness                 | 6                         |  |  |  |
| Grade 3 Redness             | 0                         |  |  |  |
| Any Swelling                | 5                         |  |  |  |
| Grade 3 Swelling            | 1                         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited general symptoms.

|   |   |
|---|---|
| End point title   | Number of subjects with solicited general symptoms. |
| End point description:  |   |
| Solicited general symptoms assessed were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain), headache and temperature. Any = occurrence of any general |   |

symptoms reported irrespective of intensity grade and relationship to study vaccination. Any temperature = axillary temperature greater than or equal to ( $\geq$ )37.5 degrees Celsius ( $^{\circ}\text{C}$ ). Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 temperature = axillary temperature above 39.0 $^{\circ}\text{C}$ . Related = symptoms considered by the investigator to have a causal relationship to vaccination.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| During the 4-day (Days 0-3) post primary (naïve control group) and booster vaccination. |           |

| End point values                  | Menactra<br>Booster Group |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type                | Reporting group           |  |  |  |
| Number of subjects analysed       | 37                        |  |  |  |
| Units: Subjects                   |                           |  |  |  |
| Any Fatigue                       | 7                         |  |  |  |
| Grade 3 Fatigue                   | 0                         |  |  |  |
| Related Fatigue                   | 6                         |  |  |  |
| Any Gastrointestinal symptoms     | 8                         |  |  |  |
| Grade 3 Gastrointestinal symptoms | 0                         |  |  |  |
| Related Gastrointestinal symptoms | 8                         |  |  |  |
| Any Headache                      | 10                        |  |  |  |
| Grade 3 Headache                  | 0                         |  |  |  |
| Related Headache                  | 10                        |  |  |  |
| Any Temperature                   | 0                         |  |  |  |
| Grade 3 Temperature               | 0                         |  |  |  |
| Related Temperature               | 0                         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with unsolicited adverse events (AEs).

|   |   |
|---|---|
| End point title   | Number of subjects with unsolicited adverse events (AEs). |
| End point description:  |   |
| Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| During the 31-day (Days 0-30) following primary (naïve control group) and booster vaccination.  |   |

|                             |                           |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| <b>End point values</b>     | Menactra<br>Booster Group |  |  |  |
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 38                        |  |  |  |
| Units: Subjects             |                           |  |  |  |
| Any AE(s)                   | 9                         |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting new onset chronic illness(es) (NOCIs).

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting new onset chronic illness(es) (NOCIs). |
|-----------------|---|

End point description:

Examples of NOCIs include autoimmune disorders, asthma, type 1 diabetes and allergies.

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

End point timeframe:

During the 6-month period following the primary (naïve control group) and booster vaccination.

|                             |                           |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| <b>End point values</b>     | Menactra<br>Booster Group |  |  |  |
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 38                        |  |  |  |
| Units: Subjects             |                           |  |  |  |
| Any NOCI(s)                 | 0                         |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with SAEs.

|                 |                               |
|-----------------|-------------------------------|
| End point title | Number of subjects with SAEs. |
|-----------------|-------------------------------|

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

During the 6-month period following the primary (naïve control group) and booster vaccination.

|                             |                           |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| <b>End point values</b>     | Menactra<br>Booster Group |  |  |  |
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 38                        |  |  |  |
| Units: Subjects             |                           |  |  |  |
| Any SAE(s)                  | 0                         |  |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs = From 6 months up to 5 years after primary vaccination and up to 6 months after vaccination in booster phase. Solicited and unsolicited symptoms during 4 days (Days 0-3) and 31-days (Days 0-30) after vaccination in booster phase respectively.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the number of participants at risk included those from Total Vaccinated cohort who had the symptom sheet completed.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Nimenrix Pooled Group |
|-----------------------|-----------------------|

Reporting group description:

Pooled group of subjects 10-25 years of age from Nimenrix 1 and Nimenrix 2 groups in the primary study (NCT00454909) who had received 1 dose of Nimenrix vaccine in that study and will receive a booster dose in this current study.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Menactra Booster Group |
|-----------------------|------------------------|

Reporting group description:

Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and received 1 dose of Nimenrix vaccine administered intramuscularly into the non-dominant deltoid in this current study during booster vaccination phase at Year 5.

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Nimenrix Naïve Group |
|-----------------------|----------------------|

Reporting group description:

Naïve control group of subjects 15 to <31 years at the time of primary vaccination with 1 dose of Nimenrix vaccine administered intramuscularly into the non-dominant deltoid in this current study during booster vaccination phase at Year 5.

| Serious adverse events                            | Nimenrix Pooled Group | Menactra Booster Group | Nimenrix Naïve Group |
|---|-----------------------|------------------------|----------------------|
| Total subjects affected by serious adverse events |                       |                        |                      |
| subjects affected / exposed                       | 3 / 183 (1.64%)       | 0 / 38 (0.00%)         | 0 / 101 (0.00%)      |
| number of deaths (all causes)                     | 0                     | 0                      | 0                    |
| number of deaths resulting from adverse events    | 0                     | 0                      | 0                    |
| Psychiatric disorders                             |                       |                        |                      |
| Depression  |                       |                        |                      |
| subjects affected / exposed                       | 1 / 183 (0.55%)       | 0 / 38 (0.00%)         | 0 / 101 (0.00%)      |
| occurrences causally related to treatment / all   | 0 / 1                 | 0 / 0                  | 0 / 0                |
| deaths causally related to treatment / all        | 0 / 0                 | 0 / 0                  | 0 / 0                |
| Infections and infestations                       |                       |                        |                      |
| Appendicitis                                      |                       |                        |                      |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 183 (0.55%) | 0 / 38 (0.00%) | 0 / 101 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Malaria</b>                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 183 (0.55%) | 0 / 38 (0.00%) | 0 / 101 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | <b>Nimenrix Pooled Group</b> | <b>Menactra Booster Group</b> | <b>Nimenrix Naïve Group</b> |
|---|------------------------------|-------------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                              |                               |                             |
| subjects affected / exposed                           | 100 / 183 (54.64%)           | 20 / 38 (52.63%)              | 55 / 101 (54.46%)           |
| General disorders and administration site conditions  |                              |                               |                             |
| Pain  |                              |                               |                             |
| alternative assessment type: Systematic               |                              |                               |                             |
| subjects affected / exposed <sup>[1]</sup>            | 100 / 170 (58.82%)           | 20 / 37 (54.05%)              | 55 / 91 (60.44%)            |
| occurrences (all)                                     | 100                          | 20                            | 55                          |
| Redness   |                              |                               |                             |
| alternative assessment type: Systematic               |                              |                               |                             |
| subjects affected / exposed <sup>[2]</sup>            | 39 / 170 (22.94%)            | 6 / 37 (16.22%)               | 17 / 91 (18.68%)            |
| occurrences (all)                                     | 39                           | 6                             | 17                          |
| Swelling  |                              |                               |                             |
| alternative assessment type: Systematic               |                              |                               |                             |
| subjects affected / exposed <sup>[3]</sup>            | 27 / 170 (15.88%)            | 5 / 37 (13.51%)               | 14 / 91 (15.38%)            |
| occurrences (all)                                     | 27                           | 5                             | 14                          |
| Fatigue   |                              |                               |                             |
| alternative assessment type: Systematic               |                              |                               |                             |
| subjects affected / exposed <sup>[4]</sup>            | 58 / 170 (34.12%)            | 7 / 37 (18.92%)               | 30 / 91 (32.97%)            |
| occurrences (all)                                     | 58                           | 7                             | 30                          |
| Gastrointestinal symptoms                             |                              |                               |                             |
| alternative assessment type: Systematic               |                              |                               |                             |
| subjects affected / exposed <sup>[5]</sup>            | 28 / 170 (16.47%)            | 8 / 37 (21.62%)               | 20 / 91 (21.98%)            |
| occurrences (all)                                     | 28                           | 8                             | 20                          |

|   |                         |                        |                        |
|---|-------------------------|------------------------|------------------------|
| Headache<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[6]</sup><br>occurrences (all)               | 61 / 170 (35.88%)<br>61 | 10 / 37 (27.03%)<br>10 | 22 / 91 (24.18%)<br>22 |
| Temperature/(Axillary)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[7]</sup><br>occurrences (all) | 4 / 170 (2.35%)<br>4    | 0 / 37 (0.00%)<br>0    | 3 / 91 (3.30%)<br>3    |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 183 (1.64%)<br>3    | 2 / 38 (5.26%)<br>2    | 0 / 101 (0.00%)<br>0   |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 11 May 2011      | The primary objective of the current study is to evaluate the long-term persistence of the immunogenicity induced by MenACWY-TT vaccine as compared to Menactra at 11-25 years of age in terms of the percentage of subjects with N. meningitidis serogroup A, C; W-135 and Y titers 1:8 as measured by a serum bactericidal assay using human complement (hSBA) at 1, 3 and 5 year after vaccine administration. In addition, to support the data obtained by hSBA testing, antibody concentrations against meningococcal polysaccharides are planned to be assessed by ELISA. The ELISA testing will be performed at 1 year after vaccine administration, but the sponsor decided not to perform the ELISA testing at 3 and 5 years after vaccine administration for the following reasons: <ul style="list-style-type: none"><li>- the World Health Organization (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines.</li><li>- circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non- functional antibodies against meningococcal polysaccharides.</li></ul> |
| 01 December 2011 | The instructions on reconstitution of the MenACWY-TT vaccine have been updated.  |
| 16 February 2012 | The co-ordinating author and several contributing author's names have been changed.<br>The saline diluent to reconstitute the MenACWY-TT vaccine has been changed from vial presentation to a pre-filled syringe.  |
| 02 May 2012      | The Interval for coming back for the Year 5 post-vaccination visit (Visit 3) has been extended 4 weeks, from 5 years + 16 weeks post-vaccination to 5 years + 20 week post-vaccination. This was done because a booster vaccination will also be administered at this visit, and the extension was needed to ensure that vaccine would be available at the study site.   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported