# Clinical trial results:
# A phase III, randomized, multinational study, double-blinded for the immunogenicity and consistency evaluation of 3 Hib-MenCY-TT vaccine lots and single-blinded and controlled for the evaluation of safety and immunogenicity of GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis serogroups C and Y-tetanus toxoid conjugate vaccine combined (Hib-MenCY-TT) compared to monovalent Hib vaccine in healthy infants at 2, 4, 6, and 12 to 15 months of age.

## Summary

| | |
|---|---|
| EudraCT number | 2005-002352-18 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 26 February 2008 |

**Results information**

| | |
|---|---|
| Result version number | v3 (current) |
| This version publication date | 08 April 2023 |
| First version publication date | 02 July 2015 |
| Version creation reason | • Correction of full data set<br>Results have been amended to account for consistency with other registries. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 103813,105067 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00289783 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

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

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No | No |

| | |
|---|---|
| 1901/2006 apply to this trial? | |
| 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 | 21 April 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 August 2007 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 February 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate: the lot-to-lot consistency of 3 lots of Hib-MenCY-TT co-administered with DTPa-HBV-IPV following 3 doses, in terms of PRP, MenC and MenY; the immune response to PRP in the group that received 3 doses of Hib-MenCY-TT and a 4th dose of Hib-MenCY-TT was non-inferior to the group that received Hib and Hib-OMP. To evaluate the immunogenicity of a 4th dose of Hib-MenCY-TT co-administered with DTPa-HBV-IPV, MMR and Var. To evaluate the effect of a 4th dose of Hib-MenCY-TT co-administered with MMR and Var, in terms of a vaccine response; the non-inferiority of Hib-MenCY-TT compared to Hib, co-administered with DTPa-HBV-IPV, in terms of PRP; the non-inferiority of MMR when co-administered with a 4th dose of Hib-MenCY-TT compared to MMR co-administered with a 4th dose of Hib-OMP, co-administered with Var; the non-inferiority of Var co-administered with a 4th dose of Hib-MenCY-TT compared to Var co-administered with a 4th dose of Hib-OMP, co-administered with MMR.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 22 February 2006 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 3037 |
| Country: Number of subjects enrolled | Australia: 604 |
| Country: Number of subjects enrolled | Mexico: 800 |
| Worldwide total number of subjects | 4441 |
| 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) | 4441 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were randomized at the beginning of the primary phase and kept their group assignment during the fourth dose vaccination phase. The study protocol identified 3 different study cohorts : United States (US) Safety and Immunogenicity (Cohort 1), Safety Only (Cohort 2: from all investigation sites), Non-US Safety and Immunogenicity (Cohort 3).

### Pre-assignment

Screening details:

The data for 261 subjects from one study center in the US were not included in the analyses as vaccine accountability could not be fully reconciled (i.e. treatment group assignment for the different subjects could not be verified).

### Period 1

| | |
|---|---|
| Period 1 title | Primary phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

Blinding implementation details:

Double-blind for the immunogenicity and consistency evaluation of the 3 Hib-MenCY-TT vaccine lots and single-blind and controlled for the evaluation of safety and immunogenicity of Hib-MenCY-TT compared to monovalent Hib vaccine, randomized study with 4 parallel treatment groups (1:1:1:1).

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Menhibrix Group |

Arm description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis 792014 vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-doses administered at 2, 4 and 6 months of age, and 1 booster dose at 12 to 15 months of age.The vaccines were administered intramuscularly in the right upper thigh.

| | |
|---|---|
| Investigational medicinal product name | Pediarix |
| Investigational medicinal product code | |
| Other name | Infanrix penta |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A 3-dose injection at 2, 4 and 6 months of age, administered intramuscularly in the left upper thigh.

| | |
|---|---|
| Investigational medicinal product name | Prevnar |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection at 2, 4 and 6 months of age, and 1 booster dose by intramuscular injection at 12 to 15 months of age.

| | |
|---|---|
| Investigational medicinal product name | M-M-R II |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

1 booster dose by subcutaneous injection at 12 to 15 months of age.

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

Dosage and administration details:

1 booster dose by subcutaneous injection at 12 to 15 months of age

| | |
|---|---|
| **Arm title** | ActHIB Group |

Arm description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | ActHIB |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose injection administered at 2, 4 and 6 months of age, intramuscularly in the right upper thigh.

| | |
|---|---|
| Investigational medicinal product name | PedvaxHIB |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 booster dose by intramuscular injection at 12 to 15 months of age, administered in the left lower deltoid or tight

| **Number of subjects in period 1[1]** | Menhibrix Group | ActHIB Group |
|---|---|---|
| Started | 3136 | 1044 |
| Completed | 2888 | 961 |
| Not completed | 248 | 83 |
| Adverse event, serious fatal | 7 | - |

| | | |
|---|---|---|
| Consent withdrawn by subject | 93 | 40 |
| Adverse event, non-fatal | 3 | 1 |
| Unspecified | 32 | 12 |
| Lost to follow-up | 60 | 14 |
| Migration from the study area | 26 | 10 |
| Protocol deviation | 27 | 6 |

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: The data for 261 subjects from one study center in the US were not included in the analyses as vaccine accountability could not be fully reconciled (i.e. treatment group assignment for the different subjects could not be verified).

## Period 2

| | |
|---|---|
| Period 2 title | Fourth dose phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Menhibrix Group |

Arm description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK Biologicals' Haemophilus influenzae type b and Neisseria meningitidis 792014 vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-doses administered at 2, 4 and 6 months of age, and 1 booster dose at 12 to 15 months of age.The vaccines were administered intramuscularly in the right upper thigh.

| | |
|---|---|
| Investigational medicinal product name | Pediarix |
| Investigational medicinal product code | |
| Other name | Infanrix penta |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A 3-dose injection at 2, 4 and 6 months of age, administered intramuscularly in the left upper thigh.

| | |
|---|---|
| Investigational medicinal product name | Prevnar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

| | |
|---|---|
| Dosage and administration details: | |
| 3-dose intramuscular injection at 2, 4 and 6 months of age, and 1 booster dose by intramuscular injection at 12 to 15 months of age. | |
| Investigational medicinal product name | M-M-R II |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 1 booster dose by subcutaneous injection at 12 to 15 months of age. | |
| Investigational medicinal product name | Varivax |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 1 booster dose by subcutaneous injection at 12 to 15 months of age | |
| **Arm title** | ActHIB Group |
| Arm description: | |
| Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm. | |
| Arm type | Active comparator |
| Investigational medicinal product name | ActHIB |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 3-dose injection administered at 2, 4 and 6 months of age, intramuscularly in the right upper thigh. | |
| Investigational medicinal product name | PedvaxHIB |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 1 booster dose by intramuscular injection at 12 to 15 months of age, administered in the left lower deltoid or tight | |

| **Number of subjects in period 2[2]** | Menhibrix Group | ActHIB Group |
|---|---|---|
| Started | 2769 | 923 |
| Completed | 2682 | 899 |
| Not completed | 87 | 24 |
| Consent withdrawn by subject | 10 | 1 |
| Adverse event | 1 | - |

| | | |
|---|---|---|
| Unspecified | 22 | 10 |
| Lost to follow-up | 53 | 12 |
| Migration from the study area | 1 | 1 |

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: Subjects were randomized at the beginning of the primary phase and kept their group assignment during the fourth dose vaccination phase.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Menhibrix Group |
| Reporting group description: | |
| Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm. | |
| Reporting group title | ActHIB Group |
| Reporting group description: | |
| Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm. | |

| Reporting group values | Menhibrix Group | ActHIB Group | Total |
|---|---|---|---|
| Number of subjects | 3136 | 1044 | 4180 |
| 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: months | | | |
| arithmetic mean | 2.11 | 2.11 | |
| standard deviation | ± 0.26 | ± 0.27 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 1523 | 498 | 2021 |
| Male | 1613 | 546 | 2159 |

### End points reporting groups

| Reporting group title | Menhibrix Group |
|---|---|

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Reporting group title | ActHIB Group |
|---|---|

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Reporting group title | Menhibrix Group |
|---|---|

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Reporting group title | ActHIB Group |
|---|---|

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Subject analysis set title | Menhibrix A Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Subject analysis set title | Menhibrix B Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot B co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Subject analysis set title | Menhibrix C Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh,

respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

## Primary: Anti-Polyribosyl Ribitol Phosphate (PRP) antibody concentrations

| End point title | Anti-Polyribosyl Ribitol Phosphate (PRP) antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 518 | 171 | 162 | 180 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 11.021 (10.027 to 12.114) | 6.463 (5.288 to 7.9) | 10.17 (8.855 to 11.681) | 11.424 (9.71 to 13.441) |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 11.438 (9.503 to 13.768) | | | |

### Statistical analyses

| Statistical analysis title | GMC ratio anti-PRP LotB / LotA |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

| Comparison groups | Menhibrix B Group v Menhibrix A Group |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 342 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| Parameter estimate | GMC ratio |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.42 |

Notes:

[1] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMC ratio anti-PRP LotC / LotA |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

| | |
|---|---|
| Comparison groups | Menhibrix A Group v Menhibrix C Group |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| Parameter estimate | GMC ratio |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.42 |

Notes:

[2] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMC ratio anti-PRP LotC / LotB |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for polyribosylribitol phosphate (PRP) as measured by ELISA.

| | |
|---|---|
| Comparison groups | Menhibrix B Group v Menhibrix C Group |
| Number of subjects included in analysis | 356 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| Parameter estimate | GMC ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1.26 |

Notes:

[3] - Criteria for lot-to-lot consistency (1 month after primary vaccination):
For each pair of lots and for the immune response to anti-PRP measured by ELISA the two-sided 95% confidence interval (CI) on the geometric mean concentrations (GMCs) ratio between lots is within the [0.5; 2.0] interval.

## Primary: Neisseria meningitidis serogroup C (MenC) serum bactericidal assay using human complement (hSBA) antibody titers

| End point title | Neisseria meningitidis serogroup C (MenC) serum bactericidal assay using human complement (hSBA) antibody titers |
|---|---|

End point description:

Titers were expressed as Geometric Mean Titers (GMTs). This analysis occured on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 491 | 164 | 158 | 168 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC | 967.6 (864 to 1083.5) | 2.5 (2.2 to 2.9) | 910 (754.6 to 1097.3) | 1118 (931.1 to 1342.5) |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 165 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC | 885.7 (712.4 to 1101.2) | | | |

### Statistical analyses

| Statistical analysis title | GMT ratio hSBA-MenC Lot B/Lot A |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

| Comparison groups | Menhibrix A Group v Menhibrix B Group |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 326 |
| Analysis specification | Pre-specified |
| Analysis type | other[4] |
| Parameter estimate | GMT ratio |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.93 |
| upper limit | 1.62 |

Notes:

[4] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMT ratio hSBA-MenC Lot C/Lot A |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

| | |
|---|---|
| Comparison groups | Menhibrix C Group v Menhibrix A Group |
| Number of subjects included in analysis | 323 |
| Analysis specification | Pre-specified |
| Analysis type | other[5] |
| Parameter estimate | GMT ratio |
| Point estimate | 0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.74 |
| upper limit | 1.29 |

Notes:

[5] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMT ratio hSBA-MenC Lot C/Lot B |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup C (MenC) as measured by a serum bactericidal assay using human complement (hSBA).

| | |
|---|---|
| Comparison groups | Menhibrix B Group v Menhibrix C Group |
| Number of subjects included in analysis | 333 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| Parameter estimate | GMT ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.04 |

Notes:

[6] - For each pair of lots and for the immune response to hSBA-MenC, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

## Primary: Neisseria meningitidis serogroup Y (MenY) serum bactericidal assay using human complement (hSBA) antibody titers

| End point title | Neisseria meningitidis serogroup Y (MenY) serum bactericidal assay using human complement (hSBA) antibody titers |
|---|---|

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 481 | 162 | 150 | 168 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenY | 236.6 (205.7 to 272.1) | 2.2 (2 to 2.4) | 178.9 (136.4 to 234.6) | 288.1 (232.8 to 356.6) |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 163 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenY | 249.6 (195.6 to 318.7) | | | |

## Statistical analyses

| Statistical analysis title | GMT ratio hSBA-MenY Lot B/Lot A |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

| Comparison groups | Menhibrix A Group v Menhibrix B Group |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 318 |
| Analysis specification | Pre-specified |
| Analysis type | other[7] |
| Parameter estimate | GMT ratio |
| Point estimate | 1.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.14 |
| upper limit | 2.27 |

Notes:

[7] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMT ratio hSBA-MenY Lot C/Lot A |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

| | |
|---|---|
| Comparison groups | Menhibrix A Group v Menhibrix C Group |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[8] |
| Parameter estimate | GMT ratio |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.99 |
| upper limit | 1.97 |

Notes:

[8] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

| **Statistical analysis title** | GMT ratio hSBA-MenC Lot C/Lot B |
|---|---|

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Hib-MenCY-TT vaccine co-administered with DTPa-HBV-IPV vaccine following 3 primary doses in terms of immunogenicity for N. meningitidis serogroup Y (MenY) as measured by a serum bactericidal assay using human complement (hSBA).

| | |
|---|---|
| Comparison groups | Menhibrix B Group v Menhibrix C Group |
| Number of subjects included in analysis | 331 |
| Analysis specification | Pre-specified |
| Analysis type | other[9] |
| Parameter estimate | GMT ratio |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 1.21 |

Notes:

[9] - For each pair of lots and for the immune response to hSBA-MenY, the two-sided 95% confidence interval (CI) on the geometric mean titers (GMTs) ratio between lots is within the [0.5; 2.0] interval.

## Primary: hSBA-MenC antibody titers

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

End point description:

Titers are expressed as Geometric Mean Titers (GMTs). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 331 | 119 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC [post-dose 4] (N=331;119) | 2039.8 (1746.3 to 2382.6) | 4.3 (3.2 to 5.8) | | |
| hSBA-MenC [pre-dose 4] (N=329;104) | 180.3 (155.6 to 208.8) | 3 (2.4 to 3.7) | | |

## Statistical analyses

| **Statistical analysis title** | 1.hSBA-MenC GMT ratio - Post-dose 4/Pre-dose 4 |
|---|---|

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenC.

| Comparison groups | Menhibrix Group v ActHIB Group |
|---|---|
| Number of subjects included in analysis | 450 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[10] |
| Parameter estimate | GMT ratio |
| Point estimate | 12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.4 |
| upper limit | 13.8 |

Notes:

[10] - Criteria for immunogenicity of MenC (42 days after the fourth dose): Lower limit of the asymptotic 95% CI for the geometric mean of individual ratio of post-dose 4/pre-dose 4 is ≥ 2.

| **Statistical analysis title** | 2.hSBA-MenC GMT ratio - Post-dose 4/Pre-dose 4 |
|---|---|

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenC.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |
| Number of subjects included in analysis | 450 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[11] |
| Parameter estimate | GMT ratio |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.4 |
| upper limit | 1.4 |

Notes:

[11] - Point estimate = Lower limit (LL) = Upper limit (UL) as LL and UL values were not available due to the departure from lognormal distribution (large number of imputed values).

## Primary: hSBA-MenY antibody titers

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

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 342 | 120 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenY [post-dose 4] (N=342;120) | 1389.5 (1205 to 1602.2) | 48.6 (31.9 to 74) | | |
| hSBA-MenY [pre-dose 4] (N=329;103) | 119.1 (101.1 to 140.3) | 2.5 (2.1 to 2.9) | | |

## Statistical analyses

| Statistical analysis title | 1.hSBA-MenY GMT ratio - Post-dose 4/Pre-dose 4 |
|---|---|

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenY.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |

| | |
|---|---|
| Number of subjects included in analysis | 462 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[12] |
| Parameter estimate | GMT ratio |
| Point estimate | 11.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.2 |
| upper limit | 13.8 |

Notes:

[12] - Criteria for immunogenicity of MenY (42 days after the fourth dose): Lower limit of the asymptotic 95% CI for the geometric mean of individual ratio of post-dose 4/pre-dose 4 is ≥ 2.

| **Statistical analysis title** | 2.hSBA-MenY GMT ratio - Post-dose 4/Pre-dose 4 |
|---|---|

Statistical analysis description:

To evaluate the specific effect of a fourth dose of Menhibrix vaccine co-administered with M-M-R II and Varivax vaccines at 12 to 15 months of age in terms of a fourth dose vaccine response as measured by hSBA-MenY.

| | |
|---|---|
| Comparison groups | ActHIB Group v Menhibrix Group |
| Number of subjects included in analysis | 462 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[13] |
| Parameter estimate | GMT ratio |
| Point estimate | 21.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 21.1 |
| upper limit | 21.1 |

Notes:

[13] - Point estimate = Lower limit (LL) = Upper limit (UL) as LL and UL values were not available due to the departure from lognormal distribution (large number of imputed values).

## Primary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)

| End point title | Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)[14] |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 518 | 171 | 162 | 180 |
| Units: Subjects | | | | |
| Anti-PRP | 499 | 156 | 158 | 175 |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Subjects | | | | |
| Anti-PRP | 166 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with hSBA-MenC titer equal to or above 1:8

| End point title | Number of subjects with hSBA-MenC titer equal to or above 1:8[15] |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after the fourth dose

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 331 | 119 | | |
| Units: Subjects | | | | |
| hSBA-MenC | 326 | 26 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with hSBA-MenY titer equal to or above 1:8

| End point title | Number of subjects with hSBA-MenY titer equal to or above |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after the fourth dose

Notes:

[16] - 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** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 342 | 120 | | |
| Units: Subjects | | | | |
| hSBA-MenY | 338 | 87 | | |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Number of subjects with anti-measles antibody concentrations equal to or above 150 milli-international units per milliliter (mIU/mL)**

| End point title | Number of subjects with anti-measles antibody concentrations equal to or above 150 milli-international units per milliliter (mIU/mL) |
|---|---|

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. Co-administration with MMR-II vaccine

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

End point timeframe:

42 days after the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 852 | 286 | | |
| Units: Subjects | | | | |
| Anti-measles | 815 | 274 | | |

**Statistical analyses**

| **Statistical analysis title** | Serostatus for anti-measles antibodies |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of

Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |
| Number of subjects included in analysis | 1138 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[17] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.56 |
| upper limit | 3.06 |

Notes:

[17] - Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with seroconversion ≥ 150 mIU/mL, in initially seronegative subjects (<150 mIU/mL), for anti-measles antibody is ≥-5% (clinical limit for non-inferiority).

### Primary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter

| | |
|---|---|
| End point title | Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter |

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 126 | | |
| Units: Subjects | | | | |
| Anti-PRP | 358 | 125 | | |

### Statistical analyses

| **Statistical analysis title** | Serostatus for anti-PRP |
|---|---|

Statistical analysis description:

To demonstrate that, following a fourth dose, the immune response to Hib polysaccharide (PRP) in the group that received 3 primary vaccine doses of Menhibrix vaccine and a fourth dose of Menhibrix vaccine coadministered with M-M-R II and Varivax vaccines was non-inferior to the corresponding immune response in the group that received 3 primary vaccine doses of ActHIB vaccine and a fourth dose of PedvaxHIB vaccine co-administered with M-M-R II and Varivax vaccines.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |

| | |
|---|---|
| Number of subjects included in analysis | 487 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[18] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.78 |
| upper limit | 3.57 |

Notes:

[18] - Criteria for non-inferiority (42 days after the fourth dose): Lower limit of the two-sided standardized asymptotic 95% CI on the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with anti-PRP concentration ≥ 1.0 µg/mL is ≥ -10% (clinical limit for non-inferiority).

## Primary: Number of subjects with anti-mumps titer equal to or above 28 estimated dose 50 (ED50)

| | |
|---|---|
| End point title | Number of subjects with anti-mumps titer equal to or above 28 estimated dose 50 (ED50) |

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-mumps antibody titers below 28 ED50. Co-administration with MMR-II vaccine.

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

End point timeframe:

42 days after the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 601 | 191 | | |
| Units: Subjects | | | | |
| Anti-mumps | 595 | 191 | | |

## Statistical analyses

| Statistical analysis title | Serostatus for anti-mumps antibodies ≥ 28 ED50 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M--M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[19] |
| Parameter estimate | Difference in percentage |
| Point estimate | -1 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.16 |
| upper limit | 0.98 |

Notes:

[19] - Criterion for non-inferiority (42 days after fourth dose vaccination): Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with a seroconversion ≥28 ED50, in subjects with initial anti-mumps antibody < 28 ED50, for anti-mumps antibody is ≥ -5% (clinical limit for non-inferiority).

## Primary: Number of subjects with anti-rubella antibody concentrations equal to or above 10 international units per millilitre (IU/mL)

| | |
|---|---|
| End point title | Number of subjects with anti-rubella antibody concentrations equal to or above 10 international units per millilitre (IU/mL) |

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. Co-administration with MMR-II vaccine.

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

End point timeframe:

42 days after the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 850 | 285 | | |
| Units: Subjects | | | | |
| Anti-rubella | 848 | 284 | | |

## Statistical analyses

| **Statistical analysis title** | Serostatus for anti-rubella antibodies ≥ 10 IU/mL |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

| | |
|---|---|
| Comparison groups | Menhibrix Group v ActHIB Group |
| Number of subjects included in analysis | 1135 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[20] |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.57 |
| upper limit | 1.73 |

Notes:

[20] - To demonstrate the non-inferiority of M-M-R II vaccine when co-administered with a fourth dose of Menhibrix vaccine compared to M-M-R II vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with Varivax vaccine.

## Primary: Number of subjects with anti-varicella titers equal to or above 1:5

| End point title | Number of subjects with anti-varicella titers equal to or above 1:5 |
|---|---|

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody titers below 1:5. Co-administration with Varivax vaccine.

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

End point timeframe:

42 days after the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 723 | 223 | | |
| Units: Subjects | | | | |
| Anti-varicella | 722 | 223 | | |

### Statistical analyses

| **Statistical analysis title** | Serostatus for anti-varicella antibodies (≥ 1:5) |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of Varivax vaccine co-administered with a fourth dose of Menhibrix vaccine compared to Varivax vaccine co-administered with a fourth dose of PedvaxHIB vaccine, each co-administered with M-M-R II vaccine in terms of immunogenicity to varicella as measured by fluorescent antibody to membrane antigen (FAMA).

| Comparison groups | Menhibrix Group v ActHIB Group |
|---|---|
| Number of subjects included in analysis | 946 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[21] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.78 |
| upper limit | 1.56 |

Notes:

[21] - Criterion for non-inferiority (42 days after the fourth dose vaccination): Lower limit of the standardized asymptotic 95% CI for the difference (Menhibrix vaccine fourth dose group minus ActHIB fourth dose group) in the percentage of subjects with seroconversion ≥ 1:5 dilution, in initially seronegative subjects (< 1:5), for anti-varicella antibody is ≥ -10% (clinical limit for non-inferiority).

## Secondary: Number of subjects with anti-tetanus (anti-T) and anti-diphtheria toxoid (anti-D) antibody concentrations equal to or above 0.1 international units per millilitre (IU/mL)

| End point title | Number of subjects with anti-tetanus (anti-T) and anti- |
|---|---|

| | |
|---|---|
| | diphtheria toxoid (anti-D) antibody concentrations equal to or above 0.1 international units per millilitre (IU/mL) |

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 365 | 120 | | |
| Units: Subjects | | | | |
| Anti-D | 365 | 120 | | |
| Anti-T | 365 | 120 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-D and anti-T antibody concentrations

| | |
|---|---|
| End point title | Anti-D and anti-T antibody concentrations |

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in international units per milliliter (IU/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 365 | 120 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D | 2 (1.9 to 2.2) | 2.2 (2 to 2.5) | | |
| Anti-T | 3.9 (3.7 to 4.1) | 1.9 (1.7 to 2.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above 10.0 milli-international units per millilitre (mIU/mL)

| End point title | Number of subjects with anti hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above 10.0 milli-international units per millilitre (mIU/mL) |
|---|---|

End point description:

Results are stratified by the presence or absence of a birth dose of hepatitis B vaccine. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 194 | 47 | | |
| Units: Subjects | | | | |
| Anti-HBs with Hepatitis B at birth (N=194;47) | 193 | 47 | | |
| Anti-HBs without Hepatitis B at birth (N=18;8) | 17 | 8 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-HBs antibody concentrations

| End point title | Anti-HBs antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in milli-International units per milliliter (mIU/mL) Results are stratified by the presence or absence of a birth dose of hepatitis B vaccine. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 194 | 47 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs with Hepatitis B at birth (N=194;47) | 1963.2 (1684.8 to 2287.7) | 2187.6 (1551.4 to 3084.5) | | |
| Anti-HBs without Hepatitis B at birth (N=18;8) | 1672.7 (730.9 to 3827.8) | 3593.2 (1499.4 to 8611.1) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations equal to or above 5 ELISA units per millilitre (EL.U/mL)

| End point title | Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations equal to or above 5 ELISA units per millilitre (EL.U/mL) |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 327 | 101 | | |
| Units: Subjects | | | | |
| Anti-PT (N=327;100) | 327 | 100 | | |
| Anti-FHA (N=324;97) | 324 | 97 | | |
| Anti-PRN (N=322;101) | 321 | 99 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

| End point title | Anti-PT, anti-FHA and anti-PRN antibody concentrations |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 327 | 101 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT (N=327;100) | 57.7 (54 to 61.7) | 65.6 (58.3 to 73.9) | | |
| Anti-FHA (N=324;97) | 243.8 (227.9 to 260.9) | 293.6 (261.4 to 329.8) | | |
| Anti-PRN (N=322;101) | 98.6 (89.5 to 108.6) | 103.1 (82.8 to 128.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-poliovirus types 1, 2 and 3 equal to or above 8 estimated dose 50 (ED50)

| End point title | Number of subjects with anti-poliovirus types 1, 2 and 3 equal to or above 8 estimated dose 50 (ED50) |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 90 | | |
| Units: Subjects | | | | |
| Anti-Polio 1 (N=285;90) | 285 | 90 | | |
| Anti-Polio 2 (N=285;90) | 285 | 90 | | |
| Anti-Polio 3 (N=285;89) | 285 | 89 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-poliovirus types 1, 2 and 3 titers

| End point title | Anti-poliovirus types 1, 2 and 3 titers |
|---|---|

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 90 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1 (N=285;90) | 591.8 (525 to 667) | 590.7 (462.7 to 754.1) | | |
| Anti-Polio 2 (N=285;90) | 496.7 (435.9 to 566) | 452.7 (360.3 to 568.8) | | |
| Anti-Polio 3 (N=285;89) | 1367.7 (1209.9 to 1546) | 1239.2 (973.5 to 1577.6) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with antibodies to Neisseria meningitidis serogroup C and Y polysaccharide capsule (anti-PSC and anti-PSY) concentrations equal to or above the cut-off values

| End point title | Number of subjects with antibodies to Neisseria meningitidis serogroup C and Y polysaccharide capsule (anti-PSC and anti-PSY) concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 microgram per milliliter (µg/mL) and >=2.0 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 421 | 404 | | |
| Units: Subjects | | | | |
| Anti-PSC >=0.3 µg/mL (N=421;119) | 418 | 5 | | |
| Anti-PSY >=0.3 µg/mL (N=404;109) | 402 | 1 | | |
| Anti-PSC >=2.0 µg/mL (N=421;119) | 379 | 2 | | |
| Anti-PSY >=2.0 µg/mL (N=404;109) | 396 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PSC and anti-PSY antibody concentrations

| End point title | Anti-PSC and anti-PSY antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per milliliter (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after primary vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 421 | 119 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PSC (N=421;119) | 5.8 (5.3 to 6.2) | 0.2 (0.2 to 0.2) | | |
| Anti-PSY (N=404;109) | 17.5 (16 to 19.1) | 0.2 (0.1 to 0.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

| End point title | Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 microgram per milliliter (µg/mL) and >=1.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 134 | 46 | 49 | 42 |
| Units: Subjects | | | | |
| Anti-PRP >=0.15 µg/mL | 134 | 46 | 49 | 42 |
| Anti-PRP >=1.0 µg/mL | 134 | 46 | 49 | 42 |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 43 | | | |
| Units: Subjects | | | | |
| Anti-PRP >=0.15 µg/mL | 43 | | | |
| Anti-PRP >=1.0 µg/mL | 43 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values

| End point title | Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 microgram per milliliter (µg/mL) and >=1.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: Subjects | | | | |
| Anti-PRP pre-dose 4 >=0.15 µg/mL (N=38;12) | 38 | 12 | | |
| Anti-PRP pre-dose 4 >=1.0 µg/mL (N=38;12) | 33 | 11 | | |
| Anti-PRP post-dose 4 >=0.15 µg/mL (N=40;13) | 40 | 13 | | |
| Anti-PRP post-dose 4 >=1.0 µg/mL (N=40;13) | 40 | 13 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

| End point title | Anti-PRP antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 134 | 46 | 49 | 42 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 23.165 (20.012 to 26.815) | 29.759 (22.729 to 38.965) | 24.984 (19.674 to 31.728) | 24.05 (18.327 to 31.561) |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 43 | | | |

| | | | | |
|---|---|---|---|---|
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 20.489 (15.653 to 26.819) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

| End point title | Anti-PRP antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP Pre-dose 4 (N=38;12) | 3.34 (2.407 to 4.636) | 4.123 (1.981 to 8.583) | | |
| Anti-PRP Post-dose 4 (N=40;13) | 132.965 (97.131 to 182.019) | 92.8 (45.636 to 188.709) | | |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

hSBA-MenC/Y antibody cut-off values assessed were >=1:4 and >=1:8. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| **End point values** | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 135 | 46 | 49 | 42 |
| Units: Subjects | | | | |
| hSBA-MenC >=1:4 (N=134;46;48;42;44) | 133 | 2 | 47 | 42 |
| hSBA-MenC >=1:8 (N=134;46;48;42;44) | 133 | 2 | 47 | 42 |
| hSBA-MenY >=1:4 (N=135;45;49;42;44) | 134 | 1 | 48 | 42 |
| hSBA-MenY >=1:8 (N=135;45;49;42;44) | 134 | 1 | 48 | 42 |

| **End point values** | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 44 | | | |
| Units: Subjects | | | | |
| hSBA-MenC >=1:4 (N=134;46;48;42;44) | 44 | | | |
| hSBA-MenC >=1:8 (N=134;46;48;42;44) | 44 | | | |
| hSBA-MenY >=1:4 (N=135;45;49;42;44) | 44 | | | |
| hSBA-MenY >=1:8 (N=135;45;49;42;44) | 44 | | | |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

hSBA-MenC/Y antibody cut-off values assessed were >=1:4 and >=1:8. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: Subjects | | | | |
| hSBA-MenC pre-dose 4 >=1:4 (N=39;13) | 39 | 2 | | |
| hSBA-MenC pre-dose 4 >=1:8 (N=39;13) | 39 | 2 | | |
| hSBA-MenC post-dose 4 >=1:4 (N=39;13) | 39 | 1 | | |
| hSBA-MenC post-dose 4 >=1:8 (N=39;13) | 39 | 1 | | |
| hSBA-MenY pre-dose 4 >=1:4 (N=39;13) | 39 | 3 | | |
| hSBA-MenY pre-dose 4 >=1:8 (N=39;13) | 39 | 3 | | |
| hSBA-MenY post-dose 4 >=1:4 (N=40;13) | 40 | 7 | | |
| hSBA-MenY post-dose 4 >=1:8 (N=40;13) | 40 | 7 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA-MenC and hSBA-MenY antibody titers

| End point title | hSBA-MenC and hSBA-MenY antibody titers |
|---|---|

End point description:

Titres are expressed as Geometric Mean Titers (GMTs). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 135 | 46 | 49 | 42 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC (N=134;46;48;42;44) | 3172.6 (2657.9 to 3786.8) | 2.4 (1.8 to 3.1) | 3055.8 (2096.8 to 4453.6) | 3370.7 (2545.4 to 4463.6) |

| | | | | |
|---|---|---|---|---|
| hSBA-MenY (N=135;45;49;42;44) | 837.2 (696.4 to 1006.3) | 2.2 (1.8 to 2.5) | 666.5 (464 to 957.3) | 916.7 (666.9 to 1260.1) |

| **End point values** | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 44 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC (N=134;46;48;42;44) | 3119.3 (2418.9 to 4022.4) | | | |
| hSBA-MenY (N=135;45;49;42;44) | 989.6 (756.7 to 1294.2) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA-MenC and hSBA-MenY antibody titers

| End point title | hSBA-MenC and hSBA-MenY antibody titers |
|---|---|

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenC pre-dose 4 (N=39;13) | 504.7 (366.2 to 695.5) | 3.6 (1.5 to 8.7) | | |
| hSBA-MenC post-dose 4 (N=39;13) | 10132.9 (8008 to 12821.7) | 2.5 (1.6 to 3.8) | | |
| hSBA-MenY pre-dose 4 (N=39;13) | 446.5 (328.3 to 607.3) | 5.3 (1.7 to 16.7) | | |
| hSBA-MenY post-dose 4 (N=40;13) | 5775.8 (4488.9 to 7431.7) | 27.4 (5.8 to 129) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

| End point title | Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 microgram per milliliter (µg/mL) and >=2.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 134 | 46 | | |
| Units: Subjects | | | | |
| Anti-PSC >=0.3 µg/mL (N=134;46) | 134 | 2 | | |
| Anti-PSC >=2.0 µg/mL (N=134;46) | 134 | 1 | | |
| Anti-PSY >=0.3 µg/mL (N=130;46) | 130 | 1 | | |
| Anti-PSY >=2.0 µg/mL (N=130;46) | 130 | 1 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

| End point title | Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 µg/mL and >=2.0 µg/mL. The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: Subjects | | | | |
| Anti-PSC pre-dose 4 >=0.3 µg/mL (N=40;13) | 40 | 0 | | |
| Anti-PSC pre-dose 4 >=2.0 µg/mL (N=40;13) | 22 | 0 | | |
| Anti-PSC post-dose 4 >=0.3 µg/mL (N=39;13) | 39 | 0 | | |
| Anti-PSC post-dose 4 >=2.0 µg/mL (N=39;13) | 39 | 0 | | |
| Anti-PSY pre-dose 4 >=0.3 µg/mL (N=40;13) | 40 | 0 | | |
| Anti-PSY pre-dose 4 >=2.0 µg/mL (N=40;13) | 36 | 0 | | |
| Anti-PSY post-dose 4 >=0.3 µg/mL (N=40;13) | 40 | 0 | | |
| Anti-PSY post-dose 4 >=2.0 µg/mL (N=40;13) | 40 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PSC and anti-PSY antibodies concentrations

| End point title | Anti-PSC and anti-PSY antibodies concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per milliliter (µg/mL). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 134 | 46 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PSC (N=134;46) | 13.4 (12.1 to 15) | 0.2 (0.1 to 0.2) | | |

| | | | | |
|---|---|---|---|---|
| Anti-PSY (N=130;46) | 36.7 (32.2 to 41.8) | 0.2 (0.1 to 0.2) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PSC and anti-PSY antibody concentrations

| End point title | Anti-PSC and anti-PSY antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). The analysis was performed on the cohort 3 (Non-US Safety and Immunogenicity): Cohort 3 was to include the subjects enrolled at 1 center in Mexico. Only descriptive immunogenicity results were reported for this cohort. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 13 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PSC pre-dose 4 (N=40;13) | 2.2 (1.72 to 2.83) | 0.15 (0.15 to 0.15) | | |
| Anti-PSC post-dose 4 (N=39;13) | 15.63 (13.3 to 18.37) | 0.15 (0.15 to 0.15) | | |
| Anti-PSY pre-dose 4 (N=40;13) | 5.7 (4.18 to 7.78) | 0.15 (0.15 to 0.15) | | |
| Anti-PSY post-dose 4 (N=40;13) | 64.66 (52.35 to 79.86) | 0.15 (0.15 to 0.15) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off value

| End point title | Number of subjects with anti-PRP antibody concentrations equal to or above the cut-off value |
|---|---|

End point description:

Anti-PRP antibody cut-off values assessed were >=0.15 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 518 | 171 | 162 | 180 |
| Units: Subjects | | | | |
| Anti-PRP post-primary >=0.15 µg/mL | 518 | 168 | 162 | 180 |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Subjects | | | | |
| Anti-PRP post-primary >=0.15 µg/mL | 176 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PRP antibody concentrations

| End point title | Anti-PRP antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course and prior to the fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 469 | 160 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP post-primary (N=469;160) | 10.802 (9.767 to 11.947) | 6.086 (4.897 to 7.564) | | |
| Anti-PRP pre-dose 4 (N=441;147) | 1.615 (1.439 to 1.812) | 0.832 (0.664 to 1.042) | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

hSBA-MenC and hSBA-MenY antibody cut-off values assessed were >=1:4 and >=1:8. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

One month after the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | Menhibrix A Group | Menhibrix B Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 491 | 164 | 158 | 168 |
| Units: Subjects | | | | |
| hSBA-MenC >=1:4 (N=491;164;158;168;165) | 485 | 11 | 156 | 167 |
| hSBA-MenC >=1:8 (N=491;164;158;168;165) | 485 | 11 | 156 | 167 |
| hSBA-MenY >=1:4 (N=481;162;150;168;163) | 463 | 3 | 141 | 165 |
| hSBA-MenY >=1:8 (N=481;162;150;168;163) | 461 | 3 | 140 | 165 |

| End point values | Menhibrix C Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 165 | | | |
| Units: Subjects | | | | |
| hSBA-MenC >=1:4 (N=491;164;158;168;165) | 162 | | | |
| hSBA-MenC >=1:8 (N=491;164;158;168;165) | 162 | | | |
| hSBA-MenY >=1:4 (N=481;162;150;168;163) | 157 | | | |
| hSBA-MenY >=1:8 (N=481;162;150;168;163) | 156 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values

| End point title | Number of subjects with anti-PSC and anti-PSY antibody concentrations equal to or above the cut-off values |
|---|---|

End point description:

Anti-PSC and anti-PSY antibody cut-off values assessed were >=0.3 µg/mL and >=2.0 µg/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 334 | 109 | | |
| Units: Subjects | | | | |
| Anti-PSC pre-dose 4 >=0.3 µg/mL (N=327;99) | 300 | 3 | | |
| Anti-PSC pre-dose 4 >=2.0 µg/mL (N=327;99) | 73 | 0 | | |
| Anti-PSC post-dose 4 >=0.3 µg/mL (N=316;106) | 313 | 9 | | |
| Anti-PSC post-dose 4 >=2.0 µg/mL (N=316;106) | 262 | 6 | | |
| Anti-PSY pre-dose 4 >=0.3 µg/mL (N=325;93) | 320 | 1 | | |
| Anti-PSY pre-dose 4 >=2.0 µg/mL (N=325;93) | 235 | 0 | | |
| Anti-PSY post-dose 4 >=0.3 µg/mL (N=334;109) | 332 | 6 | | |
| Anti-PSY post-dose 4 >=2.0 µg/mL (N=334;109) | 325 | 4 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-PSC and anti-PSY antibody concentrations

| End point title | Anti-PSC and anti-PSY antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL). This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth dose vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 334 | 109 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PSC pre-dose 4 (N=327;99) | 1.04 (0.94 to 1.16) | 0.16 (0.15 to 0.17) | | |
| Anti-PSC post-dose 4 (N=316;106) | 4.81 (4.33 to 5.34) | 0.19 (0.16 to 0.23) | | |
| Anti-PSY pre-dose 4 (N=325;93) | 3.15 (2.83 to 3.5) | 0.15 (0.15 to 0.15) | | |
| Anti-PSY post-dose 4 (N=334;109) | 18.26 (16.41 to 20.31) | 0.18 (0.15 to 0.21) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRP antibody concentrations equal to or above 0.15 microgram per milliliter (µg/mL)

| End point title | Number of subjects with anti-PRP antibody concentrations equal to or above 0.15 microgram per milliliter (µg/mL) |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 126 | | |
| Units: Subjects | | | | |
| Anti-PRP [post-dose 4] (N=361;126) | 361 | 126 | | |
| Anti-PRP [pre-dose 4] (N=341;112) | 329 | 98 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

| End point title | Anti-PRP antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in microgram per millilitre (µg/mL) This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth vaccination and 42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 126 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP [post-dose 4] (N=361;126) | 34.851 (30.664 to 39.61) | 20.2 (16.373 to 24.92) | | |
| Anti-PRP [pre-dose 4] (N=341;112) | 1.617 (1.42 to 1.842) | 0.759 (0.589 to 0.978) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody concentrations equal to or above 1:4

| End point title | Number of subjects with hSBA-MenC and hSBA-MenY antibody concentrations equal to or above 1:4 |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination and 42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 342 | 120 | | |
| Units: Subjects | | | | |
| hSBA-MenC [post-dose 4] (N=331;119) | 326 | 26 | | |
| hSBA-MenY [post-dose 4](N=342;120) | 338 | 87 | | |
| hSBA-MenC [pre-dose 4] (N=329;104) | 318 | 12 | | |
| hSBA-MenY [pre-dose 4](N=329;103) | 309 | 6 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-measles antibody concentrations equal to or above 200 milli-international units per millilitre (mIU/mL)

| End point title | Number of subjects with anti-measles antibody concentrations equal to or above 200 milli-international units per millilitre (mIU/mL) |
|---|---|

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after the fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 852 | 286 | | |
| Units: Subjects | | | | |
| Anti-measles | 812 | 273 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-measles antibody concentrations

| End point title | Anti-measles antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in milli-international units per milliliter (mIU/mL). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody concentrations below 150 mIU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 852 | 286 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-measles | 1990 (1852.2 to 2138) | 1989.5 (1765.4 to 2242.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-mumps titer equal to or above the cut-off values

| End point title | Number of subjects with anti-mumps titer equal to or above the cut-off values |
|---|---|

End point description:

Anti-mumps antibody cut-off values assessed were >=28 estimated dose 50 (ED50) and >=51 ED50. The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-mumps antibody titers below 24 ED50. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 536 | 176 | | |
| Units: Subjects | | | | |
| Anti-mumps >=28 ED50 | 532 | 176 | | |
| Anti-mumps >=51 ED50 | 490 | 160 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-mumps antibody titers

| End point title | Anti-mumps antibody titers |
|---|---|

End point description:

Titers are expressed as Geometric Mean Titers (GMTs). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-measles antibody titers below 24 ED50. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 536 | 176 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-mumps | 123.9 (116.9 to 131.3) | 114.3 (103.7 to 126) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-rubella antibody concentrations equal to or above 4 international units per millilitre (IU/mL)

| End point title | Number of subjects with anti-rubella antibody concentrations equal to or above 4 international units per millilitre (IU/mL) |
|---|---|

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 850 | 285 | | |
| Units: Subjects | | | | |
| Anti-rubella | 850 | 285 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-rubella antibody concentrations

| End point title | Anti-rubella antibody concentrations |
|---|---|

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) and are expressed in international units per milliliter (IU/mL). The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-rubella antibody concentrations below 4 IU/mL. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 850 | 285 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-rubella | 81.4 (77.5 to 85.4) | 74.9 (68.9 to 81.4) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-varicella titer equal to or above 1:40

| End point title | Number of subjects with anti-varicella titer equal to or above 1:40 |
|---|---|

End point description:

The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody concentrations below 1:5 This analysis occurred on the cohort 1: Cohort 1 was to

include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 723 | 223 | | |
| Units: Subjects | | | | |
| Anti-varicella | 722 | 223 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-varicella antibody titers

| End point title | Anti-varicella antibody titers |
|---|---|

End point description:

Titers are expressed as Geometric Mean Titers (GMTs) The analysis was performed on initially seronegative subjects. Seronegative subjects are subjects with anti-varicella antibody titers below 1:5 This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

42 days after fourth vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 723 | 223 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-varicella | 407.1 (389.4 to 425.5) | 394.1 (364.6 to 426) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-H1N1, anti-H3N2 and anti-influenza-B (anti B) antibody titers equal to or above 1:40

| End point title | Number of subjects with anti-H1N1, anti-H3N2 and anti-influenza-B (anti B) antibody titers equal to or above 1:40 |
|---|---|

End point description:

Anti-H1N1, anti-H3N2 and anti-influenza-B (anti-B) antibody were measured by hemagglutination inhibition assay (HIA), in subjects who received 2 doses of influenza vaccine within the same influenza season of which at least one dose is concomitant with the study vaccine. For the purposes of this study, concomitant administration of influenza vaccine was defined as administration within 28 days before to 7 days after administration of study vaccines. This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based.

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

End point timeframe:

Prior to the fourth dose vaccination and one month after the fourth dose vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 4 | | |
| Units: Subjects | | | | |
| Anti-H1N1 pre-dose 4 (N=5;3) | 0 | 0 | | |
| Anti-H1N1 post-dose 4 (N=4;4) | 2 | 1 | | |
| Anti-H3N2 pre-dose 4 (N=5;3) | 0 | 0 | | |
| Anti-H3N2 post-dose 4 (N=4;4) | 3 | 1 | | |
| Anti-B pre-dose 4 (N=5;3) | 0 | 0 | | |
| Anti-B post-dose 4 (N=4;4) | 1 | 1 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

| End point title | Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit |
|---|---|

End point description:

Fever is defined as temperature (rectal or axillary/tympanic) above 39.5 degrees Celsius (°C) or 103.1 degrees Fahrenheit (°F).

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

End point timeframe:

In the 4-day (Day 0-3) follow-up period after primary vaccination course

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3089 | 1015 | | |
| Units: Subjects | | | | |
| Fever >39.5°C | 46 | 16 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit

| End point title | Number of subjects reporting fever above 39.5 degrees Celsius/103.1 degrees Fahrenheit |
|---|---|

End point description:

Fever is defined as temperature (rectal or axillary/tympanic) above 39.5 degrees Celsius (°C) or 103.1 degrees Fahrenheit (°F).

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

End point timeframe:

In the 4-day (Day0-3) follow-up period after the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2527 | 831 | | |
| Units: Subjects | | | | |
| Fever >39.5°C | 18 | 5 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting solicited local and general symptoms

| End point title | Number of subjects reporting solicited local and general symptoms |
|---|---|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Solicited general symptoms assessed were fever, irritability/fussiness, drowsiness and loss of appetite. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C.

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

End point timeframe:

Within the 4 days (Day 0-3) following each dose of the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3089 | 1016 | | |
| Units: Subjects | | | | |
| Pain Dose 1 (N=3056;1008) | 1849 | 672 | | |
| Pain Dose 2 (N=2903;954) | 1679 | 596 | | |
| Pain Dose 3 (N=2740;904) | 1454 | 522 | | |
| Pain Across Doses (N=3088;1016) | 2419 | 819 | | |
| Redness Dose 1 (N=3056;1008) | 1152 | 401 | | |
| Redness Dose 2 (N=2903;954) | 1455 | 483 | | |
| Redness Dose 3 (N=2740;904) | 1409 | 495 | | |
| Redness Across Doses (N=3088;1016) | 2052 | 691 | | |
| Swelling Dose 1 (N=3056;1008) | 893 | 281 | | |
| Swelling Dose 2 (N=2903;954) | 1091 | 350 | | |
| Swelling Dose 3 (N=2740;904) | 1110 | 381 | | |
| Swelling Across Doses (N=3088;1016) | 1707 | 568 | | |
| Drowsiness Dose 1 (N=3055;1008) | 1864 | 655 | | |
| Drowsiness Dose 2 (N=2900;952) | 1588 | 552 | | |
| Drowsiness Dose 3 (N=2736;905) | 1260 | 444 | | |
| Drowsiness Across doses (N=3088;1015) | 2418 | 804 | | |
| Temperature Dose 1 (N=3056;1008) | 688 | 228 | | |
| Temperature Dose 2 (N=2900;951) | 803 | 276 | | |
| Temperature Dose 3 (N=2736;905) | 609 | 206 | | |
| Temperature Across doses (N=3089;1015) | 1434 | 463 | | |
| Irritability Dose 1 (N=3055;1008) | 2156 | 782 | | |
| Irritability Dose 2 (N=2900;952) | 2074 | 708 | | |
| Irritability Dose 3 (N=2736;905) | 1771 | 600 | | |
| Irritability Across doses (N=3088;1015) | 2740 | 926 | | |
| Loss of appetite Dose 1 (N=3055;1008) | 1024 | 375 | | |
| Loss of appetite Dose 2 (N=2900;952) | 921 | 317 | | |
| Loss of appetite Dose 3 (N=2736;905) | 828 | 285 | | |
| Loss of appetite Across doses (N=3088;1015) | 1764 | 609 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting solicited local and general symptoms

| End point title | Number of subjects reporting solicited local and general symptoms |
|---|---|

End point description:

Solicited local symptoms assessed were pain, redness, swelling and an increase in limb circumference. Solicited general symptoms assessed were fever, irritability/fussiness, drowsiness and lost of appetite. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C

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

End point timeframe:

Within the 4 days (Day 0-3) post-vaccination period following the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Pain (N=2528;832) | 1319 | 494 | | |
| Redness (N=2528;833) | 1213 | 463 | | |
| Swelling (N=2526;832) | 936 | 334 | | |
| Increase in limb circumference (N=2769;923) | 1489 | 503 | | |
| Drowsiness (N=2526;830) | 1088 | 381 | | |
| Fever (N=2527;831) | 341 | 134 | | |
| Irritability (N=2526;830) | 1482 | 534 | | |
| Loss of appetite (N=2526;830) | 825 | 287 | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Number of subjects reporting 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:

Within 31 days (Day 0-30) following the primary vaccination course

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| AEs | 1820 | 602 | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Number of subjects reporting 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:

Within 31 days (Day 0-30) following the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| AEs | 1010 | 334 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting increased circumferential swelling at the injection limb(s)

| End point title | Number of subjects reporting increased circumferential swelling at the injection limb(s) |
|---|---|

End point description:

Increased circumferential swelling defined as either swelling with a diameter of >50 mm or a >50 mm increase in the circumference of the mid-limb when compared to the baseline (pre-vaccination) measurement, or any diffuse swelling that interferes with or prevents everyday activities (for example, active playing, eating, sleeping).

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

End point timeframe:

Within 4 days (Day 0 to Day 3) after fourth dose vaccination

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Increase in circumference | 1489 | 503 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting general symptoms specific to measles,

| mumps, rubella and varicella vaccination | |
|---|---|
| End point title | Number of subjects reporting general symptoms specific to measles, mumps, rubella and varicella vaccination |

End point description:

Symptoms assessed were fever, rash/exanthem, parotid/salivary gland swelling, and any suspected signs of meningism including febrile convulsions. Fever is defined as temperature (rectal or axillary/tympanic) equal to or above 38.0°C.

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

End point timeframe:

Within 43 days (Day 0 through Day 42) after vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 545 | 175 | | |
| Units: Subjects | | | | |
| Meningismus (N=541;173) | 0 | 0 | | |
| Parotiditis (N=541;173) | 0 | 0 | | |
| Rash (N=544;175) | 59 | 19 | | |
| Fever (N=545;173) | 211 | 70 | | |

## Statistical analyses

No statistical analyses for this end point

| Secondary: Number of subjects reporting Serious Adverse Events (SAEs) | |
|---|---|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) |

End point description:

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

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

End point timeframe:

From Dose 0 through 6 months after the last primary dose or untill administration of the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| SAEs | 126 | 50 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting Serious Adverse Events (SAEs)

| End point title | Number of subjects reporting Serious Adverse Events (SAEs) |
|---|---|

End point description:

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

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

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| SAEs | 47 | 18 | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

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

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| Any NOCIs | 163 | 52 | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

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

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Any NOCIs | 85 | 33 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting rash

| End point title | Number of subjects reporting rash |
|---|---|

End point description:

Rash assessed was hives, idiopathic thrombocytopenic purpura, petechiae.

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

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| Any rash(es) | 470 | 154 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting rash

| End point title | Number of subjects reporting rash |
|---|---|

End point description:

Rash assessed was hives, idiopathic thrombocytopenic purpura, petechiae.

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

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Any rash(es) | 265 | 94 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting adverse events resulting in emergency room (ER) visits

| End point title | Number of subjects reporting adverse events resulting in emergency room (ER) visits |
|---|---|

End point description:

Emergency room (ER) visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

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

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| Any AEs | 217 | 72 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting adverse events resulting in physicians

**(MD) office visits.**

| End point title | Number of subjects reporting adverse events resulting in physicians (MD) office visits. |
|---|---|

End point description:

Physicians (MD) office visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

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

End point timeframe:

From Dose 0 through 6 months after the last primary dose or until administration of the fourth dose

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3136 | 1044 | | |
| Units: Subjects | | | | |
| Any AEs | 1336 | 433 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects reporting adverse events resulting in emergency room (ER) visits**

| End point title | Number of subjects reporting adverse events resulting in emergency room (ER) visits |
|---|---|

End point description:

Emergency room (ER) visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

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

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

| **End point values** | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Any AEs | 137 | 54 | | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Number of subjects reporting adverse events resulting in physicians (MD) office visits

| End point title | Number of subjects reporting adverse events resulting in physicians (MD) office visits |
|---|---|

End point description:

Physicians (MD) office visits were not related to well-child care, vaccination, injury or common acute illness such as upper respiratory tract infections; otitis media, pharyngitis, gastroenteritis.

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

End point timeframe:

From the fourth dose through the end of the 6-month safety follow-up

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2769 | 923 | | |
| Units: Subjects | | | | |
| Any AEs | 668 | 205 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL)

| End point title | Number of subjects with anti-PRP antibody concentration equal to or above 1.0 microgram per milliliter (µg/mL) |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 341 | 112 | | |
| Units: Subjects | | | | |
| Anti-PRP [pre-dose 4] (N=341;112) | 227 | 52 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with hSBA-MenC and hSBA-MenY antibody titer equal to or above 1:8

| End point title | Number of subjects with hSBA-MenC and hSBA-MenY antibody titer equal to or above 1:8 |
|---|---|

End point description:

This analysis occurred on the cohort 1: Cohort 1 was to include subjects in the US on which all immunogenicity analyses were to be based. These subjects also contributed to the safety analysis.

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

End point timeframe:

Prior to the fourth dose vaccination

| End point values | Menhibrix Group | ActHIB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 329 | 104 | | |
| Units: Subjects | | | | |
| hSBA-MenC [pre-dose 4] (N=329;104) | 318 | 12 | | |
| hSBA-MenY [pre-dose 4] (N=329;103) | 306 | 6 | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs: From Day 0 after Dose 1 through the day preceding the fourth dose; From the fourth dose phase through the end of the safety follow-up; AEs: within the 31-day (Day 0-30) post vaccination period; Solicited AEs: During the 4-day post vaccination period

Adverse event reporting additional description:

Results are presented for the primary phase and the fourth dose phase.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Menhibrix Group |

Reporting group description:

Subjects were primed with 3 doses of Menhibrix vaccine Lot A, B or C co-administered with Pediarix and boosted with 1 dose of Menhibrix vaccine, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. Menhibrix and Pediarix vaccines were administered intramuscularly in the right or left upper thigh, respectively. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| | |
|---|---|
| Reporting group title | ActHIB Group |

Reporting group description:

Subjects were primed with 3 doses of ActHIB co-administered with Pediarix and boosted with 1 dose of PedvaxHIB, with co-administration of M-M-R II and Varivax. Subjects received vaccination at approximately 2, 4, 6 months and the fourth dose at 12-15 months of age. ActHIB, PedvaxHIB vaccines were administered intramuscularly in the right upper thigh and Pediarix vaccine in the left upper thigh. M-M-R II and Varivax vaccines were administered subcutaneously respectively in the upper left arm and the upper right arm.

| Serious adverse events | Menhibrix Group | ActHIB Group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 126 / 3136 (4.02%) | 50 / 1044 (4.79%) | |
| number of deaths (all causes) | 4 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Haemangioma | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroblastoma | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 3136 (0.16%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Irritability | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden infant death syndrome | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity (fourth dose) | | | |
| subjects affected / exposed[1] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory distress (primary) | | | |
| subjects affected / exposed | 5 / 3136 (0.16%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma (primary) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3136 (0.10%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial hyperreactivity (primary) | | | |
| subjects affected / exposed | 3 / 3136 (0.10%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 3 / 3136 (0.10%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Apparent life threatening event | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Apnoea | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory disorder | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stridor | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wheezing (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma (fourth dose) | | | |
| subjects affected / exposed[2] | 4 / 2769 (0.14%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial hyperreactivity (fourth dose) | | | |
| subjects affected / exposed[3] | 1 / 2769 (0.04%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress (fourth dose) | | | |
| subjects affected / exposed[4] | 1 / 2769 (0.04%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wheezing (fourth dose) | | | |
| subjects affected / exposed[5] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Aspiration bronchial | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury, poisoning and procedural complications | | | |
| Respiratory syncytial virus bronchiolitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 3136 (0.26%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Child maltreatment syndrome | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Foreign body trauma | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury (fourth dose) | | | |
| subjects affected / exposed[6] | 1 / 2769 (0.04%) | 2 / 923 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental drug intake by child | | | |
| subjects affected / exposed[7] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental exposure | | | |
| subjects affected / exposed[8] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns first degree | | | |
| subjects affected / exposed[9] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns second degree | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[10] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple injuries | | | |
| subjects affected / exposed[11] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Seroma | | | |
| subjects affected / exposed[12] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed[13] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thermal burn | | | |
| subjects affected / exposed[14] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Coarctation of the aorta | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberous sclerosis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular septal defect (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular septal defect (fourth dose) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[15] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Febrile convulsion (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Convulsion (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar ataxia | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotonia | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infantile spasms | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Convulsion (fourth dose) | | | |
| subjects affected / exposed[16] | 2 / 2769 (0.07%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion (fourth dose) | | | |
| subjects affected / exposed[17] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Lymphoid tissue hyperplasia | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic thrombocytopenic purpura | | | |
| subjects affected / exposed[18] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenitis | | | |
| subjects affected / exposed[19] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed[20] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed[21] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryostenosis acquired | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Intussusception | | | |
| subjects affected / exposed | 4 / 3136 (0.13%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|---|---|
| Vomiting (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain (fourth dose) | | | |
| subjects affected / exposed[22] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting (fourth dose) | | | |
| subjects affected / exposed[23] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |

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|---|---|---|---|
| Erythema multiforme | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash papular | | | |
| subjects affected / exposed[24] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed[25] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis (primary) | | | |
| subjects affected / exposed | 19 / 3136 (0.61%) | 7 / 1044 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Bronchiolitis (primary) | | | |
| subjects affected / exposed | 18 / 3136 (0.57%) | 5 / 1044 (0.48%) | |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media (primary) | | | |
| subjects affected / exposed | 8 / 3136 (0.26%) | 4 / 1044 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection (primary) | | | |
| subjects affected / exposed | 11 / 3136 (0.35%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus (primary) | | | |
| subjects affected / exposed | 8 / 3136 (0.26%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia (primary) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 3136 (0.26%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection (primary) | | | |
| subjects affected / exposed | 8 / 3136 (0.26%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 4 / 3136 (0.13%) | 4 / 1044 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 3 / 1044 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 3 / 1044 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection (primary) | | | |
| subjects affected / exposed | 4 / 3136 (0.13%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection (primary) | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral (primary) | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3136 (0.06%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral skin infection | | | |
| subjects affected / exposed | 2 / 3136 (0.06%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acarodermatitis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis viral | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral (primary) | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Group b streptococcus neonatal sepsis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HIV infection | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar pneumonia (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis viral | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pertussis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection (primary) | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Typhoid fever | | | |
| subjects affected / exposed | 0 / 3136 (0.00%) | 1 / 1044 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vulval abscess | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis (fourth dose) | | | |
| subjects affected / exposed[26] | 5 / 2769 (0.18%) | 4 / 923 (0.43%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection (fourth dose) | | | |
| subjects affected / exposed[27] | 5 / 2769 (0.18%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious (fourth dose) | | | |

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|---|---|---|---|
| subjects affected / exposed[28] | 4 / 2769 (0.14%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis (fourth dose) | | | |
| subjects affected / exposed[29] | 2 / 2769 (0.07%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media (fourth dose) | | | |
| subjects affected / exposed[30] | 1 / 2769 (0.04%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral (fourth dose) | | | |
| subjects affected / exposed[31] | 1 / 2769 (0.04%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection (fourth dose) | | | |
| subjects affected / exposed[32] | 2 / 2769 (0.07%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess (fourth dose) | | | |
| subjects affected / exposed[33] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess neck | | | |
| subjects affected / exposed[34] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenoviral upper respiratory infection | | | |
| subjects affected / exposed[35] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis (fourth dose) | | | |

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|---|---|---|---|
| subjects affected / exposed[36] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis of male external genital organ | | | |
| subjects affected / exposed[37] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus (fourth dose) | | | |
| subjects affected / exposed[38] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed[39] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral (fourth dose) | | | |
| subjects affected / exposed[40] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar pneumonia (fourth dose) | | | |
| subjects affected / exposed[41] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection (fourth dose) | | | |
| subjects affected / exposed[42] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymph node abscess | | | |
| subjects affected / exposed[43] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |

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|---|---|---|---|
| subjects affected / exposed[44] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia (fourth dose) | | | |
| subjects affected / exposed[45] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed[46] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed[47] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection (fourth dose) | | | |
| subjects affected / exposed[48] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection (fourth dose) | | | |
| subjects affected / exposed[49] | 1 / 2769 (0.04%) | 0 / 923 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection (fourth dose) | | | |
| subjects affected / exposed[50] | 0 / 2769 (0.00%) | 1 / 923 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration (primary) | | | |
| subjects affected / exposed | 15 / 3136 (0.48%) | 2 / 1044 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3136 (0.06%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acidosis | | | |
| subjects affected / exposed | 1 / 3136 (0.03%) | 0 / 1044 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration (fourth dose) | | | |
| subjects affected / exposed[51] | 3 / 2769 (0.11%) | 2 / 923 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: The analysis was performed only on subjects who received a fourth dose of Hib-MenCY-TT vaccine.

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

| **Non-serious adverse events** | Menhibrix Group | ActHIB Group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3034 / 3136 (96.75%) | 998 / 1044 (95.59%) | |
| General disorders and administration site conditions | | | |
| Pyrexia (primary) | | | |
| subjects affected / exposed | 176 / 3136 (5.61%) | 73 / 1044 (6.99%) | |
| occurrences (all) | 176 | 73 | |
| Pyrexia (fourth dose) | | | |
| subjects affected / exposed[52] | 176 / 2769 (6.36%) | 64 / 923 (6.93%) | |
| occurrences (all) | 176 | 64 | |
| Pain (primary) | | | |
| subjects affected / exposed[53] | 2419 / 3088 (78.34%) | 819 / 1016 (80.61%) | |
| occurrences (all) | 2419 | 819 | |
| Redness (primary) | | | |
| subjects affected / exposed[54] | 2052 / 3088 (66.45%) | 691 / 1016 (68.01%) | |
| occurrences (all) | 2052 | 691 | |
| Swelling (primary) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[55] | 1707 / 3088 (55.28%) | 568 / 1016 (55.91%) | |
| occurrences (all) | 1707 | 568 | |
| Drowsiness (primary) | | | |
| subjects affected / exposed[56] | 2418 / 3088 (78.30%) | 804 / 1015 (79.21%) | |
| occurrences (all) | 2418 | 804 | |
| Fever (primary) | | | |
| subjects affected / exposed[57] | 1434 / 3089 (46.42%) | 463 / 1015 (45.62%) | |
| occurrences (all) | 1434 | 463 | |
| Irritability (primary) | | | |
| subjects affected / exposed[58] | 2740 / 3088 (88.73%) | 926 / 1015 (91.23%) | |
| occurrences (all) | 2740 | 926 | |
| Loss of appetite (primary) | | | |
| subjects affected / exposed[59] | 1764 / 3088 (57.12%) | 609 / 1015 (60.00%) | |
| occurrences (all) | 1764 | 609 | |
| Pain (fourth dose) | | | |
| subjects affected / exposed[60] | 1319 / 2528 (52.18%) | 494 / 832 (59.38%) | |
| occurrences (all) | 1319 | 494 | |
| Redness (fourth dose) | | | |
| subjects affected / exposed[61] | 1213 / 2528 (47.98%) | 463 / 833 (55.58%) | |
| occurrences (all) | 1213 | 463 | |
| Swelling (fourth dose) | | | |
| subjects affected / exposed[62] | 936 / 2526 (37.05%) | 334 / 832 (40.14%) | |
| occurrences (all) | 936 | 334 | |
| Increase in limb circumference | | | |
| subjects affected / exposed[63] | 1489 / 2769 (53.77%) | 503 / 923 (54.50%) | |
| occurrences (all) | 1489 | 503 | |
| Drowsiness (fourth dose) | | | |
| subjects affected / exposed[64] | 1088 / 2526 (43.07%) | 381 / 830 (45.90%) | |
| occurrences (all) | 1088 | 381 | |
| Fever (fourth dose) | | | |
| subjects affected / exposed[65] | 341 / 2527 (13.49%) | 134 / 831 (16.13%) | |
| occurrences (all) | 341 | 134 | |
| Irritability (fourth dose) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[66] | 1482 / 2526 (58.67%) | 534 / 830 (64.34%) | |
| occurrences (all) | 1482 | 534 | |
| Loss of appetite (fourth dose) | | | |
| subjects affected / exposed[67] | 825 / 2526 (32.66%) | 287 / 830 (34.58%) | |
| occurrences (all) | 825 | 287 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 197 / 3136 (6.28%) | 65 / 1044 (6.23%) | |
| occurrences (all) | 197 | 65 | |
| Diarrhoea | | | |
| subjects affected / exposed | 185 / 3136 (5.90%) | 57 / 1044 (5.46%) | |
| occurrences (all) | 185 | 57 | |
| Teething (primary) | | | |
| subjects affected / exposed | 180 / 3136 (5.74%) | 55 / 1044 (5.27%) | |
| occurrences (all) | 180 | 55 | |
| Teething (fourth dose) | | | |
| subjects affected / exposed[68] | 115 / 2769 (4.15%) | 46 / 923 (4.98%) | |
| occurrences (all) | 115 | 46 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 163 / 3136 (5.20%) | 50 / 1044 (4.79%) | |
| occurrences (all) | 163 | 50 | |
| Nasal congestion | | | |
| subjects affected / exposed | 146 / 3136 (4.66%) | 53 / 1044 (5.08%) | |
| occurrences (all) | 146 | 53 | |
| Infections and infestations | | | |
| Upper respiratory tract infection (primary) | | | |
| subjects affected / exposed | 524 / 3136 (16.71%) | 173 / 1044 (16.57%) | |
| occurrences (all) | 524 | 173 | |
| Otitis media (primary) | | | |
| subjects affected / exposed | 335 / 3136 (10.68%) | 104 / 1044 (9.96%) | |
| occurrences (all) | 335 | 104 | |
| Upper respiratory tract infection (fourth dose) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[69] | 152 / 2769 (5.49%) | 50 / 923 (5.42%) | |
| occurrences (all) | 152 | 50 | |
| Otitis media (fourth dose) | | | |
| subjects affected / exposed[70] | 135 / 2769 (4.88%) | 47 / 923 (5.09%) | |
| occurrences (all) | 135 | 47 | |

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## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 07 March 2006 | The aims of this trial are to demonstrate the consistency of 3 manufacturing lots of GSK Biologicals' Hib-MenCY-TT candidate vaccine in terms of immunogenicity, the immunogenicity of Hib-MenCY-TT vaccine against N. meningitidis serogroups C and Y and the non-inferiority of GSK Biologicals' Hib-MenCY-TT vaccine with respect to immunogenicity and safety compared to the control vaccine (ActHIB) when each are co-administered with Pediarix to healthy infants at 2, 4, and 6 months of age. The study will also evaluate the safety of a booster dose of Hib-MenCY-TT vaccine at 12 to 15 months of age as compared to PedvaxHIB. Finally, immunogenicity of a booster dose of Hib-MenCY-TT vaccine at 12 to 15 months co-administered with M-M-R II and Varivax will be evaluated. The booster immunogenicity will be performed on data from 2 studies: the current study and a second study with the same design, the non-US study, Hib-MenCY-TT-007/008, which is being conducted under US Investigational New Drug (IND) application. |
| 05 October 2006 | The aims of this trial are to demonstrate the consistency of 3 manufacturing lots of GSK Biologicals' Hib-MenCY-TT candidate vaccine in terms of immunogenicity, the immunogenicity of Hib-MenCY-TT vaccine against N. meningitidis serogroups C and Y and the non-inferiority of GSK Biologicals' Hib-MenCY-TT vaccine with respect to immunogenicity and safety compared to the control vaccine (ActHIB) when each are co-administered with Pediarix to healthy infants at 2, 4, and 6 months of age. The study will also evaluate the safety of a fourth dose of Hib-MenCY-TT vaccine at 12 to 15 months of age as compared to PedvaxHIB. Finally, immunogenicity of a fourth dose of Hib-MenCY-TT vaccine at 12 to 15 months coadministered with M-M-R II and Varivax will be evaluated. The M-M-R II and Varivax co-administration analysis will be performed on data from 2 studies: the current study and a second study with the same design, the non-US study, Hib-MenCY-TT-007/008, which is being conducted under US Investigational New Drug (IND) application. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported