



## Clinical trial results:

**A phase III, open, randomized, controlled primary vaccination study to demonstrate the non-inferiority of meningococcal vaccine GSK134612 given intramuscularly versus Mencevax™ ACWY given subcutaneously to healthy subjects aged 2 through 10 years of age**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2012-000283-23  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 06 January 2009 |

### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v3 (current)   |
| This version publication date  | 11 October 2020  |
| First version publication date | 25 April 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Minor corrections of the full study results.</li></ul> |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 109495 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00514904 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline Biologicals  |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330   |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000429-PIP01-08 |
| 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                       | 20 May 2009       |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 03 September 2008 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 06 January 2009   |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

Within 4 days after vaccination, in all subjects:

- To demonstrate the non-inferiority of meningococcal vaccine GSK134612 as compared to the licensed Mencevax ACWY in terms of the incidence of any grade 3 systemic symptoms.

One month after vaccination, in the immunogenicity subset corresponding to the first 1125 enrolled subjects:

- To demonstrate the non-inferiority of the vaccine response induced by meningococcal vaccine GSK134612 when compared to the licensed Mencevax ACWY in terms of serum bactericidal antibodies.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the day of vaccination and the subsequent 30 days after the last vaccination administration.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 18 September 2007 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | No                |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Saudi Arabia: 102 |
| Country: Number of subjects enrolled | Lebanon: 201      |
| Country: Number of subjects enrolled | Philippines: 800  |
| Country: Number of subjects enrolled | India: 401        |
| Worldwide total number of subjects   | 1504              |
| EEA total number of subjects         | 0                 |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|  |      |
|--|------|
| Infants and toddlers (28 days-23 months) | 0    |
| Children (2-11 years)                    | 1504 |
| Adolescents (12-17 years)                | 0    |
| Adults (18-64 years)                     | 0    |
| From 65 to 84 years                      | 0    |
| 85 years and over                        | 0    |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Pre-assignment period milestones

|                              |      |
|------------------------------|------|
| Number of subjects started   | 1504 |
| Number of subjects completed | 1501 |

### Pre-assignment subject non-completion reasons

|                            |                   |
|----------------------------|-------------------|
| Reason: Number of subjects | No vaccination: 3 |
|----------------------------|-------------------|

### Period 1

|                              |                                    |
|------------------------------|------------------------------------|
| Period 1 title               | Active+ESFU Phase (overall period) |
| 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 Group |

Arm description:

Subjects received 1 dose of Nimenrix vaccine at Month 0. Nimenrix vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Nimenrix  |
| Investigational medicinal product code |   |
| Other name                             | MenACWY-TT, GSK134612A, GSK Biologicals' meningococcal serogroups A, C, W-135, Y-tetanus toxoid conjugate vaccine |
| Pharmaceutical forms                   | Powder and solvent for solution for injection   |
| Routes of administration               | Intramuscular use   |

Dosage and administration details:

Single dose, intramuscular injection into the deltoid region of the non-dominant arm at Month 0.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Mencevax ACWY Group |
|------------------|---------------------|

Arm description:

Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.

|  |   |
|--|---|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Mencevax ACWY   |
| Investigational medicinal product code |   |
| Other name                             | MenACWY, GSK Biologicals' meningococcal serogroups A, C, W-135 and Y plain polysaccharide vaccine |
| Pharmaceutical forms                   | Powder and solvent for solution for injection   |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Single dose, subcutaneous injection into the upper region of the non-dominant arm.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Nimenrix Group | Mencevax ACWY Group |
|---|----------------|---------------------|
| Started   | 1125           | 376                 |
| Completed   | 1101           | 371                 |
| Not completed                                       | 24             | 5                   |
| Consent withdrawn by subject                        | 3              | 2                   |
| Lost to follow-up                                   | 21             | 3                   |

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Notes:

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

Justification: Details provided in the Pre-assignment period.

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Subjects received 1 dose of Nimenrix vaccine at Month 0. Nimenrix vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Mencevax ACWY Group |
|-----------------------|---------------------|

Reporting group description:

Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.

| Reporting group values                             | Nimenrix Group | Mencevax ACWY Group | Total |
|--|----------------|---------------------|-------|
| Number of subjects                                 | 1125           | 376                 | 1501  |
| Age categorical<br>Units: Subjects                 |                |                     |       |
| In utero   |                |                     | 0     |
| Preterm newborn infants (gestational age < 37 wks) |                |                     | 0     |
| Newborns (0-27 days)                               |                |                     | 0     |
| Infants and toddlers (28 days-23 months)           |                |                     | 0     |
| Children (2-11 years)                              |                |                     | 0     |
| Adolescents (12-17 years)                          |                |                     | 0     |
| Adults (18-64 years)                               |                |                     | 0     |
| From 65-84 years                                   |                |                     | 0     |
| 85 years and over                                  |                |                     | 0     |
| Age continuous<br>Units: years                     |                |                     |       |
| arithmetic mean                                    | 5.6            | 5.5                 |       |
| standard deviation                                 | ± 2.49         | ± 2.45              | -     |
| Gender categorical<br>Units: Subjects              |                |                     |       |
| Female   | 526            | 175                 | 701   |
| Male   | 599            | 201                 | 800   |
| Race/Ethnicity<br>Units: Subjects                  |                |                     |       |
| Asian - Central/South Asian heritage               | 300            | 101                 | 401   |
| Asian - Japanese heritage                          | 2              | 1                   | 3     |
| Asian - South East Asian heritage                  | 597            | 199                 | 796   |
| Native Hawaiian or other Pacific Islander          | 1              | 0                   | 1     |
| White - Arabic/ North African heritage             | 221            | 74                  | 295   |
| White - Caucasian/ European heritage               | 4              | 1                   | 5     |

## End points

### End points reporting groups

|  |                     |
|--|---------------------|
| Reporting group title  | Nimenrix Group      |
| Reporting group description:<br>Subjects received 1 dose of Nimenrix vaccine at Month 0. Nimenrix vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.        |                     |
| Reporting group title  | Mencevax ACWY Group |
| Reporting group description:<br>Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm. |                     |

### Primary: Number of subjects with vaccine response to N. meningitidis serogroups A (MenA), MenC, MenY and MenW-135

|   |  |
|---|--|
| End point title   | Number of subjects with vaccine response to N. meningitidis serogroups A (MenA), MenC, MenY and MenW-135 |
| End point description:<br>Vaccine response was defined as an rSBA titer of at least 1:32 in subjects initially seronegative (< 1:8) and as 4-fold increase in titer from pre- to post-vaccination in subjects initially seropositive (≥ 1:8). |  |
| End point type  | Primary  |
| End point timeframe:<br>One month after vaccination (Post-vaccination, study Month 1)   |  |

| End point values            | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 723             | 240                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| rSBA-MenA [N=594;192]       | 529             | 124                 |  |  |
| rSBA-MenC [N=691;234]       | 664             | 210                 |  |  |
| rSBA-MenW-135 [N=691;236]   | 673             | 195                 |  |  |
| rSBA-MenY [N=723;240]       | 670             | 165                 |  |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | Difference vaccine response to anti-rSBA-MenW135 |
| Statistical analysis description:<br>To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup W-135 in terms of serum bactericidal antibodies using baby rabbit complement (rSBA). |  |
| Comparison groups  | Nimenrix Group v Mencevax ACWY Group             |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 963                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| Parameter estimate                      | Difference in percentage       |
| Point estimate                          | 14.77                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 10.26                          |
| upper limit                             | 20.23                          |

Notes:

[1] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI]  $\geq -10\%$ .

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Difference vaccine response to anti-rSBA-MenA |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for *Neisseria meningitidis* serogroup A in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).

|   |                                      |
|---|--------------------------------------|
| Comparison groups                       | Nimenrix Group v Mencevax ACWY Group |
| Number of subjects included in analysis | 963                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | non-inferiority <sup>[2]</sup>       |
| Parameter estimate                      | Difference in percentage             |
| Point estimate                          | 24.47                                |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 17.52                                |
| upper limit                             | 31.87                                |

Notes:

[2] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI]  $\geq -10\%$ .

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Difference vaccine response to anti-rSBA-MenC |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for *Neisseria meningitidis* serogroup C in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).

|   |                                      |
|---|--------------------------------------|
| Comparison groups                       | Nimenrix Group v Mencevax ACWY Group |
| Number of subjects included in analysis | 963                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | non-inferiority <sup>[3]</sup>       |
| Parameter estimate                      | Difference in percentage             |
| Point estimate                          | 6.35                                 |
| Confidence interval                     |                                      |
| level                                   | 95 %                                 |
| sides                                   | 2-sided                              |
| lower limit                             | 2.68                                 |
| upper limit                             | 11.08                                |

Notes:

[3] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI]  $\geq -10\%$ .

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Difference in vaccine response to anti-rSBA-MenY |
| Statistical analysis description:<br>To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup Y in terms of serum bactericidal antibodies using baby rabbit complement (rSBA). |  |
| Comparison groups  | Nimenrix Group v Mencevax ACWY Group             |
| Number of subjects included in analysis  | 963  |
| Analysis specification   | Pre-specified                                    |
| Analysis type  | non-inferiority <sup>[4]</sup>                   |
| Parameter estimate   | Difference in percentage                         |
| Point estimate   | 23.92  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | 18.02  |
| upper limit  | 30.3   |

Notes:

[4] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI]  $\geq -10\%$ .

### Primary: Number of subjects with grade 3 general symptoms (solicited and unsolicited)

|   |  |
|---|--|
| End point title   | Number of subjects with grade 3 general symptoms (solicited and unsolicited) |
| End point description:<br>Grade 3 symptom= symptom that prevented normal, everyday activities |  |
| End point type  | Primary  |
| End point timeframe:<br>During the 4-day (Days 0-3) post-vaccination period                   |  |

| End point values            | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 1125            | 376                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Subjects                    | 10              | 1                   |  |  |

### Statistical analyses

|   |                                      |
|---|--------------------------------------|
| <b>Statistical analysis title</b>   | Relative Risk for Grade 3 symptoms   |
| Statistical analysis description:<br>To demonstrate the non-inferiority of Nimenrix conjugate vaccine as compared to Mencevax ACWY vaccine in terms of the incidence of any grade 3 general (solicited and unsolicited) symptoms. |                                      |
| Comparison groups   | Nimenrix Group v Mencevax ACWY Group |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 1501                           |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[5]</sup> |
| P-value                                 | = 0.2202                       |
| Method                                  | Chi-squared                    |
| Parameter estimate                      | Risk ratio (RR)                |
| Point estimate                          | 3.34                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.56                           |
| upper limit                             | 20.25                          |

Notes:

[5] - Criterion for assessment: upper limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the ratio between Nimenrix Group and Mencevax ACWY Group being lower than or equal to the pre-defined clinical limit ratio of 3.0 in the percentage of subjects with any grade 3 general symptoms.

### **Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers greater than or equal to the cut-off values**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers greater than or equal to the cut-off values |
|-----------------|--|

End point description:

The cut-off values for the rSBA titers were  $\geq 1:8$  and  $\geq 1:128$  respectively.

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

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1)

| <b>End point values</b>                   | Nimenrix Group  | Mencevax ACWY Group |  |  |
|---|-----------------|---------------------|--|--|
| Subject group type                        | Reporting group | Reporting group     |  |  |
| Number of subjects analysed               | 742             | 250                 |  |  |
| Units: Subjects                           |                 |                     |  |  |
| rSBA-MenA $\geq 1:8$ , M0 [N=599;194]     | 491             | 162                 |  |  |
| rSBA-MenA $\geq 1:8$ , M1 [N=739;247]     | 739             | 246                 |  |  |
| rSBA-MenA $\geq 1:128$ , M0 [N=599;194]   | 476             | 155                 |  |  |
| rSBA-MenA $\geq 1:128$ , M1 [N=739;247]   | 739             | 246                 |  |  |
| rSBA-MenC $\geq 1:8$ , M0 [N=692;237]     | 224             | 77                  |  |  |
| rSBA-MenC $\geq 1:8$ , M1 [N=742;248]     | 738             | 241                 |  |  |
| rSBA-MenC $\geq 1:128$ M0 [N=692;237]     | 157             | 51                  |  |  |
| rSBA-MenC $\geq 1:128$ M1 [N=742;248]     | 736             | 234                 |  |  |
| rSBA-MenW-135 $\geq 1:8$ , M0 [N=693;237] | 455             | 152                 |  |  |
| rSBA-MenW-135 $\geq 1:8$ , M1 [N=742;250] | 742             | 245                 |  |  |
| rSBA-MenW-135 $\geq 1:128$ M0 [N=693;237] | 389             | 133                 |  |  |
| rSBA-MenW-135 $\geq 1:128$ M1 [N=742;250] | 742             | 245                 |  |  |
| rSBA-MenY $\geq 1:8$ , M0 [N=725;241]     | 630             | 198                 |  |  |
| rSBA-MenY $\geq 1:8$ , M1 [N=742;250]     | 742             | 248                 |  |  |

|                                       |     |     |  |  |
|---------------------------------------|-----|-----|--|--|
| rSBA-MenY $\geq$ 1:128 M0 [N=725;241] | 590 | 188 |  |  |
| rSBA-MenY $\geq$ 1:128 M1 [N=742;250] | 742 | 246 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers

|   |   |
|---|---|
| End point title   | rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers |
| End point description:<br>Antibody titers were expressed as geometric mean titers (GMTs).   |   |
| End point type  | Secondary   |
| End point timeframe:<br>Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1) |   |

| End point values                         | Nimenrix Group               | Mencevax ACWY Group       |  |  |
|--|------------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group              | Reporting group           |  |  |
| Number of subjects analysed              | 742                          | 250                       |  |  |
| Units: Titer                             |                              |                           |  |  |
| geometric mean (confidence interval 95%) |                              |                           |  |  |
| rSBA-MenA, M0 [N=599;194]                | 219.1 (186.5 to 257.4)       | 227.7 (172.9 to 299.9)    |  |  |
| rSBA-MenA, M1 [N=739;247]                | 6343.3 (5998.3 to 6708.1)    | 2283.2 (2022.6 to 2577.3) |  |  |
| rSBA-MenC, M0 [N=692;237]                | 14.5 (12.5 to 16.7)          | 14.2 (11.1 to 18.1)       |  |  |
| rSBA-MenC, M1 [N=742;248]                | 4813.1 (4342.1 to 5335.3)    | 1317 (1042.9 to 1663.3)   |  |  |
| rSBA-MenW-135, M0 [N=693;237]            | 80.1 (67.4 to 95.3)          | 68.8 (51.3 to 92.3)       |  |  |
| rSBA-MenW-135, M1 [N=742;250]            | 11543.2 (10872.7 to 12255.1) | 2157.8 (1815.2 to 2565.1) |  |  |
| rSBA-MenY, M0 [N=725;241]                | 310 (268.8 to 357.3)         | 241.7 (185.3 to 315.3)    |  |  |
| rSBA-MenY, M1 [N=742;250]                | 10825.1 (10232.7 to 11451.7) | 2613.1 (2236.9 to 3052.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-tetanus toxoid (anti-TT) concentrations greater than or equal to the cut-off values

|  |  |
|--|--|
| End point title  | Number of subjects with anti-tetanus toxoid (anti-TT) concentrations greater than or equal to the cut-off values |
| End point description:<br>The cut-off values for anti-TT concentrations were $\geq 0.1$ international units (IU/mL) and $\geq 1.0$ IU/mL respectively. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1)                  |  |

| End point values                         | Nimenrix Group  | Mencevax ACWY Group |  |  |
|--|-----------------|---------------------|--|--|
| Subject group type                       | Reporting group | Reporting group     |  |  |
| Number of subjects analysed              | 743             | 250                 |  |  |
| Units: Subjects                          |                 |                     |  |  |
| Anti-TT $\geq 0.1$ IU/mL, M0 [N=743;250] | 635             | 220                 |  |  |
| Anti-TT $\geq 0.1$ IU/mL, M1 [N=740;249] | 733             | 218                 |  |  |
| Anti-TT $\geq 1.0$ IU/mL, M0 [N=743;250] | 296             | 107                 |  |  |
| Anti-TT $\geq 1.0$ IU/mL, M1 [N=740;249] | 720             | 107                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-tetanus toxoid (anti-TT) antibody concentrations

|   |   |
|---|---|
| End point title   | Anti-tetanus toxoid (anti-TT) antibody concentrations |
| End point description:<br>Antibody concentrations were expressed as geometric mean concentrations (GMCs)                              |   |
| End point type  | Secondary   |
| End point timeframe:<br>Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1) |   |

| End point values                         | Nimenrix Group        | Mencevax ACWY Group    |  |  |
|--|-----------------------|------------------------|--|--|
| Subject group type                       | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed              | 743                   | 250                    |  |  |
| Units: Titer                             |                       |                        |  |  |
| geometric mean (confidence interval 95%) |                       |                        |  |  |
| Anti-TT, M0 [N=743;250]                  | 0.65 (0.577 to 0.731) | 0.744 (0.609 to 0.908) |  |  |

|                         |                           |                        |  |  |
|-------------------------|---------------------------|------------------------|--|--|
| Anti-TT, M1 [N=740;249] | 21.731 (19.821 to 23.825) | 0.709 (0.581 to 0.866) |  |  |
|-------------------------|---------------------------|------------------------|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-polysaccharide (anti-PS) concentrations greater than or equal to the cut-off values

|                 |  |
|-----------------|--|
| End point title | Number of subjects with anti-polysaccharide (anti-PS) concentrations greater than or equal to the cut-off values |
|-----------------|--|

End point description:

The cut-off values for anti-PS concentrations were  $\geq 0.3$  micrograms per milliliter ( $\mu\text{g/mL}$ ) and  $\geq 2.0$   $\mu\text{g/mL}$  respectively FOR THE ant- PSA, anti-PSC, anti-PSW-135 and anti-PSY antibodies respectively. One half of the subjects (50%, randomized) of the ATP cohort for immunogenicity was tested for anti-PSA and anti-PSC and the other half for anti-PSW-135 and anti-PSY.

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

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1)

| End point values  | Nimenrix Group  | Mencevax ACWY Group |  |  |
|---|-----------------|---------------------|--|--|
| Subject group type  | Reporting group | Reporting group     |  |  |
| Number of subjects analysed                               | 370             | 128                 |  |  |
| Units: Subjects   |                 |                     |  |  |
| Anti-PSA $\geq 0.3$ $\mu\text{g/mL}$ , M0 [N=354;124]     | 154             | 41                  |  |  |
| Anti-PSA $\geq 0.3$ $\mu\text{g/mL}$ , M1 [N=370;128]     | 369             | 126                 |  |  |
| Anti-PSA $\geq 2.0$ $\mu\text{g/mL}$ , M0 [N=354;124]     | 59              | 12                  |  |  |
| Anti-PSA $\geq 2.0$ $\mu\text{g/mL}$ , M1 [N=370;128]     | 368             | 123                 |  |  |
| Anti-PSC $\geq 0.3$ $\mu\text{g/mL}$ , M0 [N=368;127]     | 29              | 7                   |  |  |
| Anti-PSC $\geq 0.3$ $\mu\text{g/mL}$ , M1 [N=366;127]     | 365             | 127                 |  |  |
| Anti-PSC $\geq 2.0$ $\mu\text{g/mL}$ , M0 [N=368;127]     | 12              | 2                   |  |  |
| Anti-PSC $\geq 2.0$ $\mu\text{g/mL}$ M1 [N=366;127]       | 363             | 125                 |  |  |
| Anti-PSW-135 $\geq 0.3$ $\mu\text{g/mL}$ , M0 [N=364;121] | 18              | 11                  |  |  |
| Anti-PSW-135 $\geq 0.3$ $\mu\text{g/mL}$ , M1 [N=370;121] | 368             | 121                 |  |  |
| Anti-PSW-135 $\geq 2.0$ $\mu\text{g/mL}$ M0 [N=364;121]   | 5               | 2                   |  |  |
| Anti-PSW-135 $\geq 2.0$ $\mu\text{g/mL}$ M1 [N=370;121]   | 353             | 112                 |  |  |
| Anti-PSY $\geq 0.3$ $\mu\text{g/mL}$ , M0 [N=368;121]     | 28              | 16                  |  |  |
| Anti-PSY $\geq 0.3$ $\mu\text{g/mL}$ , M1 [N=370;122]     | 369             | 122                 |  |  |
| Anti-PSY $\geq 2.0$ $\mu\text{g/mL}$ , M0 [N=368;121]     | 11              | 4                   |  |  |
| Anti-PSY $\geq 2.0$ $\mu\text{g/mL}$ , M1 [N=370;122]     | 362             | 118                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-polysaccharide (anti-PS) antibody concentrations

|                 |   |
|-----------------|---|
| End point title | Anti-polysaccharide (anti-PS) antibody concentrations |
|-----------------|---|

End point description:

Anti-PS concentrations were expressed as geometric mean concentrations (GMCs) and expressed in µg/mL. One half of the subjects (50%, randomized) of the ATP cohort for immunogenicity was tested for anti-PSA and anti-PSC and the other half for anti-PSW-135 and anti-PSY.

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

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1)

| End point values                         | Nimenrix Group         | Mencevax ACWY Group    |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 370                    | 128                    |  |  |
| Units: µg/mL                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| Anti-PSA, M0 [N=354,124]                 | 0.4 (0.35 to 0.46)     | 0.29 (0.24 to 0.36)    |  |  |
| Anti-PSA, M1 [N=370,128]                 | 81.1 (71.34 to 92.2)   | 25.43 (19.66 to 32.9)  |  |  |
| Anti-PSC, M0 [N=368,127]                 | 0.18 (0.17 to 0.19)    | 0.17 (0.15 to 0.18)    |  |  |
| Anti-PSC, M1 [N=366,127]                 | 22.61 (20.24 to 25.25) | 25.69 (21.3 to 30.99)  |  |  |
| Anti-PSW-135, M0 [N=364,121]             | 0.17 (0.16 to 0.18)    | 0.17 (0.16 to 0.19)    |  |  |
| Anti-PSW-135, M1 [N=370,121]             | 12.8 (11.32 to 14.48)  | 13.85 (10.93 to 17.53) |  |  |
| Anti-PSY, M0 [N=368,121]                 | 0.18 (0.17 to 0.2)     | 0.2 (0.17 to 0.23)     |  |  |
| Anti-PSY, M1 [N=370,122]                 | 19.26 (17.1 to 21.69)  | 22.71 (18.13 to 28.46) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects < 6 years of age with solicited local symptoms

|  |   |
|--|---|
| End point title  | Number of subjects < 6 years of age with solicited local symptoms |
| End point description:<br>Solicited local symptoms assessed were pain, redness and swelling. |   |
| End point type   | Secondary   |
| End point timeframe:<br>During the 4-day (Days 0-3) follow-up period after vaccination       |   |

| End point values            | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 575             | 188                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Any Pain                    | 104             | 39                  |  |  |
| Any Redness                 | 82              | 31                  |  |  |
| Any Swelling                | 31              | 15                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects ≥ 6 years of age with solicited local symptoms

|   |   |
|---|---|
| End point title   | Number of subjects ≥ 6 years of age with solicited local symptoms |
| End point description:<br>Solicited local symptoms assessed were pain, redness and swelling |   |
| End point type  | Secondary   |
| End point timeframe:<br>During the 4-day (Days 0-3) follow-up period after vaccination.     |   |

| End point values            | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 542             | 186                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Any Pain                    | 105             | 50                  |  |  |
| Any Redness                 | 107             | 36                  |  |  |
| Any Swelling                | 54              | 16                  |  |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: Number of subjects < 6 years of age with solicited general symptoms**

|                 |   |
|-----------------|---|
| End point title | Number of subjects < 6 years of age with solicited general symptoms |
|-----------------|---|

End point description:

Solicited general symptoms assessed were drowsiness, fever (measured orally and temperature  $\geq 37.5^{\circ}\text{C}$  ), irritability and loss of appetite

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination

| End point values                  | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------------|-----------------|---------------------|--|--|
| Subject group type                | Reporting group | Reporting group     |  |  |
| Number of subjects analysed       | 575             | 188                 |  |  |
| Units: Subjects                   |                 |                     |  |  |
| Any Drowsiness                    | 34              | 5                   |  |  |
| Fever $\geq 37.5^{\circ}\text{C}$ | 50              | 12                  |  |  |
| Any Irritability                  | 31              | 6                   |  |  |
| Any Loss of aptite                | 35              | 6                   |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects  $\geq 6$  years of age with solicited general symptoms**

|                 |  |
|-----------------|--|
| End point title | Number of subjects $\geq 6$ years of age with solicited general symptoms |
|-----------------|--|

End point description:

Solicited general symptoms assessed were fatigue, fever (measured orally and temperature  $\geq 37.5^{\circ}\text{C}$  ), gastrointestinal and headache

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination.

| End point values                  | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------------|-----------------|---------------------|--|--|
| Subject group type                | Reporting group | Reporting group     |  |  |
| Number of subjects analysed       | 542             | 186                 |  |  |
| Units: Subjects                   |                 |                     |  |  |
| Any Fatigue                       | 33              | 19                  |  |  |
| Fever $\geq 37.5^{\circ}\text{C}$ | 48              | 19                  |  |  |
| Any Gastrointestinal              | 25              | 15                  |  |  |
| Any Headache                      | 51              | 19                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting specific adverse events (AEs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting specific adverse events (AEs) |
|-----------------|--|

End point description:

Specific AEs include:

- rash (hives, idiopathic thrombocytopenic purpura, petechiae),
- new onset of chronic illness(es) (NOCI) (e.g. autoimmune disorders, asthma, type I diabetes and allergies), and/or:
- conditions prompting emergency room (ER) visits or or non-routine physician office visits (i.e. office visits not related to well-being care, vaccination, injury or common acute illnesses such as upper respiratory tract infections, otitis media, pharyngitis, gastroenteritis)

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

End point timeframe:

From Day 0 up to 6 months after vaccination

| End point values            | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 1125            | 376                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Rash (es)                   | 45              | 16                  |  |  |
| NOCI (s)                    | 3               | 1                   |  |  |
| ER visit (s)                | 15              | 4                   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any unsolicited symptoms

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting any unsolicited symptoms |
|-----------------|---|

End point description:

Unsolicited symptom covers any symptom 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:

Up to one month (Day 0-Day 30) after vaccination

| <b>End point values</b>     | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 1125            | 376                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Any (AE's)                  | 198             | 75                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any serious adverse events (SAEs)

|   |  |
|---|--|
| End point title   | Number of subjects reporting any serious adverse events (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:  |  |
| From Day 0 up to 6 months after vaccination   |  |

| <b>End point values</b>     | Nimenrix Group  | Mencevax ACWY Group |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 1125            | 376                 |  |  |
| Units: Subjects             |                 |                     |  |  |
| Any (SAE's)                 | 15              | 7                   |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events: from Day 0 up to 6 months after vaccination. Solicited symptoms: during the 4-day (Day 0-Day 3) follow-up period after vaccination.

Adverse event reporting additional description:

This is specific for each SAE/AE that is entered.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Mencevax ACWY Group |
|-----------------------|---------------------|

Reporting group description:

Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.

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

Reporting group description:

Subjects received 1 dose of Nimenrix vaccine at Month 0. Nimenrix vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.

| Serious adverse events                            | Mencevax ACWY Group | Nimenrix Group    |  |
|---|---------------------|-------------------|--|
| Total subjects affected by serious adverse events |                     |                   |  |
| subjects affected / exposed                       | 7 / 376 (1.86%)     | 15 / 1125 (1.33%) |  |
| number of deaths (all causes)                     | 0                   | 0                 |  |
| number of deaths resulting from adverse events    | 0                   | 0                 |  |
| Injury, poisoning and procedural complications    |                     |                   |  |
| Arthropod bite                                    |                     |                   |  |
| subjects affected / exposed                       | 0 / 376 (0.00%)     | 1 / 1125 (0.09%)  |  |
| occurrences causally related to treatment / all   | 0 / 0               | 0 / 1             |  |
| deaths causally related to treatment / all        | 0 / 0               | 0 / 0             |  |
| Gastrointestinal disorders                        |                     |                   |  |
| Enteritis   |                     |                   |  |
| subjects affected / exposed                       | 0 / 376 (0.00%)     | 1 / 1125 (0.09%)  |  |
| occurrences causally related to treatment / all   | 0 / 0               | 0 / 1             |  |
| deaths causally related to treatment / all        | 0 / 0               | 0 / 0             |  |
| Hyperchlorhydria                                  |                     |                   |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| 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 |                 |                  |  |
| Asthma  |                 |                  |  |
| subjects affected / exposed                     | 1 / 376 (0.27%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Rhinitis allergic                               |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |                 |                  |  |
| Rash  |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Infections and infestations                     |                 |                  |  |
| Upper respiratory tract infection               |                 |                  |  |
| subjects affected / exposed                     | 3 / 376 (0.80%) | 3 / 1125 (0.27%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Typhoid fever                                   |                 |                  |  |
| subjects affected / exposed                     | 2 / 376 (0.53%) | 2 / 1125 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Urinary tract infection                         |                 |                  |  |
| subjects affected / exposed                     | 1 / 376 (0.27%) | 3 / 1125 (0.27%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Dengue fever                                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 2 / 1125 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| Otitis media                                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 2 / 1125 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Viral infection                                 |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 2 / 1125 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Amoebic dysentery                               |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Gastroenteritis                                 |                 |                  |  |
| subjects affected / exposed                     | 1 / 376 (0.27%) | 0 / 1125 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Parasitic gastroenteritis                       |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Pharyngotonsillitis                             |                 |                  |  |
| subjects affected / exposed                     | 1 / 376 (0.27%) | 0 / 1125 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Pneumonia                                       |                 |                  |  |
| subjects affected / exposed                     | 1 / 376 (0.27%) | 0 / 1125 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Respiratory tract infection                     |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Metabolism and nutrition disorders              |                 |                  |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| Food intolerance                                |                 |                  |  |
| subjects affected / exposed                     | 0 / 376 (0.00%) | 1 / 1125 (0.09%) |  |
| 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 %

| Non-serious adverse events                            | Mencevax ACWY Group  | Nimenrix Group      |  |
|---|--|---------------------|--|
| Total subjects affected by non-serious adverse events |  |                     |  |
| subjects affected / exposed                           | 155 / 376 (41.22%)   | 416 / 1125 (36.98%) |  |
| General disorders and administration site conditions  |  |                     |  |
| Pain (< 6 years of age)                               | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age. |                     |  |
| subjects affected / exposed <sup>[1]</sup>            | 39 / 188 (20.74%)  | 104 / 575 (18.09%)  |  |
| occurrences (all)                                     | 39   | 104                 |  |
| Redness (< 6 years of age)                            | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age. |                     |  |
| subjects affected / exposed <sup>[2]</sup>            | 31 / 188 (16.49%)  | 82 / 575 (14.26%)   |  |
| occurrences (all)                                     | 31   | 82                  |  |
| Swelling (< 6 years of age)                           | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects 2-5 years of age. |                     |  |
| subjects affected / exposed <sup>[3]</sup>            | 15 / 188 (7.98%)   | 31 / 575 (5.39%)    |  |
| occurrences (all)                                     | 15   | 31                  |  |
| Pain (≥ 6 years of age)                               | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age  |                     |  |
| subjects affected / exposed <sup>[4]</sup>            | 50 / 186 (26.88%)  | 105 / 542 (19.37%)  |  |
| occurrences (all)                                     | 50   | 105                 |  |
| Redness (≥ 6 years of age)                            | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age  |                     |  |
| subjects affected / exposed <sup>[5]</sup>            | 36 / 186 (19.35%)  | 107 / 542 (19.74%)  |  |
| occurrences (all)                                     | 36   | 107                 |  |
| Swelling (≥ 6 years of age)                           | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age. |                     |  |
| subjects affected / exposed <sup>[6]</sup>            | 16 / 186 (8.60%)   | 54 / 542 (9.96%)    |  |
| occurrences (all)                                     | 16   | 54                  |  |
| Drowsiness  | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age  |                     |  |
| subjects affected / exposed <sup>[7]</sup>            | 5 / 188 (2.66%)  | 34 / 575 (5.91%)    |  |
| occurrences (all)                                     | 5  | 34                  |  |
| Fever (Orally) (< 6 years of age)                     | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age  |                     |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed <sup>[8]</sup>  | 12 / 188 (6.38%)  | 50 / 575 (8.70%) |  |
| occurrences (all)                           | 12  | 50               |  |
| Irritability                                | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age |                  |  |
| subjects affected / exposed <sup>[9]</sup>  | 6 / 188 (3.19%)   | 31 / 575 (5.39%) |  |
| occurrences (all)                           | 6   | 31               |  |
| Loss of appetite                            | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age |                  |  |
| subjects affected / exposed <sup>[10]</sup> | 6 / 188 (3.19%)   | 35 / 575 (6.09%) |  |
| occurrences (all)                           | 6   | 35               |  |
| Fatigue                                     | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age |                  |  |
| subjects affected / exposed <sup>[11]</sup> | 19 / 186 (10.22%)   | 33 / 542 (6.09%) |  |
| occurrences (all)                           | 19  | 33               |  |
| Fever (Orally) (≥ 6 years of age)           | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age |                  |  |
| subjects affected / exposed <sup>[12]</sup> | 19 / 186 (10.22%)   | 48 / 542 (8.86%) |  |
| occurrences (all)                           | 19  | 48               |  |
| Gastrointestinal                            | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age |                  |  |
| subjects affected / exposed <sup>[13]</sup> | 15 / 186 (8.06%)  | 25 / 542 (4.61%) |  |
| occurrences (all)                           | 15  | 25               |  |
| Headache                                    | Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age |                  |  |
| subjects affected / exposed <sup>[14]</sup> | 19 / 186 (10.22%)   | 51 / 542 (9.41%) |  |
| occurrences (all)                           | 19  | 51               |  |

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.

[8] - 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.

[9] - 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.

[10] - 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.

[11] - 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.

[12] - 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.

[13] - 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.

[14] - 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? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported