

**Clinical trial results:****Immunogenicity and Safety Study of a Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) at 3, 5, 11 to 12 Months of Age in Healthy Infants in Europe.****Summary**

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-001054-26 |
| Trial protocol | SE FI |
| Global end of trial date | 10 January 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 08 February 2016 |
| First version publication date | 14 February 2015 |

Trial information**Trial identification**

| | |
|-----------------------|-------|
| Sponsor protocol code | A3L38 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | U1111-1122-2235 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi Pasteur SA |
| Sponsor organisation address | 2, avenue Pont Pasteur, Lyon Cedex 07, France, F-69367 |
| Public contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43, emmanuel.feroldi@sanofipasteur.com |
| Scientific contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43, emmanuel.feroldi@sanofipasteur.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001201-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 12 August 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the Hexaxim vaccine to the licensed Infanrix hexa vaccine, both co-administered with Prevenar 13, in terms of seroprotection or vaccine response rates to all antigens contained in both investigational and control vaccines, 1 month after a 2+1-dose schedule.

Protection of trial subjects:

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

Background therapy:

Prevenar 13 was co-administered with both the investigational and control vaccines in order to document the concomitant administration with the investigational vaccine as compared to its co-administration with the licensed vaccine.

Evidence for comparator:

Infanrix hexa was chosen as the comparator vaccine as it was the only licensed hexavalent vaccine in Europe at the time of study start and was licensed but not used in Sweden and Finland.

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|---|------------------|
| Actual start date of recruitment | 01 November 2012 |
| 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: 43 |
| Country: Number of subjects enrolled | Finland: 511 |
| Worldwide total number of subjects | 554 |
| EEA total number of subjects | 554 |

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 | 554 |

| | |
|---------------------------|---|
| months) | |
| 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 01 November 2012 to 12 March 2014 in 11 centers in Finland and 2 centers in Sweden.

Pre-assignment

Screening details:

A total of 546 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

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 | Investigator, Subject |

Blinding implementation details:

Neither the Investigator, the subject's parent(s)/legally representative(s), nor the Sponsor knew the vaccine administered. The product preparation and administration, and the assessment of safety were performed by 2 different individuals in separate rooms. The Investigator or delegate included subjects and evaluated the immediate safety post- vaccination. The nurse/vaccinator prepared and administered the vaccine in a separate room and had sole access to the product accountability forms.

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | DTaP-IPV-HB-Hib+Prevenar 13 |

Arm description:

Subjects who received 3 doses of DTaP-IPV-HB-Hib vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Hexaxim |
| Investigational medicinal product code | DTaP-IPV-HepB-PRP-T |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL dose, intramuscular injection into the anterolateral area of the right thigh, 3 doses at 3, 5, and 11 to 12 months of age.

| | |
|------------------|---------------------------|
| Arm title | Infanrix hexa+Prevenar 13 |
|------------------|---------------------------|

Arm description:

Subjects who received 3 doses of Infanrix hexa vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Infanrix hexa |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection, Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL dose, intramuscular injection into the anterolateral area of the right thigh, 3 doses at 3, 5, and 11 to 12 months of age.

| Number of subjects in period 1^[1] | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 |
|---|-----------------------------|---------------------------|
| Started | 271 | 275 |
| Completed | 266 | 267 |
| Not completed | 5 | 8 |
| Consent withdrawn by subject | 4 | 6 |
| Adverse event, non-fatal | 1 | 2 |

Notes:

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

Justification: The number of subjects enrolled at baseline (N=546) represents subjects who were vaccinated at V01 and included in the Full Analysis Set.

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | DTaP-IPV-HB-Hib+Prevenar 13 |
|-----------------------|-----------------------------|

Reporting group description:

Subjects who received 3 doses of DTaP-IPV-HB-Hib vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| | |
|-----------------------|---------------------------|
| Reporting group title | Infanrix hexa+Prevenar 13 |
|-----------------------|---------------------------|

Reporting group description:

Subjects who received 3 doses of Infanrix hexa vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| Reporting group values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | Total |
|--|-----------------------------|---------------------------|-------|
| Number of subjects | 271 | 275 | 546 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 271 | 275 | 546 |
| 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: days | | | |
| arithmetic mean | 89.6 | 89 | |
| standard deviation | ± 3.2 | ± 3 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 130 | 142 | 272 |
| Male | 141 | 133 | 274 |

End points

End points reporting groups

| | |
|--|-----------------------------|
| Reporting group title | DTaP-IPV-HB-Hib+Prevenar 13 |
| Reporting group description: | |
| Subjects who received 3 doses of DTaP-IPV-HB-Hib vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age. | |
| Reporting group title | Infanrix hexa+Prevenar 13 |
| Reporting group description: | |
| Subjects who received 3 doses of Infanrix hexa vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age. | |

Primary: Percentage of Subjects with Seroprotection or Vaccine Response Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

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|-----------------|---|
| End point title | Percentage of Subjects with Seroprotection or Vaccine Response Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) ^[1] |
|-----------------|---|

End point description:

Anti-Diphtheria antibodies (Ab) were measured by a diphtheria micrometabolic inhibition test; Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay; Anti-Polio types were measured by neutralization assay; Anti-hepatitis B (Hep B) Ab were measured by the VITROS ECi/ECiQ Immunodiagnostic System; and Anti-polyribosyl ribitol phosphate (PRP) Ab were measured using a Farr-type radioimmunoassay. Seroprotection was defined as Anti-Diphtheria and anti-Tetanus Ab concentrations ≥ 0.1 international units (IU)/mL, Anti-poliovirus 1, 2, and 3 Ab titers ≥ 8 (1/dil), Anti-Hep B Ab concentrations ≥ 10 mIU/mL, and Anti-PRP Ab concentrations ≥ 1 μ g/mL. Vaccine response for PT and FHA was defined as Post-Dose 3 Ab concentrations $\geq 4 \times$ Lower Level Of Quantitation (LLOQ), if pre-Dose 1 Ab concentrations $< 4 \times$ LLOQ; Post-Dose 3 Ab concentrations \geq pre-Dose 1 Ab concentrations, if pre-Dose 1 Ab concentrations $\geq 4 \times$ LLOQ.

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| 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 | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|-------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Diphtheria | 100 | 99.2 | | |
| Anti-Tetanus | 100 | 100 | | |
| Anti-PT | 98 | 99.6 | | |
| Anti-FHA | 100 | 99.6 | | |
| Anti-Polio 1 | 100 | 100 | | |
| Anti-Polio 2 | 100 | 100 | | |

| | | | | |
|--------------|------|------|--|--|
| Anti-Polio 3 | 99.6 | 99.6 | | |
| Anti-Hep B | 96.4 | 99.6 | | |
| Anti-PRP | 93.5 | 85.2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Vaccine Antibodies' Titers Before and After Dose 3 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Summary of Vaccine Antibodies' Titers Before and After Dose 3 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
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End point description:

Anti-Diphtheria antibodies (Ab) were measured by a diphtheria micrometabolic inhibition test (MIT); Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay (ELISA); Anti-hepatitis B (Hep B) Ab were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System; and Anti-polyribosyl ribitol phosphate (PRP) Ab were measured using a Farr-type radioimmunoassay. The following Ab criteria were applied: Pre-Dose 3 for Anti-Diphtheria and Anti-Tetanus (≥ 0.01 IU/mL), Anti-PT and Anti-FHA (≥ 4 EU/mL), Anti-Hep B (≥ 100 mIU/mL), and Anti-PRP (≥ 0.15 μ g/mL) and Post-Dose 3 for Anti-Diphtheria and Anti-Tetanus (≥ 0.01 IU/mL), Anti-PT and Anti-FHA (≥ 4 EU/mL), Anti-Hep B (≥ 100 mIU/mL), and Anti-PRP (≥ 0.15 μ g/mL).

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| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre- and Post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|-------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Diphtheria; Pre-Dose 3 | 98.3 | 97.5 | | |
| Anti-Diphtheria; Post-Dose 3 | 100 | 99.6 | | |
| Anti-Tetanus; Pre-Dose 3 | 100 | 100 | | |
| Anti-Tetanus; Post-Dose 3 | 100 | 100 | | |
| Anti-PT; Pre-Dose 3 | 99.6 | 99.2 | | |
| Anti-PT; Post-Dose 3 | 100 | 100 | | |
| Anti-FHA; Pre-Dose 3 | 100 | 100 | | |
| Anti-FHA; Post-Dose 3 | 100 | 100 | | |
| Anti-Hep B; Pre-Dose 3 | 45.2 | 80.5 | | |
| Anti-Hep B; Post-Dose 3 | 91.2 | 98 | | |
| Anti-PRP; Pre-Dose 3 | 50.6 | 40.8 | | |
| Anti-PRP; Post-Dose 3 | 99.6 | 98.8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroconversion or Booster Response to Pertussis Toxoid and Filamentous Hemagglutinin Antibodies After Vaccinations with DTaP-IPV-Hep B-PRP-T Vaccine or Infanrix hexa™ Administered With 13-Valent Pneumococcal Conjugate Vaccine

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|-----------------|---|
| End point title | Percentage of Subjects with Seroconversion or Booster Response to Pertussis Toxoid and Filamentous Hemagglutinin Antibodies After Vaccinations with DTaP-IPV-Hep B-PRP-T Vaccine or Infanrix hexa™ Administered With 13-Valent Pneumococcal Conjugate Vaccine |
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End point description:

Anti-Pertussis toxoid (PT), and Anti- Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay (ELISA). Seroconversion for PT and FHA was defined as follows: ≥ 4 -fold Ab concentrations increase from pre-Dose 1 (V01) to post-Dose 3 (V05). Booster response for PT and FHA was defined as Post-Dose 3 Ab concentrations ≥ 4 -fold rise if pre-Dose 3 Ab concentrations $< 4 \times$ LLOQ; Post-Dose 3 Ab concentrations ≥ 2 -fold rise if pre-Dose 3 Ab concentrations $\geq 4 \times$ LLOQ.

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|----------------|-----------|
| End point type | Secondary |
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End point timeframe:

Post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|-------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-PT; Seroconversion | 94.3 | 95.5 | | |
| Anti-PT; Booster response | 94 | 99.2 | | |
| Anti-FHA; Seroconversion | 97.6 | 94.2 | | |
| Anti-FHA; Booster response | 96.6 | 95.8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Vaccine Antigens Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

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|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Antibodies Against Vaccine |
|-----------------|--|

End point description:

Anti-Diphtheria antibodies (Ab) were measured by a diphtheria micrometabolic inhibition test (MIT); Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti- Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay (ELISA); Anti-Polio types 1, 2, and 3 were measured by neutralization assay; Anti-hepatitis B (Hep B) Ab were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System; and Anti- polyribosyl ribitol phosphate (PRP) Ab were measured using a Farr-type radioimmunoassay.

End point type Secondary

End point timeframe:

Pre- and Post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria; Pre-Dose 3 | 0.08 (0.069 to 0.092) | 0.053 (0.046 to 0.06) | | |
| Anti-Diphtheria; Post-Dose 3 | 1.7 (1.54 to 1.87) | 1.2 (1.07 to 1.34) | | |
| Anti-Tetanus; Pre-Dose 3 | 0.129 (0.114 to 0.146) | 0.167 (0.149 to 0.188) | | |
| Anti-Tetanus; Post-Dose 3 | 2.23 (2.01 to 2.47) | 2.37 (2.16 to 2.6) | | |
| Anti-PT; Pre-Dose 3 | 20.5 (18.8 to 22.5) | 23.7 (21.5 to 26) | | |
| Anti-PT; Post-Dose 3 | 90.9 (84.9 to 97.4) | 129 (119 to 139) | | |
| Anti-FHA; Pre-Dose 3 | 30.6 (28.3 to 33.1) | 28.7 (26.3 to 31.4) | | |
| Anti-FHA; Post-Dose 3 | 148 (138 to 158) | 167 (155 to 179) | | |
| Anti-Polio 1; Pre-Dose 3 | 15.8 (12.8 to 19.4) | 27.3 (22.4 to 33.3) | | |
| Anti-Polio 1; Post-Dose 3 | 1749 (1494 to 2047) | 3279 (2869 to 3746) | | |
| Anti-Polio 2; Pre-Dose 3 | 14.1 (11.5 to 17.2) | 22.4 (18 to 27.8) | | |
| Anti-Polio 2; Post-Dose 3 | 1729 (1454 to 2058) | 2954 (2520 to 3462) | | |
| Anti-Polio 3; Pre-Dose 3 | 15.7 (12.8 to 19.1) | 20.9 (17.4 to 25) | | |
| Anti-Polio 3; Post-Dose 3 | 1213 (1005 to 1463) | 1906 (1594 to 2279) | | |
| Anti-Hep B; Pre-Dose 3 | 76.5 (62 to 94.4) | 260 (218 to 311) | | |
| Anti-Hep B; Post-Dose 3 | 1370 (1069 to 1757) | 5015 (4178 to 6020) | | |
| Anti-PRP; Pre-Dose 3 | 0.168 (0.137 to 0.205) | 0.115 (0.096 to 0.137) | | |

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|-----------------------|---------------------|---------------------|--|--|
| Anti-PRP; Post-Dose 3 | 9.73 (8.12 to 11.7) | 5.64 (4.66 to 6.81) | | |
|-----------------------|---------------------|---------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Immune Responses to Prevenar 13 antigens Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

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|-----------------|--|
| End point title | Percentage of Subjects with Immune Responses to Prevenar 13 antigens Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
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End point description:

Anti-pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F were measured by enzyme-linked immunosorbent assay (ELISA). Immune response was defined as subjects with antibody concentrations ≥ 0.35 $\mu\text{g/mL}$ 1 month after a 2+1-dose schedule.

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|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|-------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Serotype 1 | 99.4 | 100 | | |
| Serotype 3 | 86.3 | 88 | | |
| Serotype 4 | 99.4 | 98.8 | | |
| Serotype 5 | 95.1 | 98.1 | | |
| Serotype 6A | 100 | 98.8 | | |
| Serotype 6B | 100 | 100 | | |
| Serotype 7F | 100 | 100 | | |
| Serotype 9V | 99.4 | 99.4 | | |
| Serotype 14 | 100 | 100 | | |
| Serotype 18C | 98.2 | 100 | | |
| Serotype 19A | 100 | 100 | | |
| Serotype 19F | 100 | 100 | | |
| Serotype 23F | 100 | 99.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Prevenar Vaccine Antibodies Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Prevenar Vaccine Antibodies Following Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|---|

End point description:

Anti-pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F were measured by enzyme-linked immunosorbent assay (ELISA).

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|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 248 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 | 2.15 (1.95 to 2.36) | 2.47 (2.21 to 2.75) | | |
| Serotype 3 | 0.669 (0.605 to 0.74) | 0.824 (0.735 to 0.924) | | |
| Serotype 4 | 1.5 (1.36 to 1.66) | 1.95 (1.74 to 2.18) | | |
| Serotype 5 | 1.07 (0.973 to 1.19) | 1.32 (1.2 to 1.45) | | |
| Serotype 6A | 4.01 (3.63 to 4.44) | 4.92 (4.34 to 5.58) | | |
| Serotype 6B | 2.82 (2.51 to 3.17) | 4.29 (3.8 to 4.84) | | |
| Serotype 7F | 3.04 (2.79 to 3.31) | 3.97 (3.6 to 4.38) | | |
| Serotype 9V | 1.36 (1.24 to 1.5) | 1.7 (1.53 to 1.88) | | |
| Serotype 14 | 6.79 (6 to 7.69) | 7.77 (6.98 to 8.65) | | |
| Serotype 18C | 1.27 (1.14 to 1.41) | 1.79 (1.61 to 1.99) | | |
| Serotype 19A | 4.43 (3.88 to 5.06) | 5.78 (5.1 to 6.55) | | |
| Serotype 19F | 4.75 (4.27 to 5.3) | 6 (5.31 to 6.78) | | |
| Serotype 23F | 2.89 (2.6 to 3.22) | 4.24 (3.74 to 4.8) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Seroprotection or Vaccine Response One Month Post-dose 2 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|--|
| End point title | Percentage of Subjects with Seroprotection or Vaccine Response One Month Post-dose 2 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|--|

End point description:

Anti-Diphtheria antibodies (Ab) were measured by a diphtheria micrometabolic inhibition test (MIT); Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay (ELISA); Anti-poliovirus 1, 2, and 3 were measured by neutralization assay; Anti-hepatitis B (Hep B) Ab were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System; and Anti-polyribosyl ribitol phosphate (PRP) Ab were measured using a Farr-type radioimmunoassay. The following Ab criteria were applied 1 month Post-Dose 3: Anti-Diphtheria and Anti-Tetanus (≥ 0.01 IU/mL), Anti-Polio 1, 2, and 3 (≥ 8 1[dil]), Anti-Hep B (≥ 10 mIU/mL), and Anti-PRP (≥ 0.15 μ g/mL). Vaccine response for Anti-PT and Anti-FHA was defined as Post-Dose 2 Ab concentrations $\geq 4 \times$ Lower Level Of Quantitation (LLOQ), if pre-Dose 1 Ab concentrations $< 4 \times$ LLOQ; Post-Dose 2 Ab concentrations \geq pre-Dose 1 Ab concentrations, if pre-Dose 1 Ab concentrations $\geq 4 \times$ LLOQ.

| | |
|----------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| 1 month Post-Dose 2 | |

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|-------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 246 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Diphtheria | 99.6 | 99.6 | | |
| Anti-Tetanus | 100 | 100 | | |
| Anti-PT | 98.4 | 99.2 | | |
| Anti-FHA | 99.6 | 98.3 | | |
| Anti-Polio 1 | 90.8 | 95.4 | | |
| Anti-Polio 2 | 95 | 96.6 | | |
| Anti-Polio 3 | 96.7 | 98.3 | | |
| Anti-Hep B | 97.2 | 98.4 | | |
| Anti-PRP | 71.5 | 57.9 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers (GMTs) of Antibodies Against Vaccine Antigens One Month Post-dose 2 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies Against Vaccine Antigens One Month Post-dose 2 Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|---|

End point description:

Anti-Diphtheria antibodies (Ab) were measured by a diphtheria micrometabolic inhibition test (MIT); Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous Hemagglutinin (FHA) Ab were measured by enzyme-linked immunosorbent assay (ELISA); Anti-poliovirus 1, 2, and 3 Ab were measured by neutralization assay; Anti-hepatitis B (Hep B) Ab were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System; and Anti-polyribosyl ribitol phosphate (PRP) Ab were measured using a Farr-type radioimmunoassay.

| | |
|----------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| 1 month Post-Dose 2 | |

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 246 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria | 0.13 (0.112 to 0.152) | 0.118 (0.103 to 0.134) | | |
| Anti-Tetanus | 0.491 (0.439 to 0.549) | 0.594 (0.54 to 0.652) | | |
| Anti-PT | 105 (97.8 to 113) | 106 (97.7 to 115) | | |
| Anti-FHA | 94.9 (88.5 to 102) | 97.7 (90.5 to 105) | | |
| Anti-Polio 1 | 60 (47.6 to 75.5) | 105 (84.5 to 129) | | |
| Anti-Polio 2 | 62.1 (49.1 to 78.5) | 89.5 (70.9 to 113) | | |
| Anti-Polio 3 | 122 (97.7 to 152) | 142 (115 to 175) | | |
| Anti-Hep B | 401 (330 to 488) | 699 (577 to 847) | | |

| | | | | |
|----------|------------------------|------------------------|--|--|
| Anti-PRP | 0.507 (0.398 to 0.647) | 0.226 (0.184 to 0.277) | | |
|----------|------------------------|------------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Each Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|------------------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Each Vaccinations with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
| End point description: | Solicited injection site: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Anorexia, and Irritability. |
| End point type | Other pre-specified |
| End point timeframe: | Day 0 up to Day 7 post-each vaccination |

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|---|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 271 | 275 | | |
| Units: Percentage of subjects number (not applicable) | | | | |
| Injection site Pain; Post-Injection 1 | 43.9 | 32.1 | | |
| Injection site Pain; Post-Injection 2 | 40.1 | 29.9 | | |
| Injection site Pain; Post-Injection 3 | 65 | 56.8 | | |
| Injection site Erythema; Post-Injection 1 | 32.8 | 26.6 | | |
| Injection site Erythema; Post-Injection 2 | 46.5 | 40.6 | | |
| Injection site Erythema; Post-Injection 3 | 53.4 | 51.9 | | |
| Injection site Swelling; Post-Injection 1 | 24.7 | 18.2 | | |
| Injection site Swelling; Post-Injection 2 | 27.5 | 29.5 | | |
| Injection site Swelling; Post-Injection 3 | 28.2 | 38.7 | | |
| Pyrexia; Post-Injection 1 | 46.3 | 26.3 | | |
| Pyrexia; Post-Injection 2 | 61.7 | 49.8 | | |
| Pyrexia; Post-Injection 3 | 52.1 | 48.1 | | |
| Vomiting; Post-Injection 1 | 15.5 | 21.9 | | |
| Vomiting; Post-Injection 2 | 20.4 | 22.5 | | |
| Vomiting; Post-Injection 3 | 13.2 | 11.7 | | |
| Crying; Post-Injection 1 | 72 | 65.3 | | |
| Crying; Post-Injection 2 | 62.8 | 64.2 | | |
| Crying; Post-Injection 3 | 63.9 | 64.5 | | |

| | | | | |
|--------------------------------|------|------|--|--|
| Somnolence; Post-Injection 1 | 60.5 | 58.8 | | |
| Somnolence; Post-Injection 2 | 49.8 | 49.4 | | |
| Somnolence; Post-Injection 3 | 53 | 52.1 | | |
| Anorexia; Post-Injection 1 | 35.4 | 28.5 | | |
| Anorexia; Post-Injection 2 | 32 | 28 | | |
| Anorexia; Post-Injection 3 | 44.4 | 48.9 | | |
| Irritability; Post-Injection 1 | 81.9 | 76.6 | | |
| Irritability; Post-Injection 2 | 76.6 | 74.2 | | |
| Irritability; Post-Injection 3 | 75.6 | 74.7 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 1 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 1 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|---|

End point description:

Solicited injection site: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Anorexia, and Irritability. Grade 3 Solicited injection site reactions: Pain – Cries when injected limb is moved, or the movement of the injected limb is reduced; Erythema and Swelling – ≥ 50 mm. Grade 3 Systemic reactions: Pyrexia – $>39^{\circ}\text{C}$; Vomiting – ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying – >3 hours; Somnolence – Sleeping most of the time or difficult to wake up; Anorexia – Refuses ≥ 3 feeds/meals or refuses most meals; Irritability – Inconsolable.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 up to Day 7 post-Dose 1

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|---------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 271 | 275 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain | 43.9 | 32.1 | | |
| Grade 3 Injection site Pain | 3.3 | 2.9 | | |
| Injection site Erythema | 32.8 | 26.6 | | |
| Grade 3 Injection site Erythema | 3.3 | 1.8 | | |
| Injection site Swelling | 24.7 | 18.2 | | |
| Grade 3 Injection site Swelling | 2.6 | 1.1 | | |
| Pyrexia | 46.3 | 26.3 | | |
| Grade 3 Pyrexia | 0 | 0 | | |
| Vomiting | 15.5 | 21.9 | | |

| | | | | |
|----------------------|------|------|--|--|
| Grade 3 Vomiting | 0.4 | 0.7 | | |
| Crying | 72 | 65.3 | | |
| Grade 3 Crying | 3.3 | 0.4 | | |
| Somnolence | 60.5 | 58.8 | | |
| Grade 3 Somnolence | 1.8 | 0.7 | | |
| Anorexia | 35.4 | 28.5 | | |
| Grade 3 Anorexia | 0.7 | 0.7 | | |
| Irritability | 81.9 | 76.6 | | |
| Grade 3 Irritability | 4.8 | 6.2 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 2 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 2 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|---|

End point description:

Solicited injection site: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Anorexia, and Irritability. Grade 3 Solicited injection site reactions: Pain – Cries when injected limb is moved, or the movement of the injected limb is reduced; Erythema and Swelling – ≥ 50 mm. Grade 3 Systemic reactions: Pyrexia – $>39^{\circ}\text{C}$; Vomiting – ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying – >3 hours; Somnolence – Sleeping most of the time or difficult to wake up; Anorexia – Refuses ≥ 3 feeds/meals or refuses most meals; Irritability – Inconsolable.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 up to Day 7 post-Dose 2

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|---------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 269 | 272 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain | 40.1 | 29.9 | | |
| Grade 3 Injection site Pain | 0.4 | 1.8 | | |
| Injection site Erythema | 46.5 | 40.6 | | |
| Grade 3 Injection site Erythema | 1.1 | 0.4 | | |
| Injection site Swelling | 27.5 | 29.5 | | |
| Grade 3 Injection site Swelling | 1.5 | 0 | | |
| Pyrexia | 61.7 | 49.8 | | |
| Grade 3 Pyrexia | 0.7 | 1.5 | | |
| Vomiting | 20.4 | 22.5 | | |

| | | | | |
|----------------------|------|------|--|--|
| Grade 3 Vomiting | 1.5 | 0.4 | | |
| Crying | 62.8 | 64.2 | | |
| Grade 3 Crying | 3.3 | 1.8 | | |
| Somnolence | 49.8 | 49.4 | | |
| Grade 3 Somnolence | 0.7 | 2.2 | | |
| Anorexia | 32 | 28 | | |
| Grade 3 Anorexia | 1.5 | 0 | | |
| Irritability | 76.6 | 74.2 | | |
| Grade 3 Irritability | 4.1 | 2.2 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 3 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

| | |
|-----------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination 3 with Hexavalent DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa™ Concomitantly Administered With 13-Valent Pneumococcal Conjugate Vaccine (PCV13) |
|-----------------|---|

End point description:

Solicited injection site: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Anorexia, and Irritability. Grade 3 Solicited injection site reactions: Pain – Cries when injected limb is moved, or the movement of the injected limb is reduced; Erythema and Swelling – ≥ 50 mm. Grade 3 Systemic reactions: Pyrexia – $>39^{\circ}\text{C}$; Vomiting – ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying – >3 hours; Somnolence – Sleeping most of the time or difficult to wake up; Anorexia – Refuses ≥ 3 feeds/meals or refuses most meals; Irritability – Inconsolable.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 up to Day 7 post-Dose 3

| End point values | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | | |
|---------------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 267 | 268 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain | 65 | 56.8 | | |
| Grade 3 Injection site Pain | 6.8 | 4.1 | | |
| Injection site Erythema | 53.4 | 51.9 | | |
| Grade 3 Injection site Erythema | 2.6 | 4.1 | | |
| Injection site Swelling | 28.2 | 38.7 | | |
| Grade 3 Injection site Swelling | 1.5 | 2.3 | | |
| Pyrexia | 52.1 | 48.1 | | |
| Grade 3 Pyrexia | 2.3 | 1.5 | | |
| Vomiting | 13.2 | 11.7 | | |

| | | | | |
|----------------------|------|------|--|--|
| Grade 3 Vomiting | 0 | 0 | | |
| Crying | 63.9 | 64.5 | | |
| Grade 3 Crying | 5.3 | 2.6 | | |
| Somnolence | 53 | 52.1 | | |
| Grade 3 Somnolence | 1.1 | 1.5 | | |
| Anorexia | 44.4 | 48.9 | | |
| Grade 3 Anorexia | 2.6 | 0.8 | | |
| Irritability | 75.6 | 74.7 | | |
| Grade 3 Irritability | 3.4 | 1.9 | | |

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 30 post-final vaccination.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | DTaP-IPV-HB-Hib+Prevenar 13 |
|-----------------------|-----------------------------|

Reporting group description:

Subjects who received 3 doses of DTaP-IPV-HB-Hib vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| | |
|-----------------------|---------------------------|
| Reporting group title | Infanrix hexa+Prevenar 13 |
|-----------------------|---------------------------|

Reporting group description:

Subjects who received 3 doses of Infanrix hexa vaccine co-administered with Prevenar 13 at 3, 5, and 11 to 12 months of age.

| Serious adverse events | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | |
|---|-----------------------------|---------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 271 (5.54%) | 15 / 275 (5.45%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (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 | | | |
| Apnoea | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Petechiae | | | |
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Breath holding | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| 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 | | | |
| Inguinal mass | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 3 / 271 (1.11%) | 1 / 275 (0.36%) | |
| 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 / 271 (0.74%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 3 / 271 (1.11%) | 3 / 275 (1.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 271 (0.00%) | 1 / 275 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 1 / 271 (0.37%) | 2 / 275 (0.73%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 271 (0.37%) | 0 / 275 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | DTaP-IPV-HB-Hib+Prevenar 13 | Infanrix hexa+Prevenar 13 | |
|---|-----------------------------|---------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 222 / 271 (81.92%) | 210 / 275 (76.36%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 164 / 271 (60.52%) | 161 / 274 (58.76%) | |
| occurrences (all) | 164 | 161 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 166 / 271 (61.25%) | 135 / 274 (49.27%) | |
| occurrences (all) | 166 | 135 | |
| Injection site induration | | | |
| subjects affected / exposed | 12 / 271 (4.43%) | 17 / 275 (6.18%) | |
| occurrences (all) | 16 | 32 | |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 173 / 271 (63.84%) | 151 / 274 (55.11%) | |
| occurrences (all) | 173 | 151 | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 142 / 271 (52.40%) | 138 / 274 (50.36%) | |
| occurrences (all) | 142 | 138 | |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 75 / 271 (27.68%) | 103 / 274 (37.59%) | |
| occurrences (all) | 75 | 103 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|--|---|--|
| Diarrhoea subjects affected / exposed occurrences (all) | 23 / 271 (8.49%) 23 | 22 / 275 (8.00%) 27 | |
| Teething subjects affected / exposed occurrences (all) | 13 / 271 (4.80%) 18 | 23 / 275 (8.36%) 31 | |
| Vomiting alternative assessment type: Systematic subjects affected / exposed ^[6] occurrences (all) | 55 / 271 (20.30%) 55 | 61 / 274 (22.26%) 61 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 31 / 271 (11.44%) 35 | 26 / 275 (9.45%) 28 | |
| Psychiatric disorders Crying alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all) Irritability alternative assessment type: Systematic subjects affected / exposed ^[8] occurrences (all) | 195 / 271 (71.96%) 195 222 / 271 (81.92%) 222 | 179 / 274 (65.33%) 179 210 / 274 (76.64%) 210 | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Otitis media subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) | 62 / 271 (22.88%) 77 45 / 271 (16.61%) 52 27 / 271 (9.96%) 32 24 / 271 (8.86%) 35 | 71 / 275 (25.82%) 96 45 / 275 (16.36%) 53 26 / 275 (9.45%) 31 29 / 275 (10.55%) 33 | |

| | | | |
|--|--------------------|--------------------|--|
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[9] | 118 / 271 (43.54%) | 130 / 274 (47.45%) | |
| occurrences (all) | 118 | 130 | |

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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[5] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[6] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[7] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[8] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[9] - 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: This was a solicited adverse event recorded in a diary card within 7 days after each vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 14 November 2012 | The scale for assessment of Extensive Limb Swelling was added and the protocol was corrected with the new Sponsor's Responsible Medical Officer information. |
| 14 June 2013 | The Global Clinical Immunology (GCI) re-implemented the micrometabolic inhibition test using pH indicator for development (MIT-pH) assay for the DTaP-IPV-HB-Hib studies and discontinued the micrometabolic inhibition test using cell survival assessed by crystal violet staining (MIT-CV) method. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported