Clinical trial results:
A randomised, controlled, double blind study of the 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 given to infants using a three dose immunisation schedule (“Nordic schedule” 3-5-12 months)

Summary

EudraCT number	2005-004133-17
Trial protocol	FI SE
Global end of trial date	28 May 2007

Results information

Result version number	v1
This version publication date	05 February 2016
First version publication date	30 January 2015

Trial information

Trial identification

Sponsor protocol code	A5I15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00287092
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	Associate Vice President, Clinical Development, Sanofi Pasteur Inc, 1 570 957 3570, emilia.jordanov@sanofipasteur.com
Scientific contact	Associate Vice President, Clinical Development, 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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 September 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity post-dose 3 of PEDIACEL® (Group A) and Infanrix™–IPV+Hib (Group B) when administered to infants at 3, 5 and 12 months of age.

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 were also available on site in case of any immediate allergic reactions.

Background therapy:

The three-dose vaccination schedule assessed in this study is the vaccine schedule used in Nordic countries for infant routine vaccinations.

Evidence for comparator:

The active comparator, Infanrix-IPV+Hib, is a current pentavalent standard of care vaccine in Nordic countries.

Actual start date of recruitment	10 February 2006
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	Sweden: 15
Country: Number of subjects enrolled	Finland: 790
Worldwide total number of subjects	805
EEA total number of subjects	805

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	805
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 from 10 February 2006 to 28 May 2007 in 12 clinical centers in Finland and 1 clinical center in Sweden.

Pre-assignment

Screening details:

A total of 807 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated. However, Two subjects randomised to the PEDIACEL group did not report safety data and therefore were not part of the safety analysis set and in this report.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Assessor

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	PEDIACEL

Arm description:

Subjects who received 3 doses of PEDIACEL (diphtheria, tetanus, 5 component acellular pertussis, inactivated poliomyelitis Haemophilus influenzae type B conjugate vaccine [adsorbed]) administered at 3, 5, and 12 months.

Arm type	Experimental
Investigational medicinal product name	PEDIACEL®
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 in the anterolateral aspect of the upper thigh at 3 and 5 months and in the deltoid muscle at 12 months.

Arm title	Infanrix-IPV+Hib

Arm description:

Subjects who received Infanrix-IPV+Hib (diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated Haemophilus influenzae type b vaccine) administered at 3, 5, and 12 months.

Arm type	Active comparator
Investigational medicinal product name	Infanrix™-IPV+Hib
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 anterolateral aspect of the upper thigh at 3 and 5 months and in the deltoid muscle at 12 months.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Subjects and assessors were blinded to the product administered. Each study site designated one person who remained unblinded to the randomization procedure and vaccine administration. This person was responsible for the preparation and administration of the vaccine and did not participate in the assessment of the subject.

Number of subjects in period 1	PEDIACEL	Infanrix-IPV+Hib
Started	400	405
Completed	380	393
Not completed	20	12
Adverse event, serious fatal	7	-
Consent withdrawn by subject	7	4
Adverse event, non-fatal	4	5
Lost to follow-up	1	2
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	PEDIACEL
Reporting group description:	
Subjects who received 3 doses of PEDIACEL (diphtheria, tetanus, 5 component acellular pertussis, inactivated poliomyelitis Haemophilus influenzae type B conjugate vaccine [adsorbed]) administered at 3, 5, and 12 months.	
Reporting group title	Infanrix-IPV+Hib
Reporting group description:	
Subjects who received Infanrix-IPV+Hib (diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated Haemophilus influenzae type b vaccine) administered at 3, 5, and 12 months.	

Reporting group values	PEDIACEL	Infanrix-IPV+Hib	Total
Number of subjects	400	405	805
Age categorical			
The number of subjects reported are based on the Safety Analysis Set (N=805).			
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)	400	405	805
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	2.9	2.9	
standard deviation	± 0.27	± 0.27	-
Gender categorical			
Units: Subjects			
Female	179	194	373
Male	221	211	432

End points

End points reporting groups

Reporting group title	PEDIACEL

Reporting group description:

Subjects who received 3 doses of PEDIACEL (diphtheria, tetanus, 5 component acellular pertussis, inactivated poliomyelitis Haemophilus influenzae type B conjugate vaccine [adsorbed]) administered at 3, 5, and 12 months.

Reporting group title	Infanrix-IPV+Hib

Reporting group description:

Subjects who received Infanrix-IPV+Hib (diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated Haemophilus influenzae type b vaccine) administered at 3, 5, and 12 months.

Primary: Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine[1]

End point description:

Antibody titers were measured for polyribosylribitol phosphate capsular polysaccharide (PRP) using radioimmunoassay, for diphtheria and poliovirus by serum neutralization (SN) assay, and for tetanus by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as a titer ≥1.0 µg/mL for PRP, ≥0.1 IU/mL for diphtheria and tetanus, and ≥1:8 [1/dil] for poliovirus 1, 2, and 3.

End point type	Primary

End point timeframe:

1 month post-dose 3

Notes:

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

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Subjects				
number (not applicable)				
PRP (≥1.0 µg/mL)	303	330		
Diphtheria toxoid (≥0.1 IU/mL)	309	308		
Tetanus toxoid (≥0.1 IU/mL)	325	339		
Polio 1 (≥1:8 1/dil)	322	336		
Polio 2 (≥1:8 1/dil)	322	336		
Polio 3 (≥1:8 1/dil)	319	335		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Seroresponse Against Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Number of Subjects with Seroresponse Against Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine[2]

End point description:

Antibody titers were measured for pertussis antigens by ELISA. Seroresponse 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 for pertussis toxoid (PT), pertactin (PRN), and fimbriae types 2 and 3 (FIM) and for filamentous haemagglutinin (FHA) seroresponse 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:

1 month post-dose 3

Notes:

[2] - 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 the study vaccine administered for this outcome.

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Subjects				
number (not applicable)				
PT	318	340		
FHA	321	340		
PRN	311	335		
FIM	310	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Polyribosylribitol Phosphate Capsular Polysaccharide (PRP) Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Polyribosylribitol Phosphate Capsular Polysaccharide (PRP) Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for PRP using radioimmunassay.

End point type	Secondary

End point timeframe:

1 month post-dose 3

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Titers				
geometric mean (confidence interval 95%)				
PRP (µg/mL)	12.2 (10.46 to 14.24)	17.54 (15.38 to 20.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for polyribosylribitol phosphate capsular polysaccharide (PRP) using radioimmunassay, for diphtheria and poliovirus by serum neutralization (SN) assay, and for tetanus by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as post-dose 2 titers ≥0.15 µg/mL for PRP, ≥0.01 IU/mL for diphtheria and tetanus, and ≥1:8 [1/dil] for poliovirus 1, 2, and 3.

End point type	Secondary

End point timeframe:

1 month post-dose 2

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Subjects				
number (not applicable)				
PRP (≥0.15 µg/mL)	214	234		
Diphtheria toxoid (≥0.01 IU/mL)	297	318		
Tetanus toxoid (≥0.01 IU/mL)	316	334		
Polio 1 (≥1:8 1/dil)	304	323		
Polio 2 (≥1:8 1/dil)	290	312		
Polio 3 (≥1:8 1/dil)	300	321		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria, Tetanus and Polio Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for PRP using radioimmunassay, for diphtheria and poliovirus by serum neutralization (SN) assay, and for tetanus by enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary

End point timeframe:

1 month post-dose 2

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Titers				
geometric mean (confidence interval 95%)				
PRP (µg/mL)	0.4 (0.33 to 0.5)	0.44 (0.36 to 0.54)		
Diphtheria toxoid (IU/mL)	0.07 (0.06 to 0.08)	0.05 (0.04 to 0.05)		
Tetanus toxoid (IU/mL)	0.43 (0.39 to 0.47)	0.66 (0.61 to 0.72)		
Polio 1 (1/dil)	100.92 (83.5 to 121.99)	173.13 (142.53 to 210.3)		
Polio 2 (1/dil)	34.48 (29.1 to 40.86)	37.77 (32.02 to 44.56)		
Polio 3 (1/dil)	89.51 (74.07 to 108.15)	158.7 (129.63 to 194.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Seroresponse Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Number of Subjects with Seroresponse Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for pertussis antigens by ELISA. Seroresponse was defined as post-dose 2 ≥ 4 EU/mL if pre-dose 1 < 4 EU/mL or post-dose 2 ≥ pre-dose 1 if pre-dose 1 ≥ 4 EU/mL for pertussis toxoid (PT), pertactin (PRN), and fimbriae types 2 and 3 (FIM) and for filamentous haemagglutinin (FHA) seroresponse was defined as post-dose 2 ≥ 3 EU/mL if pre-dose 1 < 3 EU/mL or post-dose 2 ≥ pre-dose 1 if pre-dose 1 ≥ 3 EU/mL.

End point type	Secondary

End point timeframe:

1 month post-dose 2

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Subjects				
number (not applicable)				
PT	306	326		
FHA	311	320		
PRN	246	300		
FIM	297	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ≥ 2- and ≥ 4-Fold Increases in Antibodies Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Percentage of Subjects with ≥ 2- and ≥ 4-Fold Increases in Antibodies Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM]) by ELISA. A fold increase was defined as post-dose 2/pre-dose 1.

End point type	Secondary

End point timeframe:

Pre-dose 1 to 1 month post-dose 2

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Percentage of subjects				
number (not applicable)				
PT ≥2-fold increase	94.9	96.4		
PT ≥4-fold increase	87.7	90.4		
FHA ≥2-fold increase	94.9	92.7		
FHA ≥4-fold increase	85.7	84.9		
PRN ≥2-fold increase	70.4	85.5		
PRN ≥4-fold increase	55.3	75.2		
FIM ≥2-fold increase	91	0.6		
FIM ≥4-fold increase	85.5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Pertussis Antigens Post-dose 2 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM]) by ELISA.

End point type	Secondary

End point timeframe:

1 month post-dose 2

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Titers				
geometric mean (confidence interval 95%)				
PT (EU/mL)	77.3 (71.18 to 83.94)	72.76 (67.63 to 78.28)		
FHA (EU/mL)	61.54 (57.12 to 66.29)	73.72 (68.29 to 79.57)		
PRN (EU/mL)	25.21 (21.97 to 28.93)	56.89 (50.66 to 63.89)		
FIM (EU/mL)	131 (115.09 to 149.12)	2.59 (2.43 to 2.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria and Tetanus Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Number of Subjects with Seroprotection Against Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP), Diphtheria and Tetanus Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for PRP using radioimmunassay, for diphtheria by serum neutralization (SN) assay, and for tetanus by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as post-dose 3 titers ≥0.15 µg/mL for PRP and ≥0.01 IU/mL for diphtheria and tetanus.

End point type	Secondary

End point timeframe:

1 month post-dose 3

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Subjects				
number (not applicable)				
PRP (≥0.15 µg/mL)	322	340		
Diphtheria toxoid (≥0.01 IU/mL)	319	334		
Tetanus toxoid (≥0.01 IU/mL)	325	340		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Diphtheria, Tetanus and Polio Antibodies Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Geometric Mean Titers (GMTs) of Diphtheria, Tetanus and Polio Antibodies Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for diphtheria and poliovirus by serum neutralization (SN) assay and for tetanus by enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary

End point timeframe:

1 month post-dose 3

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Titers				
geometric mean (confidence interval 95%)				
Diphtheria toxoid (IU/mL)	1.28 (1.09 to 1.5)	0.7 (0.6 to 0.82)		
Tetanus toxoid (IU/mL)	3.63 (3.35 to 3.93)	3.91 (3.63 to 4.22)		

Polio 1 (1/dil)	1260.2 (1081.59 to 1468.31)	3419.53 (2987.52 to 3914.02)		
Polio 2 (1/dil)	853.26 (709.42 to 1026.26)	1870.3 (1584.01 to 2208.33)		
Polio 3 (1/dil)	1204.14 (991.42 to 1462.51)	3536.37 (2984.8 to 4189.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ≥ 2- and ≥ 4-Fold Increases in Antibodies to Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Percentage of Subjects with ≥ 2- and ≥ 4-Fold Increases in Antibodies to Pertussis Antigens Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM]) by ELISA. A fold increase was defined as post-dose 3/pre-dose 1.

End point type	Secondary

End point timeframe:

Pre-dose 1 to 1 month post-dose 3

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Percentage of subjects				
number (not applicable)				
PT ≥2-fold increase	97.8	98.5		
PT ≥4-fold increase	94.7	96.5		
FHA ≥2-fold increase	98.8	99.7		
FHA ≥4-fold increase	95.7	96.2		
PRN ≥2-fold increase	93.8	97.6		
PRN ≥4-fold increase	87.2	94.4		
FIM ≥2-fold increase	96	2.4		
FIM ≥4-fold increase	94.4	0.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Pertussis Antibodies Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point title	Geometric Mean Titers (GMTs) of Pertussis Antibodies Post-dose 3 Vaccination with Either PEDIACEL or Infanrix-IPV+Hib Vaccine

End point description:

Antibody titers were measured for pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM]) by ELISA.

End point type	Secondary

End point timeframe:

1 month post-dose 3

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	341		
Units: Titers				
geometric mean (confidence interval 95%)				
PT (EU/mL)	150.3 (138.48 to 163.14)	118.55 (110.4 to 127.29)		
FHA (EU/mL)	149.51 (138.45 to 161.46)	215.55 (200.38 to 231.87)		
PRN (EU/mL)	98.08 (88.97 to 108.13)	206.71 (188.42 to 226.78)		
FIM (EU/mL)	439.64 (384.42 to 502.79)	2.27 (2.15 to 2.4)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited Injection Site Reactions: Tenderness, Erythema, and Swelling. Solicited Systemic Reactions: Temperature (Fever), Vomiting, Crying abnormal, Drowsiness, Appetite loss, Irritability.

End point type	Secondary

End point timeframe:

Day 0 to Day 7 post any vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	405		
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness	59.5	60.2		
Injection site Erythema	61.3	62		
Injection site Swelling	44	45.9		
Fever (≥38 C)	68.7	70.4		
Vomiting	30.5	31.1		
Crying abnormal	78.5	75.8		
Drowsiness	76.8	73.3		
Appetite loss	56.3	60.5		
Irritability	88.8	89.6		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited Injection Site Reactions: Tenderness, Erythema, and Swelling. Solicited Systemic Reactions: Temperature (Fever), Vomiting, Crying abnormal, Drowsiness, Appetite loss, Irritability. Grade 3 Injection Site: Tenderness – Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling – ≥5 cm. Grade 3 Solicited 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 loss – Refuses ≥3 feeds/meals or refuses most feeds/meals; Irritability – Inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to 12 months post vaccination

End point values	PEDIACEL	Infanrix-IPV+Hib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	405		
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness Post-dose 1	37.6	29.6		
Grade 3 Injection site Tenderness Post-dose 1	6.5	1		
Injection site Tenderness Post-dose 2	26.2	26.6		
Grade 3 Injection site Tenderness Post-dose 2	4.6	2		

Injection site Tenderness Post-dose 3	36.2	46.8		
Grade 3 Injection site Tenderness Post-dose 3	2.6	3.3		
Injection site Erythema Post-dose 1	26.8	21.7		
Grade 3 Injection site Erythema Post-dose 1	3	1.2		
Injection site Erythema Post-dose 2	33.6	32.4		
Grade 3 Injection site Erythema Post-dose 2	0.5	0.3		
Injection site Erythema Post-dose 3	47.2	49.9		
Grade 3 Injection site Erythema Post-dose 3	3.9	4.9		
Injection site Swelling Post-dose 1	20.8	14.8		
Grade 3 Injection site Swelling Post-dose 1	2.5	0.5		
Injection site Swelling Post-dose 2	22.1	20.6		
Grade 3 Injection site Swelling Post-dose 2	1	0.8		
Injection site Swelling Post-dose 3	27.6	34.7		
Grade 3 Injection site Swelling Post-dose 3	0.8	3.3		
Fever Post-dose 1	25.7	24		
Grade 3 Fever Post-dose 1	0	0		
Fever Post-dose 2	43	35.5		
Grade 3 Fever Post-dose 2	0.5	0.8		
Fever Post-dose 3	39.8	53.9		
Grade 3 Fever Post-dose 3	2.1	1.8		
Vomiting Post-dose 1	17.3	15.3		
Grade 3 Vomiting Post-dose 1	1	0.5		
Vomiting Post-dose 2	14.8	16.3		
Grade 3 Vomiting Post-dose 2	0	0.8		
Vomiting Post-dose 3	7.9	11.8		
Grade 3 Vomiting Post-dose 3	1	0.3		
Crying abnormal Post-dose 1	59.6	52.1		
Grade 3 Crying abnormal Post-dose 1	3	2		
Crying abnormal Post-dose 2	50.1	45.5		
Grade 3 Crying abnormal Post-dose 2	1.8	2.8		
Crying abnormal Post-dose 3	43.8	51.2		
Grade 3 Crying abnormal Post-dose 3	1.6	2.6		
Drowsiness Post-dose 1	56.9	50.9		
Grade 3 Drowsiness Post-dose 1	2	2.2		
Drowsiness Post-dose 2	45.5	36.7		
Grade 3 Drowsiness Post-dose 2	1.3	0.8		
Drowsiness Post-dose 3	36.7	47.6		
Grade 3 Drowsiness Post-dose 3	0.8	1		
Appetite loss Post-dose 1	26.8	24.2		
Grade 3 Appetite loss Post-dose 1	0.5	1.5		
Appetite loss Post-dose 2	26.2	20.4		
Grade 3 Appetite loss Post-dose 2	0.8	1.3		
Appetite loss Post-dose 3	36.5	44.7		
Grade 3 Appetite loss Post-dose 3	4.2	4.6		
Irritability Post-dose 1	70.7	65.4		
Grade 3 Irritability Post-dose 1	6	5.4		
Irritability Post-dose 2	60.8	57.5		

Grade 3 Irritability Post-dose 2	4.1	4.5		
Irritability Post-dose 3	57	70.2		
Grade 3 Irritability Post-dose 3	1.8	3.1		

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 (post-vaccination) up to Day 28 post-any vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	7.1

Reporting groups	
Reporting group title	PEDIACEL
Reporting group description:	
Subjects who received 3 doses of PEDIACEL (diphtheria, tetanus, 5 component acellular pertussis, inactivated poliomyelitis Haemophilus influenzae type B conjugate vaccine [adsorbed]) administered at 3, 5, and 12 months.	
Reporting group title	Infanrix-IPV+Hib
Reporting group description:	
Subjects who received Infanrix-IPV+Hib (diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and adsorbed conjugated Haemophilus influenzae type b vaccine) administered at 3, 5, and 12 months.	

Serious adverse events	PEDIACEL	Infanrix-IPV+Hib	
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 400 (8.50%)	22 / 405 (5.43%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	2 / 400 (0.50%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Growth retardation			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Anaphylactic shock			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 400 (0.00%)	2 / 405 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Medical observation			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
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			
Thermal burn			
subjects affected / exposed	1 / 400 (0.25%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital atrial septal defect			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patent ductus arteriosus			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Convulsion			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorder			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 400 (0.00%)	2 / 405 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (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			
Abscess neck			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	3 / 400 (0.75%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 400 (0.50%)	2 / 405 (0.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis acute			
subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 400 (1.00%)	3 / 405 (0.74%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis rotavirus			
subjects affected / exposed	2 / 400 (0.50%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	2 / 400 (0.50%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 400 (0.25%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (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	2 / 400 (0.50%)	3 / 405 (0.74%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	3 / 400 (0.75%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 405 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			

subjects affected / exposed	0 / 400 (0.00%)	1 / 405 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PEDIACEL	Infanrix-IPV+Hib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	355 / 400 (88.75%)	363 / 405 (89.63%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	307 / 400 (76.75%)	297 / 405 (73.33%)	
occurrences (all)	307	297	
General disorders and administration site conditions			
Injection site Haemorrhage			
subjects affected / exposed	26 / 400 (6.50%)	27 / 405 (6.67%)	
occurrences (all)	28	27	
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	238 / 400 (59.50%)	244 / 405 (60.25%)	
occurrences (all)	238	244	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	245 / 400 (61.25%)	251 / 405 (61.98%)	
occurrences (all)	245	251	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	176 / 400 (44.00%)	186 / 405 (45.93%)	
occurrences (all)	176	186	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[1]	274 / 399 (68.67%)	285 / 405 (70.37%)	
occurrences (all)	274	285	
Gastrointestinal disorders			

Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	122 / 400 (30.50%)	126 / 405 (31.11%)	
occurrences (all)	122	126	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	314 / 400 (78.50%)	307 / 405 (75.80%)	
occurrences (all)	314	307	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	355 / 400 (88.75%)	363 / 405 (89.63%)	
occurrences (all)	355	363	
Metabolism and nutrition disorders			
Appetite loss			
alternative assessment type: Systematic			
subjects affected / exposed	225 / 400 (56.25%)	245 / 405 (60.49%)	
occurrences (all)	225	245	

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 number presented are those exposed subjects who returned the safety diary card during the solicited events period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2007	The assay descriptions of serology testing methodology and outsourcing along with the List of Investigators were updated
09 May 2007	The serology testing location, safety definitions, storage conditions of sera, and the List of Investigators were updated. The amended protcol was submitted on 20 December 2007.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported