

**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
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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 Prevnar 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 Prevnar 13 compared to Rotarix co-administered with PedvaxHIB, Pediarix and Prevnar 13 in terms of Rotarix IgA GMCs
- 3 doses of Prevnar 13 co-administered with Hib-MenCY-TT, Rotarix and Pediarix compared to Prevnar 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 Prevnar 13 compared to Havrix when the 1st dose is co-administered with PedvaxHIB and Prevnar 13, at 12-15 months of age
- 4 doses of Prevnar 13 co-administered with Hib-MenCY-TT and Havrix compared to Prevnar 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
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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
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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
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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
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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
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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]
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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
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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]
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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
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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]
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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
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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		
Grade3Redness;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;AcrossDoses(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;Dose1(Hib-MenCY-TT/PedHIB)[N=285,291]	32	64		
Grade3Swelling;Dose1(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
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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]
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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
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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]
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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
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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]
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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
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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]
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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]
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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
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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]
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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]
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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
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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]
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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
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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)
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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
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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
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Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	PedHIB Group
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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
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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 occurrences (all)	145 / 303 (47.85%) 216	110 / 297 (37.04%) 151	
Swelling [Epoch 001] subjects affected / exposed occurrences (all)	169 / 303 (55.78%) 312	128 / 297 (43.10%) 239	
Pain [Epoch 002] subjects affected / exposed occurrences (all)	144 / 303 (47.52%) 144	128 / 297 (43.10%) 128	
Pyrexia [Epoch 002] subjects affected / exposed occurrences (all)	32 / 303 (10.56%) 32	38 / 297 (12.79%) 38	
Swelling [Epoch 002] subjects affected / exposed occurrences (all)	100 / 303 (33.00%) 100	83 / 297 (27.95%) 83	
Gastrointestinal disorders Diarrhoea [Epoch 001] subjects affected / exposed occurrences (all)	14 / 303 (4.62%) 15	18 / 297 (6.06%) 22	
Vomiting [Epoch 001] subjects affected / exposed occurrences (all)	15 / 303 (4.95%) 16	13 / 297 (4.38%) 13	
Respiratory, thoracic and mediastinal disorders Cough [Epoch 001] subjects affected / exposed occurrences (all)	18 / 303 (5.94%) 18	14 / 297 (4.71%) 17	
Skin and subcutaneous tissue disorders Erythema [Epoch 001] subjects affected / exposed occurrences (all)	198 / 303 (65.35%) 407	166 / 297 (55.89%) 317	
Erythema [Epoch 002] subjects affected / exposed occurrences (all)	132 / 303 (43.56%) 132	126 / 297 (42.42%) 126	
Psychiatric disorders Irritability [Epoch 001] subjects affected / exposed occurrences (all)	280 / 303 (92.41%) 660	261 / 297 (87.88%) 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)	25 / 303 (8.25%) 26	17 / 297 (5.72%) 20	
Upper respiratory tract infection [Epoch 001] subjects affected / exposed occurrences (all)	22 / 303 (7.26%) 23	43 / 297 (14.48%) 50	
Otitis media [Epoch 002] subjects affected / exposed occurrences (all)	21 / 303 (6.93%) 22	23 / 297 (7.74%) 23	
Upper respiratory tract infection [Epoch 002] subjects affected / exposed occurrences (all)	12 / 303 (3.96%) 12	19 / 297 (6.40%) 20	
Metabolism and nutrition disorders			
Decreased appetite [Epoch 001] subjects affected / exposed occurrences (all)	177 / 303 (58.42%) 288	157 / 297 (52.86%) 251	
Decreased appetite [Epoch 002] subjects affected / exposed occurrences (all)	96 / 303 (31.68%) 96	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	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." Additionally, Distribution of a diary card for recording of medications/vaccinations post dose 2 of Havrix has been added. Treatment allocation is by component rather than dose. 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. The safety contact fax information has been updated. There have been a few changes in the contributing authors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported