



## 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          | v2 (current)  |
| This version publication date  | 27 November 2016  |
| First version publication date | 30 January 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Change of primary and back up users</li></ul> |

### 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                    |
| Roles blinded                | Subject, Assessor, Investigator |

Blinding implementation details:

Not applicable

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |          |
|------------------|----------|
| <b>Arm title</b> | 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.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 1</b> | 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:<br>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:<br>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 <sup>[1]</sup> |
| End point description:<br>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 $\geq 1.0$ $\mu\text{g/mL}$ for PRP, $\geq 0.1$ IU/mL for diphtheria and tetanus, and $\geq 1:8$ [1/dil] for poliovirus 1, 2, and 3. |  |
| End point type  | Primary  |
| End point timeframe:<br>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 ( $\geq 1.0$ $\mu\text{g/mL}$ )   | 303             | 330              |  |  |
| Diphtheria toxoid ( $\geq 0.1$ IU/mL) | 309             | 308              |  |  |
| Tetanus toxoid ( $\geq 0.1$ IU/mL)    | 325             | 339              |  |  |
| Polio 1 ( $\geq 1:8$ 1/dil)           | 322             | 336              |  |  |
| Polio 2 ( $\geq 1:8$ 1/dil)           | 322             | 336              |  |  |
| Polio 3 ( $\geq 1:8$ 1/dil)           | 319             | 335              |  |  |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Antibody titers were measured for pertussis antigens by ELISA. Seroresponse was defined as post-dose 3  $\geq$  4 EU/mL if pre-dose 1 < 4 EU/mL or post-dose 3  $\geq$  pre-dose 1 if pre-dose 1  $\geq$  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  $\geq$  3 EU/mL if pre-dose 1 < 3 EU/mL or post-dose 3  $\geq$  pre-dose 1 if pre-dose 1  $\geq$  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               |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**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**

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|                 |   |
|-----------------|---|
| 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 radioimmunoassay, 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  $\geq 0.15$  µg/mL for PRP,  $\geq 0.01$  IU/mL for diphtheria and tetanus, and  $\geq 1:8$  [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 ( $\geq 0.15$ µg/mL)               | 214             | 234              |  |  |
| Diphtheria toxoid ( $\geq 0.01$ IU/mL) | 297             | 318              |  |  |
| Tetanus toxoid ( $\geq 0.01$ IU/mL)    | 316             | 334              |  |  |
| Polio 1 ( $\geq 1:8$ 1/dil)            | 304             | 323              |  |  |
| Polio 2 ( $\geq 1:8$ 1/dil)            | 290             | 312              |  |  |
| Polio 3 ( $\geq 1:8$ 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 radioimmunoassay, 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  $\geq 4$  EU/mL if pre-dose 1  $< 4$  EU/mL or post-dose 2  $\geq$  pre-dose 1 if pre-dose 1  $\geq 4$  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  $\geq 3$  EU/mL if pre-dose 1  $< 3$  EU/mL or post-dose 2  $\geq$  pre-dose 1 if pre-dose 1  $\geq 3$  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 $\geq 2$ - and $\geq 4$ -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 $\geq 2$ - and $\geq 4$ -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 $\geq 2$ -fold increase    | 94.9            | 96.4             |  |  |
| PT $\geq 4$ -fold increase    | 87.7            | 90.4             |  |  |
| FHA $\geq 2$ -fold increase   | 94.9            | 92.7             |  |  |
| FHA $\geq 4$ -fold increase   | 85.7            | 84.9             |  |  |
| PRN $\geq 2$ -fold increase   | 70.4            | 85.5             |  |  |
| PRN $\geq 4$ -fold increase   | 55.3            | 75.2             |  |  |
| FIM $\geq 2$ -fold increase   | 91              | 0.6              |  |  |
| FIM $\geq 4$ -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 radioimmunoassay, for diphtheria by serum neutralization (SN) assay, and for tetanus by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as post-dose 3 titers  $\geq 0.15$   $\mu\text{g/mL}$  for PRP and  $\geq 0.01$  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 ( $\geq 0.15$ $\mu\text{g/mL}$ )   | 322             | 340              |  |  |
| Diphtheria toxoid ( $\geq 0.01$ IU/mL) | 319             | 334              |  |  |
| Tetanus toxoid ( $\geq 0.01$ 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<br>(1081.59 to<br>1468.31) | 3419.53<br>(2987.52 to<br>3914.02) |  |  |
| Polio 2 (1/dil) | 853.26 (709.42<br>to 1026.26)     | 1870.3<br>(1584.01 to<br>2208.33)  |  |  |
| Polio 3 (1/dil) | 1204.14<br>(991.42 to<br>1462.51) | 3536.37<br>(2984.8 to<br>4189.86)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with $\geq 2$ - and $\geq 4$ -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 $\geq 2$ - and $\geq 4$ -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 $\geq 2$ -fold increase    | 97.8            | 98.5             |  |  |
| PT $\geq 4$ -fold increase    | 94.7            | 96.5             |  |  |
| FHA $\geq 2$ -fold increase   | 98.8            | 99.7             |  |  |
| FHA $\geq 4$ -fold increase   | 95.7            | 96.2             |  |  |
| PRN $\geq 2$ -fold increase   | 93.8            | 97.6             |  |  |
| PRN $\geq 4$ -fold increase   | 87.2            | 94.4             |  |  |
| FIM $\geq 2$ -fold increase   | 96              | 2.4              |  |  |
| FIM $\geq 4$ -fold increase   | 94.4            | 0.3              |  |  |

## Statistical analyses

No statistical analyses for this end point

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

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|                 |   |
|-----------------|---|
| 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)        |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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

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|                 |  |
|-----------------|--|
| 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 ( $\geq 38$ 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 –  $\geq 5$  cm. Grade 3 Solicited Systemic Reactions: Fever -  $> 39.6$  C; Vomiting –  $\geq 6$  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  $\geq 3$  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

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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 %

| <b>Non-serious adverse events</b>                     | 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                           | 274 / 400 (68.50%) | 285 / 405 (70.37%) |  |
| occurrences (all)                                     | 274                | 285                |  |
| Gastrointestinal disorders                            |                    |                    |  |

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

## 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 protocol was submitted on 20 December 2007. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported