Clinical trial results:
Immunogenicity and Safety of Pediacel®, a Combined Diphtheria, Tetanus, Five Component Acellular Pertussis, Inactivated Poliomyelitis and Haemophilus Influenzae Type b Conjugate Vaccine (Adsorbed), Compared to Infanrix®–IPV+Hib when Both Vaccines are Co-Administered with Prevenar® to Infants and Toddlers at 2, 3, 4 and 12-18 Months of Age

Summary

EudraCT number	2006-001095-21
Trial protocol	Outside EU/EEA
Global end of trial date	17 June 2008

Results information

Result version number	v1 (current)
This version publication date	17 June 2016
First version publication date	17 June 2016

Trial information

Trial identification

Sponsor protocol code	A5I16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00343421
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
Public contact	Clinical Team Leader, Sanofi Pasteur Inc., 1 570 957 3570, emilia.jordanov@sanofipasteur.com
Scientific contact	Clinical Team Leader, Sanofi Pasteur Inc., 1 570 957 3570, emilia.jordanov@sanofipasteur.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	28 April 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Phase
1. To compare the post-dose 3 immunogenicity of Pediacel® to Infanrix®–IPV+Hib when both are co-administered with Prevenar® to infants at 2, 3 and 4 months of age.
2. To compare the post-dose 3 immunogenicity of Prevenar® co-administered with Pediacel® to the post-dose 3 immunogenicity of Prevenar® co-administered with Infanrix®-IPV+Hib in infants at 2, 3 and 4 months of age.
3. To describe the post-dose 3 pertussis antibody responses in both study groups.

Booster Phase
Not applicable

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	10 May 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 365
Country: Number of subjects enrolled	Poland: 219
Worldwide total number of subjects	584
EEA total number of subjects	584

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)	584
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:

Study subjects were enrolled for the booster dose from 10 May 2007 to 17 June 2008 for the dose 4 booster at 12 clinic sites in Poland and 53 clinic sites in France.

Pre-assignment

Screening details:

A total of 588 subjects who met all inclusion and none of the exclusion criteria were randomized, of which 573 received all 3 doses of study vaccine as randomized. The safety analysis set for all 3 doses included 584 subjects.

Period 1

Period 1 title	Primary phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

A double-blind study design was not feasible due to the different presentations of the study vaccines (i.e., vial versus pre-filled syringes). A single-blind study design had no impact on the primary immunogenicity objective. Laboratory personnel were blinded to the vaccine the subject received.

Arms

Are arms mutually exclusive?	Yes
Arm title	PEDIACEL

Arm description:

Infants received PEDIACEL co-administered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	PEDIACEL: Diphtheria, tetanus, five component acellular pertussis, inactivated poliomyelitis and H. influenzae type b conjugate vaccine (adsorbed)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection into the deltoid muscle, 1 injection each at 2, 3, and 4 months of age.

Investigational medicinal product name	Prevenar: Pneumococcal saccharide conjugated vaccine, adsorbed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle of the contralateral arm, 1 injection each at 2, 3, and 4 months of age.

Arm title	Infanrix-IPV+Hib

Arm description:

Infants received Infanrix-IPV+Hib coadministered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.

Arm type	Active comparator

Investigational medicinal product name	Infanrix-IPV+Hib: Diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated H. influenzae type b vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection in the deltoid muscle, 1 injection each at 2, 3, and 4 months of age.

Investigational medicinal product name	Prevenar: Pneumococcal saccharide conjugated vaccine, adsorbed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle of the contralateral arm, 1 injection each at 2, 3, and 4 months of age.

Number of subjects in period 1	PEDIACEL	Infanrix-IPV+Hib
Started	292	292
Completed	284	280
Not completed	8	12
Consent withdrawn by subject	3	6
Serious adverse events	-	2
Serious adverse event	1	-
Lost to follow-up	2	2
Protocol deviation	2	2

Period 2

Period 2 title	Booster phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

A double-blind study design was not feasible due to the different presentations of the study vaccines (i.e., vial versus pre-filled syringes). A single-blind study design had no impact on the primary immunogenicity objective. Laboratory personnel were blinded to the vaccine the subject received.

Arms

Are arms mutually exclusive?	Yes

Arm title	PEDIACEL

Arm description:

Infants received PEDIACEL co-administered with Prevenar as dose 4 booster at 12-18 months of age.

Arm type	Experimental
Investigational medicinal product name	PEDIACEL: Diphtheria, tetanus, five component acellular pertussis, inactivated poliomyelitis and H. influenzae type b conjugate vaccine (adsorbed)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection into the deltoid muscle, booster dose at 12-18 months of age.

Investigational medicinal product name	Prevenar: Pneumococcal saccharide conjugated vaccine, adsorbed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle of the contralateral arm, booster dose at 12-18 months of age.

Arm title	Infanrix-IPV+Hib

Arm description:

Infants received Infanrix-IPV+Hib coadministered with Prevenar as dose 4 booster at 12-18 months of age.

Arm type	Active comparator
Investigational medicinal product name	Infanrix-IPV+Hib: Diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated H. influenzae type be vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection in the deltoid muscle, booster at 12-18 months of age.

Investigational medicinal product name	Prevenar: Pneumococcal saccharide conjugated vaccine, adsorbed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle of the contralateral arm, booster dose at 12-18 months of age.

Number of subjects in period 2[1]	PEDIACEL	Infanrix-IPV+Hib
Started	267	264
Completed	266	263
Not completed	1	1
Consent withdrawn by subject	1	1

Notes:

[1] - 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: A total of 37 subjects withdrew from the study between the primary series and the booster dose. (20 subjects from the PEDIACEL Group and 17 subjects from the Infanrix-IPV+Hib group).

Baseline characteristics

Reporting groups	
Reporting group title	PEDIACEL
Reporting group description:	
Infants received PEDIACEL co-administered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.	
Reporting group title	Infanrix-IPV+Hib
Reporting group description:	
Infants received Infanrix-IPV+Hib coadministered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.	

Reporting group values	PEDIACEL	Infanrix-IPV+Hib	Total
Number of subjects	292	292	584
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	292	292	584
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	2.2	2.1	
standard deviation	± 0.17	± 0.16	-
Gender categorical Units: Subjects			
Female	138	139	277
Male	154	153	307

Subject analysis sets	
Subject analysis set title	PEDIACEL (Booster)
Subject analysis set type	Full analysis
Subject analysis set description:	
Infants received PEDIACEL co-administered with Prevenar as a booster vaccination at 12 to 18 months of age.	
Subject analysis set title	Infanrix-IPV+Hib (Booster)
Subject analysis set type	Full analysis
Subject analysis set description:	
Infants received Infanrix-IPV+Hib coadministered with Prevenar a booster vaccination at 12 to 18 months of age.	

Reporting group values	PEDIACEL (Booster)	Infanrix-IPV+Hib (Booster)	
Number of subjects	267	263	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	267	263	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: months			
arithmetic mean	13.8	13.9	
standard deviation	± 1.61	± 1.53	
Gender categorical Units: Subjects			
Female	126	123	
Male	141	140	

End points

End points reporting groups

Reporting group title	PEDIACEL
Reporting group description:	
Infants received PEDIACEL co-administered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.	
Reporting group title	Infanrix-IPV+Hib
Reporting group description:	
Infants received Infanrix-IPV+Hib coadministered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age.	
Reporting group title	PEDIACEL
Reporting group description:	
Infants received PEDIACEL co-administered with Prevenar as dose 4 booster at 12-18 months of age.	
Reporting group title	Infanrix-IPV+Hib
Reporting group description:	
Infants received Infanrix-IPV+Hib coadministered with Prevenar as dose 4 booster at 12-18 months of age.	
Subject analysis set title	PEDIACEL (Booster)
Subject analysis set type	Full analysis
Subject analysis set description:	
Infants received PEDIACEL co-administered with Prevenar as a booster vaccination at 12 to 18 months of age.	
Subject analysis set title	Infanrix-IPV+Hib (Booster)
Subject analysis set type	Full analysis
Subject analysis set description:	
Infants received Infanrix-IPV+Hib coadministered with Prevenar a booster vaccination at 12 to 18 months of age.	

Primary: Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide, Diphtheria, Tetanus, Polio, and Pneumococcal Serotypes Antigens After Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine with Prevenar

End point title	Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide, Diphtheria, Tetanus, Polio, and Pneumococcal Serotypes Antigens After Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine with Prevenar
End point description:	
Polyribosylribitol Phosphate (PRP) antibodies were assessed by radioimmunoassay. Diphtheria and poliovirus antibodies were assessed by serum neutralization assay. Tetanus and pneumococcal antigens antibodies were assessed by enzyme-linked immunosorbent assay. Seroprotection was defined as ≥ 0.15 µg/mL for PRP, ≥ 0.1 IU/mL for diphtheria and tetanus, ≥ 1:8 (dil) for poliovirus types 1, 2, and 3, and ≥ 0.35 µg/mL for pneumoccocal serotypes (4, 6B, 9V, 14, 18C, 19F, 23F).	
End point type	Primary
End point timeframe:	
Post-dose 3 vaccination	

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248	242		
Units: Percentage of subjects				
number (not applicable)				
PRP	91	80.8		
Diphtheria toxoid	99.2	100		
Tetanus toxoid	100	100		
Polio 1	100	100		
Polio 2	99.2	100		
Polio 3	99.6	100		
Pneumo 4	99.6	100		
Pneumo 6B	84.4	84.6		
Pneumo 9V	97.9	98.7		
Pneumo 14	99.2	100		
Pneumo 18C	97.5	96.6		
Pneumo 19F	100	100		
Pneumo 23F	90.5	91.5		

Statistical analyses

Statistical analysis title	PRP; Difference in PEDIACEL - Infanrix-IPV+Hib
Statistical analysis description:	
Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for PRP antigen.	
Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1
upper limit	16.5

Notes:

[1] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Diphtheria;Difference in PEDIACEL-Infanrix-IPV+Hib
Statistical analysis description:	
Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Diphtheria toxoid antigen.	
Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0.9

Notes:

[2] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Tetanus; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Tetanus toxoid antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.6

Notes:

[3] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 1; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Poliovirus type 1 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1.6

Notes:

[4] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 2; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Poliovirus type 2 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	0.9

Notes:

[5] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 3; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Poliovirus type 3 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.2

Notes:

[6] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 4; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 4 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.2

Notes:

[7] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 6B; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 6B antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	6.3

Notes:

[8] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 9V; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 9V antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	1.9

Notes:

[9] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 14; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 14 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	0.9

Notes:

[10] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 18C;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 18C antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	4.4

Notes:

[11] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 19F;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 19F antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1.6

Notes:

[12] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 23F;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 23F antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.3

Notes:

[13] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Primary: Summary of Seroresponse Against Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV + Hib Vaccine Co-administered with Prevenar

End point title	Summary of Seroresponse Against Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV + Hib Vaccine Co-administered with Prevenar[14]

End point description:

Pertussis antigen antibodies (Pertussis toxoid [PT], Filamentous haemagglutinin [FHA], Pertactin, and fimbriae) were assessed using enzyme-linked immunosorbent assay. Seroresponse for PT, Pertactin, and Fimbriae types 2 and 3 (Fimbriae) was defined as post-Dose 3 ≥ 4 EU/mL if pre-Dose 1 < 4 EU/mL or post-Dose 3 ≥ pre-Dose 1 if pre-Dose 1 ≥ 4 EU/mL. Seroresponse for FHA was defined as post-Dose 3 ≥ 3 EU/mL if pre-Dose 1 < 3 EU/mL or post-Dose 3 ≥ pre-Dose 1 if pre-Dose 1 ≥ 3 EU/mL

End point type	Primary

End point timeframe:

Post-dose 3 vaccination

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and study vaccines administered for this outcome.

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248	242		
Units: Percentage of subjects				
number (not applicable)				
Pertussis toxoid	98.7	99.6		
Filamentous haemagglutinin	93.2	97.4		
Pertactin	87.5	93.5		
Fimbriae	95.8	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers of Antibodies to PRP, Diphtheria, Tetanus, Polio and Pneumococcal Serotypes Antigens Post-dose 3 Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Summary of Geometric Mean Titers of Antibodies to PRP, Diphtheria, Tetanus, Polio and Pneumococcal Serotypes Antigens Post-dose 3 Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Polyribosylribitol Phosphate (PRP) antibodies were assessed by radioimmunoassay. Diphtheria and poliovirus antibodies were assessed by serum neutralization assay. Tetanus and pneumococcal antigens antibodies were assessed by enzyme-linked immunosorbent assay.

End point type	Secondary

End point timeframe:

Post-Dose 3 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248	242		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
PRP	1.38 (1.14 to 1.66)	0.59 (0.49 to 0.71)		
Diphtheria	0.09 (0.07 to 0.1)	0.07 (0.06 to 0.08)		
Tetanus	0.68 (0.62 to 0.75)	0.74 (0.68 to 0.81)		

Polio 1	238.71 (200.2 to 284.62)	340.2 (281.96 to 410.47)		
Polio 2	266.31 (216.11 to 328.18)	333.1 (272.04 to 407.88)		
Polio 3	406.18 (334.32 to 493.48)	590.95 (484.13 to 721.33)		
Pneumo 4	2.96 (2.7 to 3.25)	3.09 (2.82 to 3.4)		
Pneumo 6B	1.01 (0.88 to 1.15)	1.07 (0.93 to 1.24)		
Pneumo 9V	2.01 (1.82 to 2.21)	2.35 (2.13 to 2.6)		
Pneumo 14	9.42 (8.3 to 10.68)	8.38 (7.29 to 9.64)		
Pneumo 18C	2.01 (1.82 to 2.22)	2.07 (1.86 to 2.31)		
Pneumo 19F	4.14 (3.8 to 4.51)	4.36 (4.01 to 4.73)		
Pneumo 23F	1.48 (1.29 to 1.68)	1.54 (1.34 to 1.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers (GMTs) of Antibodies to Pertussis Antigens Before and Following a 3-Dose Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Summary of Geometric Mean Titers (GMTs) of Antibodies to Pertussis Antigens Before and Following a 3-Dose Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Pneumococcal antigens (Pertussis toxoid, Filamentous haemagglutinin [FHA], Pertactin, and Fimbriae types 2 and 3 [Fimbriae]) antibodies were assessed by enzyme-linked immunosorbent assay.

End point type	Secondary

End point timeframe:

Pre-Dose 1 and Post-Dose 3 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248	242		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Pertussis toxoid; Pre-dose 1	4.18 (3.74 to 4.68)	3.79 (3.37 to 4.25)		

Pertussis toxoid; Post-dose 3	109.58 (100.95 to 118.96)	76.69 (71.01 to 82.82)		
Filamentous Haemagglutinin; Pre-dose 1	6.07 (5.41 to 6.82)	5.3 (4.67 to 6.01)		
Filamentous Haemagglutinin; Post-dose 3	40.1 (36.7 to 43.82)	70.22 (65.08 to 75.77)		
Pertactin; Pre-dose 1	3.78 (3.36 to 4.24)	3.6 (3.23 to 4.03)		
Pertactin; Post-dose 3	33.31 (29.28 to 37.91)	64.08 (57.12 to 71.89)		
Fimbriae; Pre-dose 1	10.41 (8.93 to 12.14)	12.15 (10.29 to 14.35)		
Fimbriae; Post-dose 3	206.94 (183.56 to 233.3)	3.77 (3.3 to 4.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers (GMTs) of Antibodies to Vaccine Antigens Before and Following a Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Summary of Geometric Mean Titers (GMTs) of Antibodies to Vaccine Antigens Before and Following a Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Polyribosylribitol Phosphate (PRP) antibodies were assessed by radioimmunoassay. Diphtheria and poliovirus antibodies were assessed by serum neutralization assay. Tetanus and pneumococcal antigens antibodies were assessed by enzyme-linked immunosorbent assay.

End point type	Secondary

End point timeframe:

Pre- and Post-Booster 4 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	207		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
PRP; Pre-dose 4	0.36 (0.29 to 0.45)	0.14 (0.12 to 0.17)		
PRP; Post-dose 4	32.41 (27.35 to 38.39)	19.26 (15.77 to 23.54)		
Diphtheria; Pre-dose 4	0.13 (0.11 to 0.16)	0.11 (0.09 to 0.13)		
Diphtheria; Post-dose 4	4.72 (4.15 to 5.36)	3.83 (3.38 to 4.34)		

Tetanus; Pre-dose 4	0.17 (0.14 to 0.2)	0.13 (0.11 to 0.16)		
Tetanus; Post-dose 4	3.03 (2.7 to 3.4)	2.77 (2.49 to 3.1)		
Pertussis toxoid; Pre-dose 4	16.14 (14.48 to 18)	11.6 (10.31 to 13.04)		
Pertussis toxoid; Post-dose 4	174.68 (157.78 to 193.39)	110.43 (100 to 121.94)		
Filamentous haemagglutinin; Pre-dose 4	12.44 (11 to 14.07)	16.56 (14.62 to 18.76)		
Filamentous haemagglutinin; Post-dose 4	70.3 (63.1 to 78.31)	161.68 (146.75 to 178.13)		
Pertactin; Pre-dose 4	5.2 (4.54 to 5.95)	7.42 (6.41 to 8.58)		
Pertactin; Post-dose 4	79.59 (69.27 to 91.44)	177.82 (155.88 to 202.84)		
Fimbriae; Pre-dose 4	39.87 (34.65 to 45.89)	2.08 (2.01 to 2.16)		
Fimbriae; Post-dose 4	494.88 (435.45 to 562.42)	2.64 (2.33 to 2.99)		
Polio 1; Pre-dose 4	68.99 (55.45 to 85.84)	93.81 (75.26 to 116.93)		
Polio 1; Post-dose 4	2984.82 (2514.77 to 3542.73)	4554.02 (3817.41 to 5432.76)		
Polio 2; Pre-dose 4	87.8 (71.48 to 107.85)	89.58 (71.88 to 111.64)		
Polio 2; Post-dose 4	4220.46 (3573.91 to 4983.96)	5238.99 (4373.66 to 6275.52)		
Polio 3; Pre-dose 4	74.98 (59.95 to 93.77)	101.26 (82.17 to 124.79)		
Polio 3; Post-dose 4	4200.53 (3417.67 to 5162.71)	5870.72 (4875.47 to 7069.15)		
Pneumo 4; Pre-dose 4	0.42 (0.37 to 0.47)	0.43 (0.38 to 0.48)		
Pneumo 4; Post-dose 4	5.46 (4.83 to 6.17)	5.87 (5.16 to 6.67)		
Pneumo 6B; Pre-dose 4	0.42 (0.36 to 0.49)	0.44 (0.37 to 0.51)		
Pneumo 6B; Post-dose 4	8.51 (7.4 to 9.78)	8.43 (7.28 to 9.76)		
Pneumo 9V; Pre-dose 4	0.39 (0.35 to 0.44)	0.42 (0.37 to 0.48)		
Pneumo 9V; Post-dose 4	4.47 (4.01 to 4.99)	5.07 (4.5 to 5.72)		
Pneumo 14; Pre-dose 4	2.45 (2.14 to 2.8)	2.41 (2.07 to 2.8)		
Pneumo 14; Post-dose 4	17.54 (15.55 to 19.8)	18.33 (16.15 to 20.79)		
Pneumo 18C; Pre-dose 4	0.25 (0.23 to 0.28)	0.27 (0.24 to 0.31)		
Pneumo 18C; Post-dose 4	2.37 (2.11 to 2.66)	2.89 (2.55 to 3.27)		
Pneumo 19F; Pre-dose 4	0.88 (0.75 to 1.03)	0.85 (0.72 to 1)		
Pneumo 19F; Post-dose 4	5.86 (5.23 to 6.58)	6.9 (6.18 to 7.71)		

Pneumo 23F; Pre-dose 4	0.38 (0.33 to 0.44)	0.37 (0.32 to 0.43)		
Pneumo 23F; Post-dose 4	5.17 (4.51 to 5.92)	5.73 (4.96 to 6.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Booster Response Against Pertussis Antigens Before and Following Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV + Hib Vaccine Co-administered with Prevenar

End point title	Percentage of Subjects with Booster Response Against Pertussis Antigens Before and Following Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV + Hib Vaccine Co-administered with Prevenar

End point description:

Pneumococcal antigens (Pertussis toxoid [PT], Filamentous haemagglutinin [FHA], Pertactin, Fimbriae types 2 and 3) antibodies were assessed by enzyme-linked immunosorbent assay. Seroresponse for the pertussis antigens was defined as < 4X lower limit of quantitation (LLOQ) and ≥ 4XLLOQ. Booster response was defined as four fold-rise from pre-Dose 4, if pre-Dose 4 < 4XLLOQ or two fold-rise from pre-Dose 4 if pre-Dose 4 ≥ 4XLLOQ.

End point type	Secondary

End point timeframe:

Pre- and Post-dose 4 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	207		
Units: Percentage of subjects				
number (not applicable)				
Pertussis toxoid; < 4XLLOQ; Pre-dose 4	46.5	60		
Pertussis toxoid; ≥ 4XLLOQ; Pre-dose 4	53.5	40		
Pertussis toxoid; Booster response; Post-dose 4	96.7	95		
FHA; < 4XLLOQ; Pre-dose 4	47.4	32.3		
FHA; ≥ 4XLLOQ; Pre-dose 4	52.6	67.7		
FHA; Booster response; Post-dose 4	83.2	96		
Pertactin; < 4XLLOQ; Pre-dose 4	87	74.6		
Pertactin; ≥ 4XLLOQ; Pre-dose 4	13	25.4		
Pertactin; Booster response; Post-dose 4	86.9	98		
Fimbriae; < 4XLLOQ; Pre-dose 4	11.7	99.5		
Fimbriae; ≥ 4XLLOQ; Pre-dose 4	88.3	0.5		
Fimbriae; Booster response; Post-dose 4	95.7	5.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide, Diphtheria, Tetanus, Polio, and Pneumococcal Serotypes Antigens After a Booster With PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine With Prevenar

End point title	Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide, Diphtheria, Tetanus, Polio, and Pneumococcal Serotypes Antigens After a Booster With PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine With Prevenar

End point description:

Polyribosylribitol Phosphate (PRP) antibodies were assessed by radioimmunoassay. Diphtheria toxoid and poliovirus antibodies were assessed by serum neutralization assay. Tetanus toxoid and pneumococcal antigens antibodies were assessed by enzyme-linked immunosorbent assay. Seroprotection was defined as ≥ 1.0 µg/mL for PRP, ≥ 0.1 IU/mL for diphtheria and tetanus, ≥ 1:8 (dil) for poliovirus types 1, 2, and 3, and ≥ 0.35 µg/mL for pneumoccocal serotypes (4, 6B, 9V, 14, 18C, 19F, 23F).
Data show percentage of subjects with seroprotection against each vaccine antigen.

End point type	Secondary

End point timeframe:

Post-dose 4 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	207		
Units: Percentage of subjects				
number (not applicable)				
PRP	99.1	95.2		
Diphtheria	99.1	100		
Tetanus	100	100		
Polio 1	99.5	100		
Polio 2	99.5	100		
Polio 3	99.5	100		
Pneumo 4	99.5	100		
Pneumo 6B	99.5	99.5		
Pneumo 9V	99.5	100		
Pneumo 14	100	100		
Pneumo 18C	99.1	100		
Pneumo 19F	99.5	100		
Pneumo 23F	99.1	99		

Statistical analyses

Statistical analysis title	PRP; Difference in PEDIACEL - Infanrix-IPV+Hib
Statistical analysis description:	
Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for PRP antigen.	
Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	7.8

Notes:

[15] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Diphtheria;Difference in PEDIACEL-Infanrix-IPV+Hib
Statistical analysis description:	
Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Diphtheria antigen.	
Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1

Notes:

[16] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Tetanus; Difference in PEDIACEL-Infanrix-IPV+Hib
Statistical analysis description:	
Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Tetanus antigen.	
Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.8

Notes:

[17] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 1; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Polio 1 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	1.4

Notes:

[18] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 2; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Polio 2 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	1.4

Notes:

[19] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Polio 3; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Polio 3 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	1.4

Notes:

[20] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 4; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 4 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	1.4

Notes:

[21] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 6B; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 6B antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2.3

Notes:

[22] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 9V; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 9V antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	1.4

Notes:

[23] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 14; Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 14 antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.9

Notes:

[24] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 18C;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 18C antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1

Notes:

[25] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 19F;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 19F antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	1.4

Notes:

[26] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Statistical analysis title	Pneumo 23F;Difference in PEDIACEL-Infanrix-IPV+Hib

Statistical analysis description:

Difference in seroprotection rates in PEDIACEL and Infanrix-IPV+Hib for Pneumo 23F antigen.

Comparison groups	PEDIACEL v Infanrix-IPV+Hib

Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Parameter estimate	Difference in PEDIACEL-Infanrix-IPV+Hib
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	2.7

Notes:

[27] - The difference in the seroprotection rate was defined as PEDIACEL seroprotection rate minus Infanrix-IPV+Hib seroprotection rate. Non-inferiority was achieved if the lower limit of the two-sided 95% confidence interval of PEDIACEL - Infanrix-IPV+Hib is >-10% for PRP and pneumococcal serotypes and >-5% for diphtheria, tetanus and polio. The confidence intervals were computed using the Wilson score method without continuity correction. PEDIACEL was non-inferior to Infanrix-IPV+Hib.

Secondary: Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Any Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Any Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, Irritability.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-primary series vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	292		
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness	61.2	63.1		
Injection site Erythema	66.7	66.9		
Injection site Swelling	51.5	47.2		
Fever	51.5	50.7		
Vomiting	28.2	26.6		
Crying abnormal	59.1	57.6		
Drowsiness	54.3	59		
Appetite lost	47.1	45.2		
Irritability	69.4	68.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Each Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Each Primary Series Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 systemic reactions: Fever, ≥ 39.6°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Secondary

End point timeframe:

Post-dose 1 (2 months), post-dose 2 (3 months), and post-dose 3 (4 months)

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	292		
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; Post-dose 1 (2 months)	45	45		
Grade 3 Inj. site Tenderness; Post-dose 1 (2 mths)	4.1	1.7		
Any Inj. site Tenderness; Post-dose 2 (3 months)	37.8	38.3		
Grade 3 Inj. site Tenderness; Post-dose 2 (3 mths)	1	0		
Any Inj. site Tenderness; Post-dose 3 (4 months)	33	33.1		
Grade 3 Inj. site Tenderness; Post-dose 3 (4 mths)	0.3	0.4		
Any Inj. site Erythema; Post-dose 1 (2 months)	38.5	40.8		
Grade 3 Inj. site Erythema; Post-dose 1 (2 months)	1.7	0.7		
Any Inj. site Erythema; Post-dose 2 (3 months)	46.9	47.4		
Grade 3 Inj. site Erythema; Post-dose 2 (3 months)	1	0		
Any Inj. site Erythema; Post-dose 3 (4 months)	46.2	47.3		
Grade 3 Inj. site Erythema; Post-dose 3 (4 months)	0.7	0.4		
Any Inj. site Swelling; Post-dose 1 (2 months)	26.8	27.4		
Grade 3 Inj. site Swelling; Post-dose 1 (2 months)	1	0		

Any Inj. site Swelling; Post-dose 2 (3 months)	29.9	33.9		
Grade 3 Inj. site Swelling; Post-dose 2 (3 months)	1	0		
Any Inj. site Swelling; Post-dose 3 (4 months)	38.2	32.4		
Grade 3 Inj. site Swelling; Post-dose 3 (4 months)	0.7	0		
Any Fever; Post-dose 1 (2 months)	21	24		
Grade 3 Fever; Post-dose 1 (2 months)	0	0.3		
Any Fever; Post-dose 2 (3 months)	29.5	30.5		
Grade 3 Fever; Post-dose 2 (3 months)	0	0		
Any Fever; Post-dose 3 (4 months)	26.8	28.6		
Grade 3 Fever; Post-dose 3 (4 months)	0	0.7		
Any Vomiting; Post-dose 1 (2 months)	17.5	14.5		
Grade 3 Vomiting; Post-dose 1 (2 months)	1	0		
Any Vomiting; Post-dose 2 (3 months)	12.5	11.5		
Grade 3 Vomiting; Post-dose 2 (3 months)	0.3	0.3		
Any Vomiting; Post-dose 3 (4 months)	11.8	8.9		
Grade 3 Vomiting; Post-dose 3 (4 months)	0.7	0		
Any Crying abnormal; Post-dose 1 (2 months)	45	41.4		
Grade 3 Crying abnormal; Post-dose 1 (2 months)	2.4	1		
Any Crying abnormal; Post-dose 2 (3 months)	34.6	36.2		
Grade 3 Crying abnormal; Post-dose 2 (3 months)	1	2.4		
Any Crying abnormal; Post-dose 3 (4 months)	29.5	26.7		
Grade 3 Crying abnormal; Post-dose 3 (4 months)	2.4	1.8		
Any Drowsiness; Post-dose 1 (2 months)	41.2	39		
Grade 3 Drowsiness; Post-dose 1 (2 months)	4.5	2.8		
Any Drowsiness; Post-dose 2 (3 months)	32.9	38		
Grade 3 Drowsiness; Post-dose 2 (3 months)	0	0.7		
Any Drowsiness; Post-dose 3 (4 months)	24.7	26.7		
Grade 3 Drowsiness; Post-dose 3 (4 months)	1.4	1.1		
Any Appetite lost; Post-dose 1 (2 months)	26.8	26.9		
Grade 3 Appetite lost; Post-dose 1 (2 months)	0.3	0		
Any Appetite lost; Post-dose 2 (3 months)	22.8	28.2		
Grade 3 Appetite lost; Post-dose 2 (3 months)	0.3	1		
Any Appetite lost; Post-dose 3 (4 months)	25	22.1		
Grade 3 Appetite lost; Post-dose 3 (4 months)	0	0.7		
Any Irritability; Post-dose 1 (2 months)	53.3	50.3		

Grade 3 Irritability; Post-dose 1 (2 months)	5.2	3.4		
Any Irritability; Post-dose 2 (3 months)	48.1	48.8		
Grade 3 Irritability; Post-dose 2 (3 months)	1.7	3.8		
Any Irritability; Post-dose 3 (4 months)	42	35.6		
Grade 3 Irritability; Post-dose 3 (4 months)	2.4	1.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point title	Percentage of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Booster Vaccination with Either PEDIACEL Co-administered with Prevenar or Infanrix-IPV+Hib Vaccine Co-administered with Prevenar

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 systemic reactions: Fever, ≥ 39.6°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Secondary

End point timeframe:

Post-dose 4 vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	264		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness	56.9	63.5		
Grade 3 Injection site Tenderness	2.6	2.7		
Any Injection site Erythema	55.8	58.9		
Grade 3 Injection site Erythema	2.2	3		
Any Injection site Swelling	29.2	40.3		
Grade 3 Injection site Swelling	1.5	0.8		
Any Fever	48.3	52.9		
Grade 3 Fever	1.5	3		
Any Vomiting	4.9	8.7		
Grade 3 Vomiting	0	0		
Any Crying abnormal	32.2	34.2		
Grade 3 Crying abnormal	0.4	0.4		
Any Drowsiness	30.3	32.7		

Grade 3 Drowsiness	0	0		
Any Appetite lost	33.7	35.4		
Grade 3 Appetite lost	0.4	1.5		
Any Irritability	52.1	53.2		
Grade 3 Irritability	0.7	1.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 7 post-dose 4 vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	PEDIACEL (Primary and Booster)

Reporting group description:

Infants received PEDIACEL co-administered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age and as a booster at 12 to 18 months of age.

Reporting group title	Infanrix-IPV+Hib (Primary and Booster)

Reporting group description:

Infants received Infanrix-IPV+Hib coadministered with Prevenar as a primary series vaccination at 2, 3, and 4 months of age and as a booster vaccination at 12 to 18 months of age.

Serious adverse events	PEDIACEL (Primary and Booster)	Infanrix-IPV+Hib (Primary and Booster)	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 292 (8.56%)	22 / 292 (7.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood immunoglobulin A decreased			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Chemical poisoning			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skull fracture			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Circumcision			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 292 (0.34%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nystagmus			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope vasovagal			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immunodeficiency			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatosplenomegaly			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	4 / 292 (1.37%)	6 / 292 (2.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	5 / 292 (1.71%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis acute			
subjects affected / exposed	2 / 292 (0.68%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cystitis			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 292 (0.68%)	3 / 292 (1.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal abscess			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 292 (0.00%)	2 / 292 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Roseola			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 292 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 292 (0.68%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	1 / 292 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PEDIACEL (Primary and Booster)	Infanrix-IPV+Hib (Primary and Booster)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 292 (69.18%)	198 / 292 (67.81%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	158 / 292 (54.11%)	171 / 292 (58.56%)	
occurrences (all)	158	171	
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	178 / 292 (60.96%)	167 / 292 (57.19%)	
occurrences (all)	178	167	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	194 / 292 (66.44%)	194 / 292 (66.44%)	
occurrences (all)	194	194	
Injection site Swelling			
alternative assessment type: Systematic			

subjects affected / exposed	150 / 292 (51.37%)	137 / 292 (46.92%)	
occurrences (all)	150	137	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	150 / 292 (51.37%)	142 / 292 (48.63%)	
occurrences (all)	150	142	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 292 (28.08%)	77 / 292 (26.37%)	
occurrences (all)	82	77	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	172 / 292 (58.90%)	167 / 292 (57.19%)	
occurrences (all)	172	167	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	202 / 292 (69.18%)	198 / 292 (67.81%)	
occurrences (all)	202	198	
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed	137 / 292 (46.92%)	131 / 292 (44.86%)	
occurrences (all)	137	131	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2006	The new location of the PRP antibody testing and the list of investigators were updated.
04 December 2007	The new location of the Polio antibody testing was updated; the precision of the Restricted Concomitant Therapy Category 2 definition was increased to reflect the timing of the blood draw for the immunogenicity assessment; the definition of fever was updated; the temperature conditions for the storage of serum were clarified, and the Clinical Trial Leader was updated in the List of Investigators.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21807056