



Clinical trial results:

A phase IIIb, open, randomized, controlled, multicenter study to assess the co-administration of Rotarix (GlaxoSmithKline Biologicals') with Hib-MenCY-TT (MenHibrix)(GlaxoSmithKline Biologicals' Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine) at 2 and 4 months of age, the co-administration of Prevnar 13 (Pfizer) with Hib-MenCY-TT (MenHibrix) at 2, 4 and 6 months of age and the co-administration of Prevnar 13 and Havrix (GlaxoSmithKline Biologicals') with Hib-MenCY-TT ((MenHibrix) at 12 to 15 months of age.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-003459-39 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 18 March 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 22 December 2016 |
| First version publication date | 22 December 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 112931 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01978093 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 March 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 March 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferiority of 4 doses of Hib-MenCY-TT compared to 3 doses of PedvaxHIB, when co-administered with Pevnar 13 and Havrix, in terms of anti-PRP concentration

Epoch 001: To demonstrate non-inferiority of

- 2 doses of Rotarix co-administered with Hib-MenCY-TT, Pediarix and Pevnar 13 compared to Rotarix co-administered with PedvaxHIB, Pediarix and Pevnar 13 in terms of Rotarix IgA GMCs
- 3 doses of Pevnar 13 co-administered with Hib-MenCY-TT, Rotarix and Pediarix compared to Pevnar 13 co-administered with PedvaxHIB, Rotarix and Pediarix in terms of S. pneumoniae GMCs

Epoch 002: To demonstrate non-inferiority of

- 2 doses of Havrix when the 1st dose is co-administered with Hib-MenCY-TT and Pevnar 13 compared to Havrix when the 1st dose is co-administered with PedvaxHIB and Pevnar 13, at 12-15 months of age
- 4 doses of Pevnar 13 co-administered with Hib-MenCY-TT and Havrix compared to Pevnar 13 co-administered with PedvaxHIB and Havrix in terms of S. pneumoniae GMCs

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of anaphylaxis

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 19 February 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 600 |
| Worldwide total number of subjects | 600 |
| 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) | 600 |
| 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:

The study consists of two epochs:

- o Epoch 001: starting at Visit 1 (Day 0) and ending at the day preceding Visit 5
- o Epoch 002: starting at Visit 5 (Month 10-13) and ending at Visit 8 (Month 17-20, 31 days after the 2nd Havrix® vaccination)

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 600 |
| Number of subjects completed | 600 |

Period 1

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

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | HibCY Group |

Arm description:

Subjects received 4 doses of Hib-MenCY-TT (MenHibrix®) vaccine at Day 0, Month 2, Month 4 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Hib-MenCY-TT (MenHibrix) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Four doses administered intramuscularly in the right upper anterolateral thigh at Day 0, Month 2, Month 4 and Month 10-13.

| | |
|--|--|
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Two doses administered orally at Day 0 and Month 2.

| | |
|--|--------------------------|
| Investigational medicinal product name | Havrix 720 Junior |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses administered intramuscularly in the left upper anterolateral thigh at Month 10-13 and Month 16-19.

| | |
|--|--------------------------|
| Investigational medicinal product name | Pevnar 13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Four doses administered intramuscularly in the left lower anterolateral thigh at Day 0 and Month 2, Month 4 and Month 10-13.

| | |
|--|--------------------------|
| Investigational medicinal product name | Pediarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Three doses administered intramuscularly in the left upper anterolateral thigh at Day 0 and Month 2 and in the right upper anterolateral thigh at Month 4.

| | |
|------------------|--------------|
| Arm title | PedHIB Group |
|------------------|--------------|

Arm description:

Subjects received 3 doses of PedvaxHIB® vaccine at Day 0, Month 2 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Pevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Two doses administered orally at Day 0 and Month 2.

| | |
|--|--------------------------|
| Investigational medicinal product name | Havrix 720 Junior |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses administered intramuscularly in the left upper anterolateral thigh at Month 10-13 and Month 16-19.

| | |
|--|--------------------------|
| Investigational medicinal product name | Pevnar 13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Four doses administered intramuscularly in the left lower anterolateral thigh at Day 0 and Month 2, Month 4 and Month 10-13.

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

Dosage and administration details:

Three doses administered intramuscularly in the right upper anterolateral thigh at Day 0, Month 2 and Month 10-13.

| | |
|--|--------------------------|
| Investigational medicinal product name | Pediarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Three doses administered intramuscularly in the left upper anterolateral thigh at Day 0 and Month 2 and in the right upper anterolateral thigh at Month 4.

| Number of subjects in period 1 | HibCY Group | PedHIB Group |
|---------------------------------------|-------------|--------------|
| Started | 297 | 303 |
| Completed | 232 | 230 |
| Not completed | 65 | 73 |
| Loss of kaiser coverage | 4 | 10 |
| Adverse event, serious fatal | - | 5 |
| Consent withdrawn by subject | 29 | 25 |
| N/A for vaccine administration | - | 1 |
| Child was in care of grandmother | - | 1 |
| Mother lost custody of child | - | 1 |
| Migrated/moved from study area | 11 | 13 |
| Lost kaiser health plan no contact | 1 | - |
| Lost to follow-up | 11 | 15 |
| Subject Died | 1 | - |
| Protocol deviation | 8 | 2 |

Baseline characteristics

Reporting groups

| | |
|--|--------------|
| Reporting group title | HibCY Group |
| Reporting group description: Subjects received 4 doses of Hib-MenCY-TT (MenHibrix®) vaccine at Day 0, Month 2, Month 4 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19. | |
| Reporting group title | PedHIB Group |
| Reporting group description: Subjects received 3 doses of PedvaxHIB® vaccine at Day 0, Month 2 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19. | |

| Reporting group values | HibCY Group | PedHIB Group | Total |
|---|--------------|--------------|-------|
| Number of subjects | 297 | 303 | 600 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: weeks arithmetic mean standard deviation | 1.8 ± 0.4 | 1.9 ± 0.4 | - |
| Gender categorical Units: | | | |
| Female | 148 | 140 | 288 |
| Male | 149 | 163 | 312 |

Subject analysis sets

| | |
|--|--------------------------|
| Subject analysis set title | HibCY Group (Epoch 001) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The First three doses Total Vaccinated cohort (post 3rd dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13® or Rotarix® and those who had the vaccine administration documented. | |
| Subject analysis set title | PedHIB Group (Epoch 001) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The First three doses Total Vaccinated cohort (post 3rd dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13® or Rotarix® and those who had the vaccine administration documented. | |
| Subject analysis set title | HibCY Group (Epoch 002) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The Fourth dose Total Vaccinated cohort (post 4th dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13®, Rotarix®, PedvaxHIB® or Havrix® and those who had the vaccine administration documented. | |

| | |
|----------------------------|--------------------------|
| Subject analysis set title | PedHIB Group (Epoch 002) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Fourth dose Total Vaccinated cohort (post 4th dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13® , Rotarix®, PedvaxHIB® or Havrix® and those who had the vaccine administration documented.

| Reporting group values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | HibCY Group (Epoch 002) |
|------------------------------------|-------------------------|--------------------------|-------------------------|
| Number of subjects | 297 | 303 | 248 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------------|--------------|--------------|
| Age continuous Units: weeks arithmetic mean standard deviation | 1.8 ± 0.4 | 1.9 ± 0.4 | 1.8 ± 0.4 |
| Gender categorical Units: | | | |
| Female | 148 | 140 | 124 |
| Male | 149 | 163 | 124 |

| Reporting group values | PedHIB Group (Epoch 002) | | |
|------------------------------------|--------------------------|--|--|
| Number of subjects | 251 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------------|--|--|
| Age continuous Units: weeks arithmetic mean standard deviation | 1.8 ± 0.4 | | |
| Gender categorical Units: | | | |
| Female | 115 | | |
| Male | 136 | | |

End points

End points reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | HibCY Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 4 doses of Hib-MenCY-TT (MenHibrix®) vaccine at Day 0, Month 2, Month 4 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| | |
|-----------------------|--------------|
| Reporting group title | PedHIB Group |
|-----------------------|--------------|

Reporting group description:

Subjects received 3 doses of PedvaxHIB® vaccine at Day 0, Month 2 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | HibCY Group (Epoch 001) |
|----------------------------|-------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

The First three doses Total Vaccinated cohort (post 3rd dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13® or Rotarix® and those who had the vaccine administration documented.

| | |
|----------------------------|--------------------------|
| Subject analysis set title | PedHIB Group (Epoch 001) |
|----------------------------|--------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

The First three doses Total Vaccinated cohort (post 3rd dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13® or Rotarix® and those who had the vaccine administration documented.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | HibCY Group (Epoch 002) |
|----------------------------|-------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

The Fourth dose Total Vaccinated cohort (post 4th dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13®, Rotarix®, PedvaxHIB® or Havrix® and those who had the vaccine administration documented.

| | |
|----------------------------|--------------------------|
| Subject analysis set title | PedHIB Group (Epoch 002) |
|----------------------------|--------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

The Fourth dose Total Vaccinated cohort (post 4th dose of Rotarix®) included all vaccinated subjects for whom data were available, those who received at least one dose of any of the study vaccines: Hib-MenCY-TT (MenHibrix®), Pediarix®, Prevnar 13®, Rotarix®, PedvaxHIB® or Havrix® and those who had the vaccine administration documented.

Primary: Number of Subjects With Anti-polyribosyl-ribitol Phosphate (Anti-PRP) Antibody Concentrations Equal to or Above Cut-off Values.

| | |
|-----------------|--|
| End point title | Number of Subjects With Anti-polyribosyl-ribitol Phosphate (Anti-PRP) Antibody Concentrations Equal to or Above Cut-off Values. ^[1] |
|-----------------|--|

End point description:

The cut-off values were defined as a concentration equal to or above 1.0 microgram per milliliter (µg/mL).

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

End point timeframe:

At 1 month post-dose 4 (HibCY Group) and 1 month post-dose 3 (PedHIB Group).

Notes:

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

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

| End point values | HibCY Group | PedHIB Group | | |
|-----------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | | |
| Units: Subjects | | | | |

Notes:

[2] - Results are not available yet.

[3] - Results are not available yet.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

Solicited local symptom assessed was pain. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 pain = Cried when limb was moved/spontaneously painful. 99999 = placeholder value for group(s) with results not being applicable/missing.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|---|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Pain; Dose 1 (Total) [N= 285, 291] | 155 | 189 | | |
| Grade 3 Pain; Dose 1 (Total) [N= 285, 291] | 13 | 35 | | |
| Any Pain; Dose 1(Hib-MenCY-TT/ PedHIB) [N=285,291] | 126 | 178 | | |
| Grade 3 Pain;Dose 1(Hib-MenCY-TT/PedHIB)[N=285,291] | 8 | 30 | | |
| Any Pain; Dose 1 (DTPa-HBV-IPV) [N= 285, 291] | 144 | 167 | | |
| Grade 3 Pain; Dose 1 (DTPa-HBV-IPV) [N= 285, 291] | 11 | 30 | | |
| Any Pain; Dose 1 (Prev13) [N= 285, 291] | 132 | 171 | | |
| Grade 3 Pain; Dose 1 (Prev13) [N= 285, 291] | 13 | 28 | | |
| Any Pain; Dose 2 (Total) [N= 272, 278] | 142 | 174 | | |
| Grade 3 Pain; Dose 2 (Total) [N= 272, 278] | 12 | 24 | | |

| | | | | |
|---|-----|-------|--|--|
| Any Pain; Dose 2(Hib-MenCY-TT/ PedHIB)[N=272, 291] | 124 | 158 | | |
| Grade 3 Pain;Dose 2(Hib-MenCY- TT/PedHIB)[N=272,291] | 8 | 20 | | |
| Any Pain; Dose 2 (DTPa-HBV-IPV) [N= 272, 278] | 123 | 155 | | |
| Grade 3 Pain; Dose 2 (DTPa-HBV-IPV) [N=272, 278] | 11 | 22 | | |
| Any Pain; Dose 2 (Prev13) [N= 272, 277] | 121 | 155 | | |
| Grade 3 Pain; Dose 2 (Prev13) [N= 272, 277] | 9 | 21 | | |
| Any Pain; Dose 3 (Total) [N= 262, 264] | 124 | 141 | | |
| Grade 3 Pain; Dose 3 (Total) [N= 262, 264] | 12 | 11 | | |
| Any Pain; Dose 3 (Hib-MenCY-TT/ PedHIB) [N=260,NA] | 101 | 99999 | | |
| Grade 3 Pain;Dose 3(Hib-MenCY- TT/PedHIB)[N=260,NA] | 8 | 99999 | | |
| Any Pain; Dose 3 (DTPa-HBV-IPV) [N= 262, 264] | 112 | 134 | | |
| Grade 3 Pain; Dose 3 (DTPa-HBV-IPV) [N= 262, 264] | 11 | 10 | | |
| Any Pain; Dose 3 (Prev13) [N= 262, 264] | 104 | 126 | | |
| Grade 3 Pain; Dose 3 (Prev13) [N= 262, 264] | 11 | 8 | | |
| Any Pain; Across Doses (Total) [N= 286, 295] | 209 | 230 | | |
| Grade 3 Pain; Across Doses (Total) [N= 286, 295] | 28 | 54 | | |
| Any Pain; Across(Hib-MenCY- TT/PedHIB) [N=286,295] | 186 | 209 | | |
| Grade3Pain; Across(Hib-MenCY- TT/PedHIB)[N=286,295] | 20 | 43 | | |
| Any Pain; Across Doses (DTPa-HBV-IPV) [N= 286,295] | 193 | 212 | | |
| Grade 3 Pain;Across Doses(DTPa-HBV- IPV)[N=286,295] | 26 | 48 | | |
| Any Pain; Across Doses (Prev13) [N= 286, 295] | 188 | 217 | | |
| Grade 3 Pain; Across Doses (Prev13) [N= 286, 295] | 27 | 46 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

Solicited local symptom assessed was redness. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 redness = redness greater than 30 millimeters (mm) i.e. > 30mm. 99999 = placeholder value for group(s) with results not being applicable/missing.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|---|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Redness; Dose 1 (Total) [N= 285, 291] | 92 | 117 | | |
| Grade 3 Redness; Dose 1 (Total) [N= 285, 291] | 2 | 2 | | |
| Any Redness;Dose 1(Hib-MenCY-TT/PedHIB)[N=285,291] | 60 | 103 | | |
| Grade3Redness;Dose1(Hib-MenCY-TT/PedHIB)[N=285,291] | 2 | 1 | | |
| Any Redness; Dose 1 (DTPa-HBV-IPV) [N= 285, 291] | 77 | 73 | | |
| Grade 3 Redness; Dose 1(DTPa-HBV-IPV)[N= 285, 291] | 0 | 0 | | |
| Any Redness; Dose 1 (Prev13) [N= 285, 291] | 67 | 71 | | |
| Grade 3 Rednessn; Dose 1 (Prev13) [N= 285, 291] | 0 | 1 | | |
| Any Redness; Dose 2 (Total) [N= 272, 278] | 108 | 145 | | |
| Grade 3 Redness; Dose 2 (Total) [N= 272, 278] | 0 | 1 | | |
| Any Redness;Dose 2(Hib-MenCY-TT/PedHIB)[N=272,291] | 82 | 115 | | |
| Grade3Redness;Dose2(Hib-MenCY-TT/PedHIB)[N=272,291] | 0 | 0 | | |
| Any Redness; Dose 2 (DTPa-HBV-IPV) [N= 272, 278] | 92 | 120 | | |
| Grade 3 Rednes; Dose 2 (DTPa-HBV-IPV) [N=272, 278] | 0 | 1 | | |
| Any Redness; Dose 2 (Prev13) [N= 272, 277] | 83 | 114 | | |
| Grade 3 Redness; Dose 2 (Prev13) [N= 272, 277] | 0 | 1 | | |
| Any Redness; Dose 3 (Total) [N= 262, 264] | 116 | 145 | | |
| Grade 3 Redness; Dose 3 (Total) [N= 262, 264] | 0 | 2 | | |
| Any Redness;Dose 3(Hib-MenCY-TT/PedHIB) [N=260,NA] | 82 | 99999 | | |
| Grade3Redness;Dose 3(Hib-MenCY-TT/PedHIB)[N=260,NA] | 0 | 99999 | | |
| Any Redness; Dose 3 (DTPa-HBV-IPV) [N= 262, 264] | 100 | 133 | | |
| Grade 3 Redness;Dose 3(DTPa-HBV-IPV) [N= 262, 264] | 0 | 0 | | |
| Any Redness; Dose 3 (Prev13) [N= 262, 264] | 95 | 121 | | |
| Grade 3 Redness; Dose 3 (Prev13) [N= 262, 264] | 0 | 2 | | |

| | | | | |
|---|-----|-----|--|--|
| Any Redness; Across Doses (Total) [N= 286, 295] | 165 | 198 | | |
| Grade 3 Redness; Across Doses (Total) [N= 286, 295] | 2 | 5 | | |
| Any Redness; Across (Hib-MenCY-TT/PedHIB) [N=286,295] | 125 | 149 | | |
| Grade 3 Redness; Across (Hib-MenCY-TT/PedHIB) N=286,295 | 2 | 1 | | |
| Any Redness; Across Doses (DTPa-HBV-IPV) [N= 286,295] | 148 | 181 | | |
| Grade 3 Redness; Across Doses (DTPa-HBV-IPV) N=286,295 | 0 | 1 | | |
| Any Redness; Across Doses (Prev13) [N= 286, 295] | 137 | 169 | | |
| Grade 3 Redness; Across Doses (Prev13) [N= 286, 295] | 0 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

Solicited local symptom assessed was swelling. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 swelling = swelling greater than 30 millimeters (mm) i.e. > 30mm. 99999 = placeholder value for group(s) with results not being applicable/missing.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall.

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|--|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Swelling; Dose 1 (Total) [N= 285, 291] | 70 | 79 | | |
| Grade 3 Swelling; Dose 1 (Total) [N= 285, 291] | 2 | 4 | | |
| Any Swelling; Dose 1 (Hib-MenCY-TT/PedHIB) [N=285,291] | 32 | 64 | | |
| Grade 3 Swelling; Dose 1 (Hib-MenCY-TT/PedHIB) N=285,291 | 1 | 3 | | |
| Any Swelling; Dose 1 (DTPa-HBV-IPV) [N= 285, 291] | 53 | 47 | | |
| Grade 3 Swelling; Dose 1 (DTPa-HBV-IPV) [N= 285,291] | 2 | 1 | | |
| Any Swelling; Dose 1 (Prev13) [N= 285, 291] | 42 | 47 | | |

| | | | | |
|---|-----|-------|--|--|
| Grade 3 Swelling; Dose 1 (Prev13) [N= 285, 291] | 1 | 0 | | |
| Any Swelling; Dose 2 (Total) [N= 272, 278] | 77 | 118 | | |
| Grade 3 Swelling; Dose 2 (Total) [N= 272, 278] | 1 | 2 | | |
| Any Swelling;Dose2(Hib-MenCY-TT/PedHIB)[N=272,291] | 50 | 85 | | |
| Grade3Swelling;Dose2(Hib-MenCY-TT/PedHIB)N=272,291 | 1 | 1 | | |
| Any Swelling; Dose 2 (DTPa-HBV-IPV) [N= 272, 278] | 60 | 101 | | |
| Grade 3 Swelling;Dose 2(DTPa-HBV-IPV) [N=272, 278] | 1 | 1 | | |
| Any Swelling; Dose 2 (Prev13) [N= 272, 277] | 61 | 80 | | |
| Grade 3 Swelling; Dose 2 (Prev13) [N= 272, 277] | 1 | 1 | | |
| Any Swelling; Dose 3 (Total) [N= 262, 264] | 92 | 115 | | |
| Grade 3 Swelling; Dose 3 (Total) [N= 262, 264] | 1 | 1 | | |
| Any Swelling;Dose3(Hib-MenCY-TT/PedHIB) [N=260,NA] | 50 | 99999 | | |
| Grade3Swelling;Dose3(Hib-MenCY-TT/PedHIB)[N=260,NA] | 0 | 99999 | | |
| Any Swelling; Dose 3 (DTPa-HBV-IPV) [N= 262, 264] | 77 | 100 | | |
| Grade 3 Swelling;Dose3(DTPa-HBV-IPV) [N= 262, 264] | 1 | 0 | | |
| Any Swelling; Dose 3 (Prev13) [N= 262, 264] | 64 | 83 | | |
| Grade 3 Swelling; Dose 3 (Prev13) [N= 262, 264] | 1 | 1 | | |
| Any Swelling; Across Doses (Total) [N= 286, 295] | 128 | 169 | | |
| Grade 3 Swelling;Across Doses(Total) [N= 286, 295] | 2 | 7 | | |
| AnySwelling;Across(Hib-MenCY-TT/PedHIB)[N=286,295] | 81 | 112 | | |
| Grade3Swelling;Across(Hib-MenCY-TTPedHIB)N=286,295 | 1 | 4 | | |
| Any Swelling;Across Doses(DTPa-HBV-IPV)[N=286,295] | 110 | 147 | | |
| Grade 3Swelling;AcrossDoses(DTPa-HBV-IPV)N=286,295 | 2 | 2 | | |
| Any Swelling; Across Doses (Prev13) [N= 286, 295] | 101 | 130 | | |
| Grade 3 Swelling;Across Doses(Prev13)[N= 286, 295] | 2 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events |
|-----------------|---|

End point description:

Solicited general symptom assessed was fever. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 fever = temperature greater than (>) 40.0 °C. Related fever= symptom assessed by the investigator as causally related to study vaccination.

End point type Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|---|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Fever; Dose 1 [N= 285, 291] | 34 | 69 | | |
| Grade 3 Fever; Dose 1 [N= 285, 291] | 0 | 0 | | |
| Related Fever; Dose 1 [N= 285, 291] | 32 | 58 | | |
| Any Fever; Dose 2 [N= 273, 279] | 57 | 85 | | |
| Grade 3 Fever; Dose 2 [N= 273, 279] | 0 | 1 | | |
| Related Fever; Dose 2 [N= 273, 279] | 53 | 81 | | |
| Any Fever; Dose 3 [N= 262, 265] | 44 | 47 | | |
| Grade 3 Fever; Dose 3 [N= 262, 265] | 1 | 1 | | |
| Related Fever; Dose 3 [N= 262, 265] | 43 | 44 | | |
| Any Fever; Across Doses [N= 286, 295] | 100 | 137 | | |
| Grade 3 Fever; Across Doses [N= 286, 295] | 1 | 2 | | |
| Related Fever; Across Doses [N= 286, 295] | 94 | 129 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 001]

End point title Number of subjects reporting solicited general adverse events (AEs) [Epoch 001]

End point description:

Solicited general symptom assessed was drowsiness. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Drowsiness = prevented normal activity. Related = symptom assessed by the investigator as causally related to vaccination.

End point type Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall.

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Drowsiness; Dose 1 [N= 285, 291] | 185 | 204 | | |
| Grade 3 Drowsiness; Dose 1 (Total) [N= 285, 291] | 13 | 17 | | |
| Related Drowsiness; Dose 1 [N= 285, 291] | 178 | 200 | | |
| Any Drowsiness; Dose 2 [N= 273, 279] | 148 | 181 | | |
| Grade 3 Drowsiness; Dose 2 [N= 273, 279] | 8 | 16 | | |
| Related Drowsiness; Dose 2 [N= 273, 279] | 141 | 177 | | |
| Any Drowsiness; Dose 3 [N= 262, 265] | 128 | 139 | | |
| Grade 3 Drowsiness; Dose 3 [N= 262, 265] | 7 | 12 | | |
| Related Drowsiness; Dose 3 [N= 262, 265] | 122 | 135 | | |
| Any Drowsiness; Across Doses [N= 286, 295] | 226 | 248 | | |
| Grade 3 Drowsiness; Across Doses [N= 286, 295] | 23 | 32 | | |
| Related Drowsiness; Across Doses [N= 286, 295] | 220 | 245 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

Solicited general symptom assessed was irritability. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Irritability = crying that could not be comforted/prevented normal activity. Related = symptom assessed by the investigator as causally related to vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall.

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any Irritability; Dose 1 [N= 285, 291] | 203 | 238 | | |
| Grade 3 Irritability; Dose 1 [N= 285, 291] | 10 | 34 | | |
| Related Irritability; Dose 1 [N= 285, 291] | 196 | 231 | | |
| Any Irritability; Dose 2 [N= 273, 279] | 191 | 232 | | |
| Grade 3 Irritability; Dose 2 [N= 273, 279] | 22 | 33 | | |
| Related Irritability; Dose 2 [N= 273, 279] | 183 | 225 | | |
| Any Irritability; Dose 3 [N= 262, 265] | 173 | 184 | | |
| Grade 3 Irritability; Dose 3 [N= 262, 265] | 16 | 20 | | |
| Related Irritability; Dose 3 [N= 262, 265] | 166 | 181 | | |
| Any Irritability; Across Doses [N= 286, 295] | 260 | 280 | | |
| Grade 3 Irritability; Across Doses [N= 286, 295] | 40 | 66 | | |
| Related Irritability; Across Doses [N= 286, 295] | 253 | 275 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

Solicited general symptom assessed was loss of appetite. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Loss of appetite = did not eat at all. Related = symptom assessed by the investigator as causally related to vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and overall.

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 286 | 295 | | |
| Units: Subjects | | | | |
| Any loss of appetite; Dose 1 [N= 285, 291] | 90 | 123 | | |
| Grade 3 loss of appetite; Dose 1 [N= 285, 291] | 1 | 2 | | |

| | | | | |
|--|-----|-----|--|--|
| Related loss of appetite; Dose 1 [N= 285, 291] | 85 | 115 | | |
| Any loss of appetite; Dose 2 [N= 273, 279] | 81 | 88 | | |
| Grade 3 loss of appetite; Dose 2 [N= 273, 279] | 3 | 1 | | |
| Related loss of appetite; Dose 2 [N= 273, 279] | 77 | 87 | | |
| Any loss of appetite; Dose 3 [N= 262, 265] | 78 | 76 | | |
| Grade 3 loss of appetite; Dose 3 [N= 262, 265] | 0 | 3 | | |
| Related loss of appetite; Dose 3 [N= 262, 265] | 75 | 71 | | |
| Any loss of appetite; Across Doses [N= 286, 295] | 156 | 176 | | |
| Grade 3 loss of appetite; Across Doses [N= 286, 295] | 4 | 6 | | |
| Related loss of appetite; Across Doses [N= 286, 295] | 151 | 171 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 002]

| | |
|---|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 002] |
| End point description: | |
| Solicited local symptom assessed was pain. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 pain = Cried when limb was moved/spontaneously painful. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 4-day (Days 0-3 post-dose 4 vaccination period | |

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|--|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 | 242 | | |
| Units: Subjects | | | | |
| Any Pain; Total [N= 241, 242] | 128 | 144 | | |
| Grade 3 Pain; Total [N= 241, 242] | 6 | 14 | | |
| Any Pain; Hib-MenCY-TT/ PedHIB [N= 241, 242] | 108 | 121 | | |
| Grade 3 Pain; Hib-MenCY-TT/ PedHIB [N= 241, 242] | 3 | 11 | | |
| Any Pain; DTPa-HBV-IPV [N= 241, 242] | 102 | 136 | | |
| Grade 3 Pain; DTPa-HBV-IPV [N= 241, 242] | 3 | 13 | | |
| Any Pain; Prev13 [N= 241, 242] | 100 | 113 | | |
| Grade 3 Pain; Prev13 [N= 241, 242] | 5 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited local symptom assessed was redness. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 redness = redness greater than 30 millimeters (mm) i.e. > 30mm.

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

End point timeframe:

During the 4-day (Days 0-3) post-dose 4 vaccination period.

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|---|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 | 242 | | |
| Units: Subjects | | | | |
| Any Redness; Total [N= 241, 242] | 126 | 132 | | |
| Grade 3 Redness; Total [N= 241, 242] | 6 | 3 | | |
| Any Redness; Hib-MenCY-TT/ PedHIB [N= 241, 242] | 93 | 106 | | |
| Grade 3 Redness; Hib-MenCY-TT/ PedHIB [N= 241, 242] | 0 | 1 | | |
| Any Redness; DTPa-HBV-IPV [N= 241, 242] | 93 | 123 | | |
| Grade 3 Redness; DTPa-HBV-IPV [N= 241, 242] | 3 | 2 | | |
| Any Redness; Prev13 [N= 241, 242] | 99 | 108 | | |
| Grade 3 Redness; Prev13 [N= 241, 242] | 3 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited local adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited local symptom assessed was swelling. Any = Occurrence of the specified local symptom irrespective of intensity grade. Grade 3 swelling = swelling greater than 30 millimeters (mm) i.e. > 30mm.

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

End point timeframe:

During the 4-day (Days 0-3) post-dose 4 vaccination period.

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|---|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 241 | 242 | | |
| Units: Subjects | | | | |
| Any Swelling; Total [N= 241, 242] | 83 | 100 | | |
| Grade 3 Swelling; Total [N= 241, 242] | 5 | 3 | | |
| Any Swelling; Hib-MenCY-TT/ PedHIB [N= 241, 242] | 61 | 63 | | |
| Grade 3 Swelling;Hib-MenCY-TT/PedHIB [N= 241, 242] | 0 | 0 | | |
| Any Swelling; DTPa-HBV-IPV [N= 241, 242] | 55 | 83 | | |
| Grade 3 Swelling; DTPa-HBV-IPV [N= 241, 242] | 2 | 1 | | |
| Any Swelling; Prev13 [N= 241, 242] | 63 | 67 | | |
| Grade 3 Swelling; Prev13 [N= 241, 242] | 3 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited general symptom assessed was fever. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 fever = temperature greater than (>) 40.0 °C. Related fever= symptom assessed by the investigator as causally related to study vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-dose 4 vaccination period.

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|-----------------------------|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 242 | 241 | | |
| Units: Subjects | | | | |
| Any Fever [N= 242, 241] | 23 | 26 | | |
| Grade 3 Fever [N= 242, 241] | 0 | 0 | | |
| Related Fever [N= 242, 241] | 20 | 25 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited general symptom assessed was drowsiness. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Drowsiness = prevented normal activity. Related = symptom assessed by the investigator as causally related to vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-dose 4 vaccination period.

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|----------------------------------|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 242 | 241 | | |
| Units: Subjects | | | | |
| Any Drowsiness [N= 242, 241] | 106 | 117 | | |
| Grade 3 Drowsiness [N= 242, 241] | 7 | 6 | | |
| Related Drowsiness [N= 242, 241] | 105 | 114 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited general symptom assessed was irritability. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Irritability = crying that could not be comforted/prevented normal activity. Related = symptom assessed by the investigator as causally

related to vaccination.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the 4-day (Days 0-3) post-dose 4 vaccination period. | |

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|------------------------------------|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 242 | 241 | | |
| Units: Subjects | | | | |
| Any Irritability [N= 242, 241] | 159 | 179 | | |
| Grade 3 Irritability [N= 242, 241] | 19 | 21 | | |
| Related Irritability [N= 242, 241] | 156 | 173 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting solicited general adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

Solicited general symptom assessed was loss of appetite. Any = occurrence of the specified general symptom irrespective of intensity grade and relationship to vaccination. Grade 3 Loss of appetite = did not eat at all. Related = symptom assessed by the investigator as causally related to vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-dose 4 vaccination period.

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 242 | 241 | | |
| Units: Subjects | | | | |
| Any Loss of Appetite [N= 242, 241] | 80 | 96 | | |
| Grade 3 Loss of Appetite [N= 242, 241] | 2 | 2 | | |
| Related Loss of Appetite [N= 242, 241] | 80 | 93 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AEs) [Epoch 001]

| | |
|-----------------|---|
| End point title | Number of subjects reporting unsolicited adverse events (AEs) [Epoch 001] |
|-----------------|---|

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

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

End point timeframe:

During post Dose 1 (Day 0) and before Visit 5 (Months 10-13).

| End point values | HibCY Group (Epoch 001) | PedHIB Group (Epoch 001) | | |
|-----------------------------|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 297 | 303 | | |
| Units: Subjects | | | | |
| Any unsolicited AE(s) | 180 | 171 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AEs) [Epoch 002]

| | |
|-----------------|---|
| End point title | Number of subjects reporting unsolicited adverse events (AEs) [Epoch 002] |
|-----------------|---|

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

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

End point timeframe:

Post-dose 4 (Month 10-13)

| End point values | HibCY Group (Epoch 002) | PedHIB Group (Epoch 002) | | |
|-----------------------------|-------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 248 | 251 | | |
| Units: Subjects | | | | |
| Any unsolicited AE(s) | 99 | 105 | | |

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 result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

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

End point timeframe:

During the entire study period (Day 0 to Months 17-20)

| End point values | HibCY Group | PedHIB Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 297 | 303 | | |
| Units: Subjects | | | | |
| Any SAE(s) | 8 | 11 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events=entire study period (Day 0 to Months 17-20),Unsolicited AEs=post Dose 1 (Day 0) & before Visit 5 (Months 10-13) & post Dose 4(Months 11-14), solicited local & general symptoms= during the 4-day (Days 0-3) post-vaccination period.

Adverse event reporting additional description:

The analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen/sheet completed). SAEs are reported by the reporting groups (i.e., HibCY Group and PedHIB Group), while frequent AEs are reported by the study epochs (i.e., Epoch 001 and 002)

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | PedHIB Group |
|-----------------------|--------------|

Reporting group description:

Subjects received 3 doses of PedvaxHIB® vaccine at Day 0, Month 2 and Month 10-13, 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| | |
|-----------------------|-------------|
| Reporting group title | HibCY Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 4 doses of Hib-MenCY-TT (MenHibrix®) vaccine at Day 0, Month 2, Month 4 and Month 10-13 , 3 doses of Pediarix® vaccine at Day 0, Month 2 and Month 4, 2 doses of Rotarix® vaccine at Day 0 and Month 2, 4 doses of Prevnar 13® vaccine at Day 0 and Month 2, Month 4 and Month 10-13 and 2 doses of Havrix® vaccine at Month 10-13 and Month 16-19.

| Serious adverse events | PedHIB Group | HibCY Group | |
|---|------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 303 (3.63%) | 8 / 297 (2.69%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Vascular disorders | | | |
| Kawasaki's disease | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (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 | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Histiocytosis haematophagic | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (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 | | | |
| Hypothermia | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (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 | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Apparent life threatening event | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 303 (0.33%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 2 / 297 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 2 / 303 (0.66%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 303 (0.00%) | 1 / 297 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypernatraemia | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ketoacidosis | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 303 (0.33%) | 0 / 297 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | PedHIB Group | HibCY Group | |
|---|---------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 280 / 303 (92.41%) | 261 / 297 (87.88%) | |
| Nervous system disorders | | | |
| Somnolence [Epoch 001] | | | |
| subjects affected / exposed | 248 / 303 (81.85%) | 226 / 297 (76.09%) | |
| occurrences (all) | 524 | 462 | |
| Somnolence [Epoch 002] | | | |
| subjects affected / exposed | 117 / 303 (38.61%) | 106 / 297 (35.69%) | |
| occurrences (all) | 117 | 107 | |
| General disorders and administration site conditions | | | |
| Pain [Epoch 001] | | | |
| subjects affected / exposed | 230 / 303 (75.91%) | 209 / 297 (70.37%) | |
| occurrences (all) | 504 | 422 | |
| Pyrexia [Epoch 001] | | | |

| | | | |
|---|--------------------|--------------------|--|
| subjects affected / exposed | 145 / 303 (47.85%) | 110 / 297 (37.04%) | |
| occurrences (all) | 216 | 151 | |
| Swelling [Epoch 001] | | | |
| subjects affected / exposed | 169 / 303 (55.78%) | 128 / 297 (43.10%) | |
| occurrences (all) | 312 | 239 | |
| Pain [Epoch 002] | | | |
| subjects affected / exposed | 144 / 303 (47.52%) | 128 / 297 (43.10%) | |
| occurrences (all) | 144 | 128 | |
| Pyrexia [Epoch 002] | | | |
| subjects affected / exposed | 32 / 303 (10.56%) | 38 / 297 (12.79%) | |
| occurrences (all) | 32 | 38 | |
| Swelling [Epoch 002] | | | |
| subjects affected / exposed | 100 / 303 (33.00%) | 83 / 297 (27.95%) | |
| occurrences (all) | 100 | 83 | |
| Gastrointestinal disorders | | | |
| Diarrhoea [Epoch 001] | | | |
| subjects affected / exposed | 14 / 303 (4.62%) | 18 / 297 (6.06%) | |
| occurrences (all) | 15 | 22 | |
| Vomiting [Epoch 001] | | | |
| subjects affected / exposed | 15 / 303 (4.95%) | 13 / 297 (4.38%) | |
| occurrences (all) | 16 | 13 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough [Epoch 001] | | | |
| subjects affected / exposed | 18 / 303 (5.94%) | 14 / 297 (4.71%) | |
| occurrences (all) | 18 | 17 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema [Epoch 001] | | | |
| subjects affected / exposed | 198 / 303 (65.35%) | 166 / 297 (55.89%) | |
| occurrences (all) | 407 | 317 | |
| Erythema [Epoch 002] | | | |
| subjects affected / exposed | 132 / 303 (43.56%) | 126 / 297 (42.42%) | |
| occurrences (all) | 132 | 126 | |
| Psychiatric disorders | | | |
| Irritability [Epoch 001] | | | |
| subjects affected / exposed | 280 / 303 (92.41%) | 261 / 297 (87.88%) | |
| occurrences (all) | 660 | 577 | |

| | | | |
|---|--|---|--|
| Irritability [Epoch 002] subjects affected / exposed occurrences (all) | 179 / 303 (59.08%) 179 | 159 / 297 (53.54%) 160 | |
| Infections and infestations Otitis media [Epoch 001] subjects affected / exposed occurrences (all) Upper respiratory tract infection [Epoch 001] subjects affected / exposed occurrences (all) Otitis media [Epoch 002] subjects affected / exposed occurrences (all) Upper respiratory tract infection [Epoch 002] subjects affected / exposed occurrences (all) | 25 / 303 (8.25%) 26 22 / 303 (7.26%) 23 21 / 303 (6.93%) 22 12 / 303 (3.96%) 12 | 17 / 297 (5.72%) 20 43 / 297 (14.48%) 50 23 / 297 (7.74%) 23 19 / 297 (6.40%) 20 | |
| Metabolism and nutrition disorders Decreased appetite [Epoch 001] subjects affected / exposed occurrences (all) Decreased appetite [Epoch 002] subjects affected / exposed occurrences (all) | 177 / 303 (58.42%) 288 96 / 303 (31.68%) 96 | 157 / 297 (52.86%) 251 80 / 297 (26.94%) 80 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 16 June 2014 | <p>In order to provide the opportunity for subjects in the control group to receive a meningococcal vaccine, which is not routinely administered in the US to this age group, the protocol has been amended to state that: "...a parent(s)/LAR(s) of a child in the PedvaxHIB control group will be offered the opportunity for their child to be vaccinated with a licensed meningococcal vaccine, which will be provided by the study sponsor, after study end as these subjects did not have the benefit of receiving any meningococcal vaccination during the study."</p> <p>Additionally,</p> <p>Distribution of a diary card for recording of medications/vaccinations post dose 2 of Havrix has been added.</p> <p>Treatment allocation is by component rather than dose.</p> <p>Text mentioning that subjects who do not continue in the booster phase will be contacted for safety information via a phone script at the ESFU timepoint has been added.</p> <p>The safety contact fax information has been updated.</p> <p>There have been a few changes in the contributing authors.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported