Clinical trial results:
A Phase III, randomized, multicenter study, double-blind for the immunogenicity and consistency evaluation of 3 lots of GSK Biologicals' Haemophilus influenzae type b (Hib) conjugate vaccine and single blind and controlled for the evaluation of safety and immunogenicity of GSK Biologicals' Hib vaccine 208108 compared to the monovalent Hib vaccine ActHIB and open for comparison with the combined DTPa-IPV-Hib vaccine Pentacel when administered to healthy infants at 2, 4, 6 and 15-18 months of age with recommended co-administrations at separate sites.

Summary

EudraCT number	2013-004194-27
Trial protocol	Outside EU/EEA
Global end of trial date	17 July 2013

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	26 July 2015

Trial information

Trial identification

Sponsor protocol code	112957

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01000974
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	17 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Consistency of the immune response post-dose 3 to PRP of 3 lots of Hiberix.
Non-inferiority of Hiberix to ActHIB in terms of post-dose 3 anti-PRP antibody conc. >= 1.0 & 0.15 µg/mL.
Non-inferiority of Pediarix co-ad with Hiberix to Pediarix co-ad with ActHIB in terms of post 3 primary vac. doses of immune response to diphtheria, tetanus, PT, FHA, PRN & polio-1, 2, 3 and acceptability of polio response.
Non-inferiority of a 3-dose primary vac. Prevnar 13 co-ad with Hiberix vs Prevnar 13 co-ad with ActHIB of S.pneumoniae GMC(s).
To rule out a 10% decrease in seroresponse to PT, FHA & PRN in subjects receiving Pediarix co-ad with Hiberix, vs subjects receiving Pediarix co-ad with ActHIB.
Noninferiority of a booster dose of HIberix vs a booster dose of ActHIB in terms of anti-PRP conc. ≥1.0 µg/mL.

Protection of trial subjects:

The vaccine recipients were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2010
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: 4009
Worldwide total number of subjects	4009
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	4009
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: -

Pre-assignment

Screening details:

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

Pre-assignment period milestones

Number of subjects started	4009
Number of subjects completed	4003

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject number allocated, no vaccine administered: 6

Period 1

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

Blinding implementation details:

The study was double-blind for the 3 Test Hib lots, single blind for the Test Hib groups vs Control Hib Group and open for Test Hib groups vs DTPa-IPV/Hib Group,

Arms

Are arms mutually exclusive?	Yes
Arm title	Hiberix Group

Arm description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' Haemophilus influenzae type b vaccine (GSK 208108)
Investigational medicinal product code	
Other name	Hiberix®
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of 3 different manufacturing lots in primary study at 2, 4 and 6 months of age as intramuscular injection and one dose as booster vaccination.

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 in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose in the booster epoch at 15-18 months of age as intramuscular injection.	
Arm title	ActHIB Group
Arm description:	
Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.	
Arm type	Active comparator
Investigational medicinal product name	ActHIB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection and one dose as a booster vaccination.	
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 in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose in the booster epoch at 15-18 months of age as intramuscular injection.	
Arm title	Pentacel Group
Arm description:	
Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.	
Arm type	Active comparator
Investigational medicinal product name	Pentacel™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection and one dose as a booster vaccination.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Engerix™-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two or three doses in primary epoch at 2,(4) and 6 months of age as intramuscular injection.

Number of subjects in period 1[1]	Hiberix Group	ActHIB Group	Pentacel Group
Started	2963	520	520
Completed	2625	470	457
Not completed	338	50	63
Consent withdrawn by subject	109	17	21
Adverse event, non-fatal	14	2	2
Unspecified	4	9	12
Lost to follow-up	171	19	26
Protocol deviation	40	3	2

Notes:

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

Justification: Out if the 4009 subjects enrolled in the study, 6 were allocated subject numbers but were not administered any vaccine, hence only 4003 subjects actually started the study.

Period 2

Period 2 title	Booster Vaccination Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Hiberix Group

Arm description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' Haemophilus influenzae type b vaccine (GSK 208108)
Investigational medicinal product code	
Other name	Hiberix®
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
Three doses of 3 different manufacturing lots in primary study at 2, 4 and 6 months of age as intramuscular injection and one dose as booster vaccination.	
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 in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
One dose in the booster epoch at 15-18 months of age as intramuscular injection.	
Arm title	ActHIB Group
Arm description:	
Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.	
Arm type	Active comparator
Investigational medicinal product name	ActHIB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection and one dose as a booster vaccination.	
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 in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: One dose in the booster epoch at 15-18 months of age as intramuscular injection.	
Arm title	Pentacel Group
Arm description: Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.	
Arm type	Active comparator
Investigational medicinal product name	Pentacel™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection and one dose as a booster vaccination.	
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Three doses in primary epoch at 2, 4 and 6 months of age as intramuscular injection.	
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 oral doses in primary epoch at 2 and 4 months of age.	
Investigational medicinal product name	Engerix™-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two or three doses in primary epoch at 2,(4) and 6 months of age as intramuscular injection.

Number of subjects in period 2[2]	Hiberix Group	ActHIB Group	Pentacel Group
Started	2337	435	400
Completed	2270	423	386
Not completed	67	12	14
Consent withdrawn by subject	3	1	1
Unspecified	24	6	4
Lost to follow-up	40	5	7
Protocol deviation	-	-	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up study. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Baseline characteristics

Reporting groups	
Reporting group title	Hiberix Group
Reporting group description:	
Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.	
Reporting group title	ActHIB Group
Reporting group description:	
Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.	
Reporting group title	Pentacel Group
Reporting group description:	
Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.	

Reporting group values	Hiberix Group	ActHIB Group	Pentacel Group
Number of subjects	2963	520	520
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: weeks			
arithmetic mean	8.6	8.6	8.7
standard deviation	± 1.08	± 1.13	± 1.12
Gender categorical Units: Subjects			
Female	1424	271	258
Male	1539	249	262

Reporting group values	Total		
Number of subjects	4003		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: weeks			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	1953		
Male	2050		

End points reporting groups

Reporting group title	Hiberix Group

Reporting group description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	ActHIB Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	Pentacel Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.

Reporting group title	Hiberix Group

Reporting group description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	ActHIB Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	Pentacel Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.

Subject analysis set title	Test-Hib A Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 3 doses of Test Hib vaccine lot A co-administered with 3 doses of DTPa-HBV-IPV and 13Pn vaccines at 2, 4 and 6 months of age and 2 doses of HRV vaccine at 2 and 4 months of age

Subject analysis set title	Test Hib B Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 3 doses of Test Hib vaccine lot B co-administered with 3 doses of DTPa-HBV-IPV and 13Pn vaccines at 2, 4 and 6 months of age and 2 doses of HRV vaccine at 2 and 4 months of age

Subject analysis set title	Test Hib C Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 3 doses of Test Hib vaccine lot C co-administered with 3 doses of DTPa-HBV-IPV and 13Pn vaccines at 2, 4 and 6 months of age and 2 doses of HRV vaccine at 2 and 4 months of age

Primary: Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations greater than or equal to (≥) 0.15 microgram per milliliter (µg/mL) and ≥ 1.0 µg/mL.

End point title	Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations greater than or equal to (≥) 0.15 microgram per milliliter (µg/mL) and ≥ 1.0 µg/mL.

End point description:

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1590	274	253	
Units: Subjects				
Anti-PRP ≥ 0.15 µg/mL	1536	265	234	
Anti-PRP ≥ 1.0 µg/mL	1291	246	198	

Statistical analyses

Statistical analysis title	Non-inferiority Anti-PRP concentration ≥ 1.0 µg/mL

Statistical analysis description:

To demonstrate the non-inferiority of Test Hib to Control Hib, each co-administered with DTPa-HBV-IPV, 13Pn and HRV vaccines, following 3 primary vaccine doses in terms of anti-PRP antibody concentration ≥ 1.0 µg/mL.

Comparison groups	ActHIB Group v Hiberix Group
Number of subjects included in analysis	1864
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage
Point estimate	-8.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.28
upper limit	-4.07

Notes:

[1] - Criterion for non-inferiority (1 month after the last dose of primary vaccination): Lower limit (LL) of the standardized asymptotic 95% CI for the difference (pooled Sub-cohorts Test Hib A-PRP, Test Hib B-PRP and Test Hib C-PRP minus Sub-cohort Control Hib) in the percentage of subjects with anti-PRP concentrations ≥ 1.0 µg/mL was ≥ -10% (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-PRP concentration ≥ 0.15 µg/m

Statistical analysis description:

To demonstrate the non-inferiority of Test Hib to Control Hib, each co-administered with DTPa-HBV-IPV, 13Pn and HRV vaccines, following 3 primary vaccine doses in terms of anti-PRP antibody concentrations ≥ 0.15 µg/mL.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1864
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentage
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.98
upper limit	2.82

Notes:

[2] - Criterion for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 95% CI for the difference (pooled Sub-cohorts Test Hib A-PRP, Test Hib B-PRP and Test Hib C-PRP minus Sub-cohort Control Hib) in the percentage of subjects with anti-PRP concentrations ≥ 0.15 µg/mL was ≥ -5% (clinical limit for non-inferiority).

Primary: Number of subjects with anti-Protein-D (anti-D) and anti-Protein-T (anti-T) antibody concentrations ≥ 0.1 International Units per milliliter (IU/mL).

End point title	Number of subjects with anti-Protein-D (anti-D) and anti-Protein-T (anti-T) antibody concentrations ≥ 0.1 International Units per milliliter (IU/mL).

End point description:

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	393	274	250	
Units: Subjects				
Anti-D [N=393,273,250]	393	273	249	
Anti-T [N=393,274,250]	393	274	249	

Statistical analyses

Statistical analysis title	Non-inferiority Anti-D antibody concentrations

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to diphtheria (Anti-D).

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	1.81

Notes:

[3] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 97.5% CIs on the differences (Subset Test Hib Co-Ad minus Sub-cohort Control Hib) in the percentages of subjects with seroprotective concentrations (≥ 0.1 IU/mL) of anti-diphtheria antibodies was ≥ -10% (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-T antibody concentrations

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to tetanus (Anti-T).

Comparison groups	ActHIB Group v Hiberix Group
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	1.8

Notes:

[4] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 97.5% CIs on the differences (Subset Test Hib Co-Ad minus Sub-cohort Control Hib) in the percentages of subjects with seroprotective concentrations (≥ 0.1 IU/mL) of anti-tetanus antibodies was ≥ -10% (clinical limit for non-inferiority).

Primary: Anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations.

End point title	Anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations.[5]

End point description:

Antibody concentrations were given as Geometric Mean Concentrations (GMCs) expressed in micrograms per milliliter (µg/mL).

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

Notes:

[5] - 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1590	274	253	
Units: µg/mL				
geometric mean (confidence interval 95%)	5.193 (4.765 to 5.658)	6.743 (5.593 to 8.129)	3.64 (2.891 to 4.583)	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous hemagglutinin (anti-FHA) antibody concentrations.

End point title	Anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous hemagglutinin (anti-FHA) antibody concentrations.

End point description:

Antibody concentrations were given as geometric mean concentrations (GMCs) expressed as enzyme-linked immuno-sorbent assay (ELISA) units per milliliter i.e. EL.U/mL.

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	792	275	251	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=792,275,251]	73.2 (69.8 to 76.6)	71.9 (66.6 to 77.6)	41.9 (38.4 to 45.8)	
Anti-PRN [N=789,275,250]	111.6 (104.5 to 119.2)	93.5 (83.7 to 104.4)	51.9 (45.4 to 59.3)	
Anti-FHA [N=791,275,249]	321.8 (307 to 337.3)	295.8 (276 to 317)	174.8 (160 to 191)	

Statistical analyses

Statistical analysis title	Non-inferiority GMC ratio anti-PT

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to pertussis toxoid [PT].

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	1.017
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.918
upper limit	1.127

Notes:

[6] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the 97.5% CIs on the GMC ratios (Subset Test Hib Co-Ad divided by Sub-cohort Control Hib) for antibodies to the pertussis antigen PT was ≥ 0.67 (clinical limit for non-inferiority)

Statistical analysis title	Non-inferiority GMC ratio anti-FHA

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to filamentous hemagglutinin [FHA].

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	GMC ratio
Point estimate	1.088
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.983
upper limit	1.204

Notes:

[7] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the 97.5% CIs on the GMC ratios (Subset Test Hib Co-Ad divided by Sub-cohort Control Hib) for antibodies to the pertussis antigen FHA was ≥ 0.67 (clinical limit for non-inferiority)

Statistical analysis title	Non-inferiority GMC ratio anti-PRN

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to pertactin [PRN].

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMC ratio
Point estimate	1.193
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.03
upper limit	1.382

Notes:

[8] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the 97.5% CIs on the GMC ratios (Subset Test Hib Co-Ad divided by Sub-cohort Control Hib) for antibodies to the pertussis antigen PRN was ≥ 0.67 (clinical limit for non-inferiority)

Primary: Anti-Streptococcus pneumoniae (S.pneumoniae) antibody concentrations.

End point title	Anti-Streptococcus pneumoniae (S.pneumoniae) antibody concentrations.

End point description:

Antibody concentrations against S.pneumoniae were given as geometric mean concentrations (GMCs) expressed as microgram per milliliter (µg/mL).

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	270	247	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-Pneumoniae 1[N = 384,268,245]	2.515 (2.318 to 2.729)	2.5 (2.278 to 2.745)	2.442 (2.19 to 2.722)	
Anti-Pneumoniae 3 [N = 382,269,245]	1.056 (0.976 to 1.142)	1.008 (0.933 to 1.089)	1.19 (1.066 to 1.329)	
Anti-Pneumoniae 4 [N = 389,268,247]	1.804 (1.684 to 1.932)	1.803 (1.662 to 1.957)	1.819 (1.645 to 2.011)	
Anti-Pneumoniae 5 [N = 379,266,246]	3.729 (3.409 to 4.079)	3.656 (3.308 to 4.04)	3.53 (3.128 to 3.984)	
Anti-Pneumoniae 6A [N = 381,267,244]	3.442 (3.177 to 3.729)	3.34 (3.032 to 3.679)	3.384 (3.046 to 3.76)	
Anti-Pneumoniae 6B [N = 383,267,245]	1.065 (0.95 to 1.196)	0.994 (0.86 to 1.148)	0.875 (0.757 to 1.013)	
Anti-Pneumoniae 7F [N = 386,269,246]	4.518 (4.192 to 4.87)	4.115 (3.777 to 4.484)	3.785 (3.412 to 4.199)	
Anti-Pneumoniae 9V [N = 386,270,246]	2.516 (2.305 to 2.746)	2.431 (2.204 to 2.681)	2.226 (1.976 to 2.507)	
Anti-Pneumoniae 14 [N = 384,267,244]	4.506 (4.105 to 4.946)	4.111 (3.672 to 4.602)	3.938 (3.472 to 4.466)	
Anti-Pneumoniae 18C [N = 380,267,244]	3.655 (3.351 to 3.986)	3.507 (3.196 to 3.848)	3.401 (3.033 to 3.814)	
Anti-Pneumoniae 19A [N = 384,266,245]	1.556 (1.433 to 1.689)	1.553 (1.391 to 1.735)	1.321 (1.175 to 1.486)	

Anti-Pneumoniae 19F [N = 384,268,245]	2.745 (2.552 to 2.952)	2.833 (2.613 to 3.072)	2.531 (2.315 to 2.766)	
Anti-Pneumoniae 23F [N = 384,268,245]	2.046 (1.846 to 2.267)	1.985 (1.765 to 2.232)	1.67 (1.444 to 1.931)	

Statistical analyses

Statistical analysis title	Non-inferiority Anti-Pneumoniae 1 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	1.006
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.873
upper limit	1.159

Notes:

[9] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 1 [anti-1] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 3 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMC ratio
Point estimate	1.048
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.921
upper limit	1.192

Notes:

[10] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 3 [anti-3] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 4 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and

DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	GMC ratio
Point estimate	1.001
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.886
upper limit	1.13

Notes:

[11] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 4 [anti-4] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 5 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	GMC ratio
Point estimate	1.02
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.874
upper limit	1.19

Notes:

[12] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 5 [anti-5] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 6A concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	GMC ratio
Point estimate	1.031
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.894
upper limit	1.188

Notes:

[13] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 6A [anti-6A] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 6B concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	GMC ratio
Point estimate	1.072
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.871
upper limit	1.32

Notes:

[14] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 6B [anti-6B] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 7F concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	GMC ratio
Point estimate	1.098
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.964
upper limit	1.251

Notes:

[15] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 7F [anti-7F] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 9V concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group

Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	GMC ratio
Point estimate	1.035
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.89
upper limit	1.204

Notes:

[16] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 9V [anti-9V] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 14 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	GMC ratio
Point estimate	1.096
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.929
upper limit	1.294

Notes:

[17] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 14 [anti-14] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 18C concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	GMC ratio
Point estimate	1.042
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.9
upper limit	1.207

Notes:

[18] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 18C [anti-18C] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 19A concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	GMC ratio
Point estimate	1.001
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.859
upper limit	1.167

Notes:

[19] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 19A [anti-19A] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 19F concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	GMC ratio
Point estimate	0.969
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.855
upper limit	1.098

Notes:

[20] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 19F [anti-19F] was ≥ 0.5 (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Pneumoniae 23F concentrations

Statistical analysis description:

To demonstrate the non-inferiority of a 3-dose primary vaccination course of 13Pn co-administered with Test Hib, HRV and DTPa-HBV-IPV compared to that of 13Pn co-administered with Control Hib, HRV and DTPa-HBV-IPV in terms of Streptococcus pneumoniae (S.pneumoniae) GMCs.

Comparison groups	Hiberix Group v ActHIB Group

Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	GMC ratio
Point estimate	1.031
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.862
upper limit	1.232

Notes:

[21] - Criteria for evaluation (1 month after the last dose of primary vaccination): LL of the 2-sided 97.5% CIs on the GMC ratio (Subset Test Hib Co-Ad over Sub-cohort Control Hib) for each S. pneumoniae serotype 23F [anti-23F] was ≥ 0.5 (clinical limit for non-inferiority).

Primary: Number of subjects with seroresponse (95%) to anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous hemagglutinin (anti-FHA).

End point title	Number of subjects with seroresponse (95%) to anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous hemagglutinin (anti-FHA).

End point description:

Seroresponse (95%) was defined as the number of subjects showing a concentration above a threshold that leads to 95% seroresponse in the ActHIB group.

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	792	275	251	
Units: Subjects				
Anti-PT [N = 792,275,251]	764	264	201	
Anti-PRN [N = 789,275,250]	762	262	213	
Anti-FHA [N=791,275,249]	744	263	191	

Statistical analyses

Statistical analysis title	Difference in seroresponse Anti-FHA

Statistical analysis description:

To rule out a 10% decrease in seroresponse to FHA in subjects receiving DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV vaccines compared to subjects receiving DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV vaccines, following 3 primary vaccine doses where seroresponse was defined as the percentage of subjects showing a concentration above a threshold that led to 95% seroresponse in the control group.

Comparison groups	Hiberix Group v ActHIB Group

Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	< 0.0001 [23]
Method	t-test, 1-sided

Notes:

[22] - Criteria for evaluation (1 month after the last dose of primary vaccination): P-value on the difference in seroresponse between groups was < 1.25% for FHA antigen (p-value was computed by integrating on the p-value for the null hypothesis that the seroresponse rate in the Subset Pertussis Co-Ad was < 85% and the a-posteriori probability of the cut-off in the Sub-cohort Control Hib).
[23] - P-value is computed by integrating on the p-values of one-sided test with alpha=0.025 and the posterior probability of the cut-off in the control group

Statistical analysis title	Difference in seroresponse Anti-PT

Statistical analysis description:

To rule out a 10% decrease in seroresponse to PT in subjects receiving DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV vaccines compared to subjects receiving DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV vaccines, following 3 primary vaccine doses where seroresponse was defined as the percentage of subjects showing a concentration above a threshold that led to 95% seroresponse in the control group.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	< 0.0001 [25]
Method	t-test, 1-sided

Notes:

[24] - Criteria for evaluation (1 month after the last dose of primary vaccination): P-value on the difference in seroresponse between groups was < 1.25% for PT antigen (p-value was computed by integrating on the p-value for the null hypothesis that the seroresponse rate in the Subset Pertussis Co-Ad was < 85% and the a-posteriori probability of the cut-off in the Sub-cohort Control Hib).
[25] - P-value is computed by integrating on the p-values of one-sided test with alpha=0.025 and the posterior probability of the cut-off in the control group

Statistical analysis title	Difference in seroresponse Anti-PRN

Statistical analysis description:

To rule out a 10% decrease in seroresponse to PRN in subjects receiving DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV vaccines compared to subjects receiving DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV vaccines, following 3 primary vaccine doses where seroresponse was defined as the percentage of subjects showing a concentration above a threshold that led to 95% seroresponse in the control group.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	1067
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	< 0.0001 [27]
Method	t-test, 1-sided

Notes:

[26] - Criteria for evaluation (1 month after the last dose of primary vaccination): P-value on the difference in seroresponse between groups was < 1.25% for PRN antigen (p-value was computed by integrating on the p-value for the null hypothesis that the seroresponse rate in the Subset Pertussis Co-Ad was < 85% and the a-posteriori probability of the cut-off in the Sub-cohort Control Hib).
[27] - P-value is computed by integrating on the p-values of one-sided test with alpha=0.025 and the posterior probability of the cut-off in the control group

Primary: Number of subjects with anti-Polio 1,2,3 antibody titres greater than or equal to cut-off value.

End point title	Number of subjects with anti-Polio 1,2,3 antibody titres greater than or equal to cut-off value.

End point description:

The cut-off value was defined as a concentration ≥ 8 ED50 (ED50 is the concentration at which the protein exhibits 50% of its maximum activity).

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	478	334	331	
Units: Subjects				
Anti-Polio 1 [N=447,322,317]	444	322	300	
Anti-Polio 2 [N=478,334,331]	473	329	323	
Anti-Polio 3 [N=456,323,311]	453	323	310	

Statistical analyses

Statistical analysis title	Non-inferiority Anti-Polio 1 concentrations

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to poliovirus 1.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	812
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	Difference in percentage
Point estimate	-0.67
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.24
upper limit	0.87

Notes:

[28] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 97.5% CIs on the differences (Subset Test Hib Co-Ad minus Sub-cohort Control Hib) in the percentages of subjects with seroprotective titres (≥8) of antibodies to each of the poliovirus antigens was ≥-5% (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Polio 2 concentration

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to poliovirus 2.

Comparison groups	Hiberix Group v ActHIB Group

Number of subjects included in analysis	812
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Parameter estimate	Difference in percentage
Point estimate	0.45
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.45
upper limit	2.91

Notes:

[29] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 97.5% CIs on the differences (Subset Test Hib Co-Ad minus Sub-cohort Control Hib) in the percentages of subjects with seroprotective titres (≥8) of antibodies to each of the poliovirus antigens was ≥-5% (clinical limit for non-inferiority).

Statistical analysis title	Non-inferiority Anti-Polio 3 concentration

Statistical analysis description:

To demonstrate the non-inferiority of DTPa-HBV-IPV co-administered with Test Hib, 13Pn and HRV to DTPa-HBV-IPV co-administered with Control Hib, 13Pn and HRV, following 3 primary vaccine doses in terms of immune response to poliovirus 3.

Comparison groups	Hiberix Group v ActHIB Group
Number of subjects included in analysis	812
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	Difference in percentage
Point estimate	-0.66
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.2
upper limit	0.88

Notes:

[30] - Criteria for non-inferiority (1 month after the last dose of primary vaccination): LL of the standardized asymptotic 97.5% CIs on the differences (Subset Test Hib Co-Ad minus Sub-cohort Control Hib) in the percentages of subjects with seroprotective titres (≥8) of antibodies to each of the poliovirus antigens was ≥-5% (clinical limit for non-inferiority).

Primary: Anti-protein-D (anti-D) and anti-protein-T (anti-T) antibody concentrations.

End point title	Anti-protein-D (anti-D) and anti-protein-T (anti-T) antibody concentrations.[31]

End point description:

Antibody concentrations were given as geometric mean concentrations (GMCs) and expressed as International Units per milliliter (IU/mL).

End point type	Primary

End point timeframe:

At 1 month after last dose of primary vaccination.

Notes:

[31] - 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	393	274	250	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D [N = 393,273,250]	2.72 (2.54 to 2.93)	2.45 (2.24 to 2.68)	1.88 (1.69 to 2.09)	
Anti-T [N = 393,274,250]	2.23 (2.07 to 2.41)	2.44 (2.2 to 2.71)	1.72 (1.55 to 1.91)	

Statistical analyses

No statistical analyses for this end point

Primary: Lot-to-Lot consistency of the 3 Test Hib formulations fro Anti-PRP

End point title	Lot-to-Lot consistency of the 3 Test Hib formulations fro Anti-PRP

End point description:

End point type	Primary

End point timeframe:

1 month after the last dose of primary vaccination

End point values	Test-Hib A Group	Test Hib B Group	Test Hib C Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	527	537	526	
Units: µg/mL				
number (not applicable)	4.994	6.323	4.416	

Statistical analyses

Statistical analysis title	GMC ratio Test Hib Lot A/B

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Test Hib co-administered with DTPa-HBV-IPV, 13Pn and HRV following 3 primary vaccine doses in terms of immune response to polyribosylribitol phosphate (PRP).

Comparison groups	Test-Hib A Group v Test Hib B Group
Number of subjects included in analysis	1064
Analysis specification	Pre-specified
Analysis type	other[32]
Parameter estimate	GMC ratio
Point estimate	0.79

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.641
upper limit	0.974

Notes:

[32] - Criterion for lot-to-lot consistency (1 month after the last dose of primary vaccination): Lot-to-lot consistency was evaluated by each pair wise ratio of geometric mean concentrations (GMC) values for anti-PRP obtained for the 3 lots of Test Hib (Sub-cohorts Test Hib A-PRP, Test Hib B-PRP and Test Hib C-PRP). The criterion for lot-to-lot consistency was that the 2-sided 95% confidence bounds on the anti-PRP GMC ratio between lots were within the [0.67; 1.5] interval for all 3 pair wise comparis

Statistical analysis title	GMC ratio Test Hib Lot A/C

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Test Hib co-administered with DTPa-HBV-IPV, 13Pn and HRV following 3 primary vaccine doses in terms of immune response to polyribosylribitol phosphate (PRP).

Comparison groups	Test-Hib A Group v Test Hib C Group
Number of subjects included in analysis	1053
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	GMC ratio
Point estimate	1.131
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.916
upper limit	1.396

Notes:

[33] - Criterion for lot-to-lot consistency (1 month after the last dose of primary vaccination): Lot-to-lot consistency was evaluated by each pair wise ratio of geometric mean concentrations (GMC) values for anti-PRP obtained for the 3 lots of Test Hib (Sub-cohorts Test Hib A-PRP, Test Hib B-PRP and Test Hib C-PRP). The criterion for lot-to-lot consistency was that the 2-sided 95% confidence bounds on the anti-PRP GMC ratio between lots were within the [0.67; 1.5] interval for all 3 pair comparisons.

Statistical analysis title	GMC ratio Test Hib Lot B/C

Statistical analysis description:

To demonstrate the lot-to-lot consistency of 3 manufacturing lots of Test Hib co-administered with DTPa-HBV-IPV, 13Pn and HRV following 3 primary vaccine doses in terms of immune response to polyribosylribitol phosphate (PRP).

Comparison groups	Test Hib B Group v Test Hib C Group
Number of subjects included in analysis	1063
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	GMC ratio
Point estimate	1.432
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.161
upper limit	1.765

Notes:

[34] - Criterion for lot-to-lot consistency (1 month after the last dose of primary vaccination): Lot-to-lot consistency was evaluated by each pair wise ratio of geometric mean concentrations (GMC) values for anti-PRP obtained for the 3 lots of Test Hib (Sub-cohorts Test Hib A-PRP, Test Hib B-PRP and Test Hib C-PRP). The criterion for lot-to-lot consistency was that the 2-sided 95% confidence bounds on the anti-PRP GMC ratio between lots were within the [0.67; 1.5] interval for all 3 pair comparisons.

Secondary: Number of subjects with any solicited local symptoms.

End point title	Number of subjects with any solicited local symptoms.

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of any symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During a 4-day follow-up period (Days 0-3) following any vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2846	503	496	
Units: Subjects				
Any pain	1932	366	370	
Any redness	1165	233	257	
Any swelling	834	174	195	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms.

End point title	Number of subjects with any solicited general symptoms.

End point description:

Assessed solicited general symptoms were drowsiness, irritability, fever and loss of appetite. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination. Any fever= Rectal temperature equal to or above (≥) 38 degrees Celsius (°C).

End point type	Secondary

End point timeframe:

During a 4-day follow-up period (Days 0-3) following any vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2848	503	496	
Units: Subjects				
Any drowsiness	2179	398	378	
Any irritability	2478	449	434	
Any loss of appetite	1450	275	253	
Any fever	1014	186	143	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events (AEs).

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 31-day (Day 0-Day 30) follow-up period after primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2963	520	520	
Units: Subjects				
Any AE(s)	1880	350	324	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

End point title	Number of subjects with serious adverse events (SAEs).

End point description:

Serious adverse events (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:

From Day 0 until 6 months following the last primary dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2963	520	520	
Units: Subjects				
Any SAE(s)	108	24	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with AEs of specific interest (AESIs).

End point title	Number of subjects with AEs of specific interest (AESIs).

End point description:

An AESI was defined as an AE including autoimmune diseases and other mediated inflammatory disorders and assessed by the investigator as specific to the treatment administration.

End point type	Secondary

End point timeframe:

From Day 0 until 6 months following the last primary dose or the receipt of the booster vaccination, whichever comes first.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2963	520	520	
Units: Subjects				
Any AESI(s)	108	22	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seroresponse (90%) to anti-PT, anti-PRN and anti-FHA.

End point title	Number of subjects with seroresponse (90%) to anti-PT, anti-PRN and anti-FHA.

End point description:

Seroresponse (90%) was defined as the number of subjects showing a concentration above a threshold that leads to 90% seroresponse in the ActHIB group.

End point type	Secondary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	792	275	251	
Units: Subjects				
Anti-PT [N = 792,275,251]	706	248	165	
Anti-PRN [N = 789,275,250]	741	250	194	
Anti-FHA [N=791,275,249]	705	248	166	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-PRN and anti-FHA antibody concentrations ≥ 5 EL.U/mL.

End point title	Number of subjects with anti-PT, anti-PRN and anti-FHA antibody concentrations ≥ 5 EL.U/mL.

End point description:

End point type	Secondary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	792	275	251	
Units: Subjects				
Anti-PT [N= 792,275,251]	789	275	249	
Anti-PRN [N = 789,275,250]	786	275	244	
Anti-FHA [N=791,275,249]	791	275	249	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B (Anti-HBs) antibody concentrations.

End point title	Anti-Hepatitis B (Anti-HBs) antibody concentrations.

End point description:

Antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as milli-international units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	363	258	239	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	3684.3 (3287 to 4129.5)	3545.6 (3067.8 to 4098)	1573.4 (1302.6 to 1900.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S.pneumoniae antibody concentrations ≥ 0.05 µg/mL, ≥ 0.2 µg/mL and ≥1.0 µg/mL.

End point title	Number of subjects with S.pneumoniae antibody concentrations ≥ 0.05 µg/mL, ≥ 0.2 µg/mL and ≥1.0 µg/mL.

End point description:

End point type	Secondary

End point timeframe:

At 1 month after the last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	270	247	
Units: Subjects				
≥ 0.05 µg/mL, Anti-Pneumoniae 1 [N = 384,268,245]	384	268	245	
≥ 0.05 µg/mL, Anti-Pneumoniae 3 [N = 382,269,245]	382	269	243	
≥ 0.05 µg/mL, Anti-Pneumoniae 4 [N = 389,268,247]	389	268	247	
≥ 0.05 µg/mL, Anti-Pneumoniae 5 [N = 379,266,246]	379	266	246	
≥ 0.05 µg/mL, Anti-Pneumoniae 6A [N = 381,267,244]	381	267	244	
≥ 0.05 µg/mL, Anti-Pneumoniae 6B [N = 383,267,245]	378	260	241	
≥ 0.05 µg/mL, Anti-Pneumoniae 7F [N = 386,269,246]	386	269	246	
≥ 0.05 µg/mL, Anti-Pneumoniae 9V [N = 386,270,246]	385	270	246	
≥ 0.05 µg/mL, Anti-Pneumoniae 14 [N = 384,267,244]	384	267	244	

≥ 0.05 µg/mL, Anti-Pneumoniae 18C [N =380,267,244]	380	267	244	
≥ 0.05 µg/mL, Anti-Pneumoniae 19A[N = 384,266,245]	383	265	244	
≥ 0.05 µg/mL, Anti-Pneumoniae 19F[N = 384,268,245]	384	268	245	
≥ 0.05 µg/mL, Anti-Pneumoniae 23F[N = 384,268,245]	384	267	244	
≥ 0.2 µg/mL, Anti-Pneumoniae 1 [N = 384,268,245]	382	267	244	
≥ 0.2 µg/mL, Anti-Pneumoniae 3 [N = 382,269,245]	379	268	243	
≥ 0.2 µg/mL, Anti-Pneumoniae 4 [N = 389,268,247]	389	267	247	
≥ 0.2 µg/mL, Anti-Pneumoniae 5 [N = 379,266,246]	377	265	245	
≥ 0.2 µg/mL, Anti-Pneumoniae 6A [N = 381,267,244]	379	265	243	
≥ 0.2 µg/mL, Anti-Pneumoniae 6B [N = 383,267,245]	351	242	224	
≥ 0.2 µg/mL, Anti-Pneumoniae 7F [N = 386,269,246]	386	269	246	
≥ 0.2 µg/mL, Anti-Pneumoniae 9V [N = 386,270,246]	385	269	243	
≥ 0.2 µg/mL, Anti-Pneumoniae 14 [N = 384,267,244]	381	265	241	
≥ 0.2 µg/mL, Anti-Pneumoniae 18C [N = 380,267,244]	377	267	244	
≥ 0.2 µg/mL, Anti-Pneumoniae 19A [N = 384,266,245]	379	259	235	
≥ 0.2 µg/mL, Anti-Pneumoniae 19F [N = 384,268,245]	383	267	244	
≥ 0.2 µg/mL, Anti-Pneumoniae 23F [N = 384,268,245]	376	265	231	
≥ 1.0 µg/mL, Anti-Pneumoniae 1 [N = 384,268,245]	334	239	213	
≥ 1.0 µg/mL, Anti-Pneumoniae 3 [N = 382,269,245]	188	140	138	
≥ 1.0 µg/mL, Anti-Pneumoniae 4 [N = 389,268,247]	318	226	199	
≥ 1.0 µg/mL, Anti-Pneumoniae 5 [N = 379,266,246]	354	250	225	
≥ 1.0 µg/mL, Anti-Pneumoniae 6A [N = 381,267,244]	357	253	229	
≥ 1.0 µg/mL, Anti-Pneumoniae 6B [N = 383,267,245]	232	151	117	
≥ 1.0 µg/mL, Anti-Pneumoniae 7F [N = 386,269,246]	379	264	239	
≥ 1.0 µg/mL, Anti-Pneumoniae 9V [N = 386,270,246]	338	234	203	
≥ 1.0 µg/mL, Anti-Pneumoniae 14 [N = 384,267,244]	360	250	223	
≥ 1.0 µg/mL, Anti-Pneumoniae 18C [N = 380,267,244]	361	256	229	
≥ 1.0 µg/mL, Anti-Pneumoniae 19A [N = 384,266,245]	290	200	164	
≥ 1.0 µg/mL, Anti-Pneumoniae 19F [N = 384,268,245]	357	254	231	
≥ 1.0 µg/mL, Anti-Pneumoniae 23F [N = 384,268,245]	297	208	180	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for Poliovirus types 1, 2 and 3.

End point title	Antibody titers for Poliovirus types 1, 2 and 3.

End point description:

Antibody titers were given as geometric mean titers(GMTs).

End point type	Secondary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	478	334	331	
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-Polio 1 [N=447,322,317]	570.8 (509.2 to 639.8)	620.9 (540.1 to 713.7)	136 (114.7 to 161.1)	
Anti-Polio 2 [N=478,334,331]	471.8 (416.7 to 534.1)	389.9 (337.3 to 450.6)	210.9 (181.9 to 244.5)	
Anti-Polio 3 [N=456,323,311]	982.8 (870.1 to 1110.2)	963.2 (843.7 to 1099.5)	297.4 (253.3 to 349.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HBs antibody concentrations greater than or equal to cut-off values.

End point title	Number of subjects with anti-HBs antibody concentrations greater than or equal to cut-off values.

End point description:

The cut-off values were defined as a concentration≥ 3.3 mIU/mL (seropositivity) and ≥ 10 mIU/mL (seroprotection).

End point type	Secondary

End point timeframe:

At 1 month after last dose of primary vaccination.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	363	258	239	
Units: Subjects				
Anti-HBs≥ 3.3 mIU/ml	362	257	239	
Anti-HBs≥ 10 mIU/ml	362	257	239	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms.

End point title	Number of subjects with any solicited local symptoms.

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of any symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) following the booster dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2224	416	379	
Units: Subjects				
Any Pain	918	179	163	
Any Redness	659	127	115	
Any Swelling	392	82	75	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms.

End point title	Number of subjects with any solicited general symptoms.

End point description:

Assessed solicited general symptoms were drowsiness, irritability, fever and loss of appetite. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination. Any fever= Axillary temperature equal to or above (≥) 38 degrees Celsius (°C).

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) following the booster dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2225	416	379	
Units: Subjects				
Any Drowsiness	857	164	119	
Any Irritability	1293	250	201	
Any Loss of appetite	614	141	85	
Any Fever	119	18	20	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with AEs of specific interest (AESIs).

End point title	Number of subjects with AEs of specific interest (AESIs).

End point description:

An AESI was defined as an AE including autoimmune diseases and other mediated inflammatory disorders and assessed by the investigator as specific to the treatment administration.

End point type	Secondary

End point timeframe:

From booster dose until 6 months following receipt of the booster dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2337	435	400	
Units: Subjects				
Any AESI(s)	47	12	7	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events (AEs).

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom

with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0 to Day 30) following the booster dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2337	435	400	
Units: Subjects				
Any AE(s)	882	159	138	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

End point title	Number of subjects with 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:

From the booster dose until 6 months following receipt of the booster dose.

End point values	Hiberix Group	ActHIB Group	Pentacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2337	435	400	
Units: Subjects				
Any SAE(s)	29	4	2	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

SAEs= Day 0 to 6 months following last primary dose and from booster dose until 6 months after receipt of booster dose. Systematically and non-systematically assessed frequent AEs=within 4 and 31 days following primary and booster vaccination respectively

Adverse event reporting additional description:

For the systematically assessed frequent AEs, the number of participants at risk included those from the Primary Total Vaccinated cohort and the Booster Total Vaccinated cohort respectively who had their symptom sheet completed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Hiberix Group

Reporting group description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	ActHIB Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	Pentacel Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.

Reporting group title	Hiberix Group

Reporting group description:

Pooled group of subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of 3 different lots of Hiberix® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Hiberix® vaccine was administered intramuscularly in the right thigh. Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	ActHIB Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of ActHIB® vaccine co-administered with 3 doses of Pediarix® and Prevnar13® vaccines at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The ActHIB® vaccine was administered intramuscularly in the right thigh. The Pediarix® vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered

intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally.

Reporting group title	Pentacel Group

Reporting group description:

Subjects, male or female between, and including, 6 and 12 weeks of age at the time of the first vaccination, who received 3 doses of Pentacel® vaccine co-administered with 3 doses of Prevnar13® vaccine, 2 or 3 doses of Engerix™-B vaccine at 2, 4 and 6 months of age and 2 doses of Rotarix® vaccine at 2 and 4 months of age. The Pentacel® vaccine was administered intramuscularly in the right thigh. The Engerix™-B vaccine was administered intramuscularly in the left thigh. The Prevnar13® vaccine was administered intramuscularly in the left thigh or deltoid. The Rotarix® vaccine was administered orally. If subjects in the Pentacel Group had received a birth dose of Hepatitis B vaccine then they were to receive Engerix™-B vaccine only at 2 and 6 months of age.

Serious adverse events	Hiberix Group	ActHIB Group	Pentacel Group
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 2963 (3.64%)	24 / 520 (4.62%)	21 / 520 (4.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinoblastoma bilateral (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Kawasaki’s disease (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Cephalhaematoma (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Pyrexia (primary phase)			
subjects affected / exposed	5 / 2963 (0.17%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Developmental delay (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory distress (primary phase)			
subjects affected / exposed	5 / 2963 (0.17%)	2 / 520 (0.38%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	2 / 520 (0.38%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apparent life threatening event (primary phase)			
subjects affected / exposed	3 / 2963 (0.10%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	1 / 520 (0.19%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome (primary phase)			

subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choking (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body aspiration (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (booster phase)			

subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Autism spectrum disorder (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breath holding (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure (primary phase)			

subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Child maltreatment syndrome (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural haematoma (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture (booster phase)			

subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage (booster phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Pyloric stenosis (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral palsy (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital aplastic anaemia (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital nystagmus (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microcephaly (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mitochondrial DNA mutation (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patent ductus arteriosus (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion (primary phase)			
subjects affected / exposed	4 / 2963 (0.13%)	3 / 520 (0.58%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion (primary phase)			
subjects affected / exposed	4 / 2963 (0.13%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drooling (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy (primary phase)			

subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle contractions involuntary (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sympathomimetic effect (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis (primary phase)			
subjects affected / exposed	3 / 2963 (0.10%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy (primary phase)			

subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal inflammation (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-weiss syndrome (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Vesicoureteric reflux (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Growth retardation (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis (primary phase)			

subjects affected / exposed	16 / 2963 (0.54%)	2 / 520 (0.38%)	2 / 520 (0.38%)
occurrences causally related to treatment / all	0 / 16	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis (primary phase)			
subjects affected / exposed	13 / 2963 (0.44%)	4 / 520 (0.77%)	2 / 520 (0.38%)
occurrences causally related to treatment / all	0 / 13	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia (primary phase)			
subjects affected / exposed	14 / 2963 (0.47%)	2 / 520 (0.38%)	2 / 520 (0.38%)
occurrences causally related to treatment / all	0 / 14	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (primary phase)			
subjects affected / exposed	9 / 2963 (0.30%)	0 / 520 (0.00%)	2 / 520 (0.38%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection (primary phase)			
subjects affected / exposed	9 / 2963 (0.30%)	2 / 520 (0.38%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious (primary phase)			
subjects affected / exposed	3 / 2963 (0.10%)	0 / 520 (0.00%)	2 / 520 (0.38%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	2 / 520 (0.38%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis (primary phase)			
subjects affected / exposed	3 / 2963 (0.10%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis (primary phase)			

subjects affected / exposed	3 / 2963 (0.10%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	2 / 520 (0.38%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess (primary phase)			
subjects affected / exposed	2 / 2963 (0.07%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck (primary phase)			

subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess (primary phase)			
subjects affected / exposed	0 / 2963 (0.00%)	1 / 520 (0.19%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis streptococcal (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis (primary)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal bacteraemia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral rash (primary phase)			

subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia (booster phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

(booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration (primary phase)			
subjects affected / exposed	10 / 2963 (0.34%)	3 / 520 (0.58%)	1 / 520 (0.19%)
occurrences causally related to treatment / all	0 / 10	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight gain poor (primary phase)			
subjects affected / exposed	1 / 2963 (0.03%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dehydration (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Hiberix Group	ActHIB Group	Pentacel Group
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 2337 (1.24%)	4 / 435 (0.92%)	2 / 400 (0.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinoblastoma bilateral (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Kawasaki’s disease (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Cephalhaematoma (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Developmental delay (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory distress (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apparent life threatening event (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choking (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body aspiration (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status asthmaticus (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity (booster phase)			
subjects affected / exposed	2 / 2337 (0.09%)	1 / 435 (0.23%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma (booster phase)			
subjects affected / exposed	2 / 2337 (0.09%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax (booster phase)			

subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Autism spectrum disorder (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breath holding (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Child maltreatment syndrome (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural haematoma (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body (booster phase)			
subjects affected / exposed	2 / 2337 (0.09%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture (booster phase)			

subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Pyloric stenosis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral palsy (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital aplastic anaemia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital nystagmus (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microcephaly (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitochondrial DNA mutation (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patient ductus arteriosus (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	1 / 435 (0.23%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drooling (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epilepsy (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle contractions involuntary (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sympathomimetic effect (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion (booster phase)			
subjects affected / exposed	5 / 2337 (0.21%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutropenia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-weiss syndrome (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Vesicoureteric reflux (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Growth retardation (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis streptococcal (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis (primary)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal bacteraemia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral rash (primary phase)			

subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious (booster phase)			
subjects affected / exposed	2 / 2337 (0.09%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess (booster phase)			
subjects affected / exposed	2 / 2337 (0.09%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

(booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection (booster phase)			
subjects affected / exposed	1 / 2337 (0.04%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight gain poor (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dehydration (booster phase)			
subjects affected / exposed	0 / 2337 (0.00%)	1 / 435 (0.23%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Hiberix Group	ActHIB Group	Pentacel Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2478 / 2963 (83.63%)	449 / 520 (86.35%)	434 / 520 (83.46%)
General disorders and administration site conditions			
Pyrexia (primary phase)			
subjects affected / exposed	196 / 2963 (6.61%)	36 / 520 (6.92%)	28 / 520 (5.38%)
occurrences (all)	196	36	28
Drowsiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	2179 / 2848 (76.51%)	398 / 503 (79.13%)	378 / 496 (76.21%)
occurrences (all)	2179	398	378
Irritability (primay phase)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	2478 / 2848 (87.01%)	449 / 503 (89.26%)	434 / 496 (87.50%)
occurrences (all)	2478	449	434
Loss of appetite (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	1450 / 2848 (50.91%)	275 / 503 (54.67%)	253 / 496 (51.01%)
occurrences (all)	1450	275	253
Fever (Rectal) (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	1014 / 2848 (35.60%)	186 / 503 (36.98%)	143 / 496 (28.83%)
occurrences (all)	1014	186	143
Pain (primary phase)			
alternative assessment type: Systematic			

subjects affected / exposed[5]	1932 / 2846 (67.88%)	366 / 503 (72.76%)	370 / 496 (74.60%)
occurrences (all)	1932	366	370
Redness (primay phase)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	1165 / 2846 (40.93%)	233 / 503 (46.32%)	257 / 496 (51.81%)
occurrences (all)	1165	233	257
Swelling (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	834 / 2846 (29.30%)	174 / 503 (34.59%)	195 / 496 (39.31%)
occurrences (all)	834	174	195
Pyrexia (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Pain (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Redness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Swelling (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Drowsiness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[11]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Irritability (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[12]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Loss of apetite (booster phase)			

alternative assessment type: Systematic			
subjects affected / exposed[13]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Fever (axillary) (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea (primary phase)			
subjects affected / exposed	162 / 2963 (5.47%)	28 / 520 (5.38%)	22 / 520 (4.23%)
occurrences (all)	162	28	22
Vomiting (primary phase)			
subjects affected / exposed	158 / 2963 (5.33%)	29 / 520 (5.58%)	21 / 520 (4.04%)
occurrences (all)	158	29	21
Teething (primary phase)			
subjects affected / exposed	128 / 2963 (4.32%)	22 / 520 (4.23%)	30 / 520 (5.77%)
occurrences (all)	128	22	30
Respiratory, thoracic and mediastinal disorders			
Cough (primary phase)			
subjects affected / exposed	307 / 2963 (10.36%)	49 / 520 (9.42%)	50 / 520 (9.62%)
occurrences (all)	307	49	50
Rhinorrhoea (primary phase)			
subjects affected / exposed	153 / 2963 (5.16%)	35 / 520 (6.73%)	27 / 520 (5.19%)
occurrences (all)	153	35	27
Nasal congestion (primary phase)			
subjects affected / exposed	155 / 2963 (5.23%)	30 / 520 (5.77%)	35 / 520 (6.73%)
occurrences (all)	155	30	35
Cough (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	568 / 2963 (19.17%)	100 / 520 (19.23%)	94 / 520 (18.08%)
occurrences (all)	568	100	94
Otitis media (primary phase)			

subjects affected / exposed	287 / 2963 (9.69%)	44 / 520 (8.46%)	55 / 520 (10.58%)
occurrences (all)	287	44	55
Upper respiratory tract infection (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0
Otitis media (booster phase)			
subjects affected / exposed	0 / 2963 (0.00%)	0 / 520 (0.00%)	0 / 520 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Hiberix Group	ActHIB Group	Pentacel Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1293 / 2337 (55.33%)	250 / 435 (57.47%)	201 / 400 (50.25%)
General disorders and administration site conditions			
Pyrexia (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Drowsiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Irritability (primay phase)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Loss of appetite (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Fever (Rectal) (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Pain (primary phase)			
alternative assessment type: Systematic			

subjects affected / exposed[5]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Redness (primay phase)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Swelling (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Pyrexia (booster phase)			
subjects affected / exposed	120 / 2337 (5.13%)	39 / 435 (8.97%)	27 / 400 (6.75%)
occurrences (all)	120	39	27
Pain (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[8]	918 / 2224 (41.28%)	179 / 416 (43.03%)	163 / 379 (43.01%)
occurrences (all)	918	179	163
Redness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[9]	659 / 2224 (29.63%)	127 / 416 (30.53%)	115 / 379 (30.34%)
occurrences (all)	659	127	115
Swelling (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[10]	392 / 2224 (17.63%)	82 / 416 (19.71%)	75 / 379 (19.79%)
occurrences (all)	392	82	75
Drowsiness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[11]	857 / 2225 (38.52%)	164 / 416 (39.42%)	119 / 379 (31.40%)
occurrences (all)	857	164	119
Irritability (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[12]	1293 / 2225 (58.11%)	250 / 416 (60.10%)	201 / 379 (53.03%)
occurrences (all)	1293	250	201

Loss of apetite (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[13]	614 / 2225 (27.60%)	141 / 416 (33.89%)	85 / 379 (22.43%)
occurrences (all)	614	141	85
Fever (axillary) (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[14]	119 / 2225 (5.35%)	18 / 416 (4.33%)	20 / 379 (5.28%)
occurrences (all)	119	18	20
Gastrointestinal disorders			
Diarrhoea (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Vomiting (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Teething (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Nasal congestion (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Cough (booster phase)			
subjects affected / exposed	108 / 2337 (4.62%)	22 / 435 (5.06%)	31 / 400 (7.75%)
occurrences (all)	108	22	31
Infections and infestations			
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0

Otitis media (primary phase)			
subjects affected / exposed	0 / 2337 (0.00%)	0 / 435 (0.00%)	0 / 400 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection (booster phase)			
subjects affected / exposed	155 / 2337 (6.63%)	22 / 435 (5.06%)	26 / 400 (6.50%)
occurrences (all)	155	22	26
Otitis media (booster phase)			
subjects affected / exposed	114 / 2337 (4.88%)	24 / 435 (5.52%)	17 / 400 (4.25%)
occurrences (all)	114	24	17

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their

symptom sheets completed.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2011	Amendment 3 for the HIB-097 protocol was developed in order to: Ensure scheduling of study visit 3 so that subjects receive final hepatitis B vaccination according to ACIP recommendations (minimum age of 24 weeks for the final hepatitis B dose, with an interval of at least 8 weeks between the 2nd and final hepatitis B dose). Update the footnote of Table 6 to clarify that it is preferred that subjects come in for Visit 6, at least 30 days after Visit 5. Update the sections on exclusion criteria for enrolment, contraindications to vaccination and warnings and precautions with information from the updated US Rotarix label. Update information for sponsor signatories, Clinical Development Manager and Global Study Manager for the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported