Clinical trial results:
Lot-to-Lot Consistency Study of DTaP-IPV-Hep B-PRP-T Vaccine Administered at 2 4 6 Months of Age in Healthy Latin American Infants Concomitantly with Prevenar™ and Rotarix™

Summary

EudraCT number	2011-004449-42
Trial protocol	Outside EU/EEA
Global end of trial date	28 September 2011

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	12 September 2014

Trial information

Trial identification

Sponsor protocol code	A3L24

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01177722
WHO universal trial number (UTN)	U1111-1111-5801

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 37 5843, emmanuel.feroldi@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 37 5843, 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)	EMEA-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 April 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the equivalence of immunogenicity on 3 lots of DTaP-IPV-Hep B-PRP-T vaccine (final bulk product [FBP]) one month after a three-dose primary series (2, 4 and 6 months) when co-administered with Prevenar™ and Rotarix™ , in terms of immunoresponses evaluated by:
- Geometric Means of Titers (GMTs) for Hep B.
- Seroprotection rates for D, T, Hep B, PRP, and polio and seroresponse rates for anti-PT and anti-FHA.
- To demonstrate the non-inferiority of the hexavalent DTaP-IPV-Hep B-PRP-T vaccine to the licensed hexavalent Infanrix hexa™ vaccine in terms of seroprotection or seroresponse rates to all antigens, one month after a three-dose primary series when co-administered with Prevenar™ and Rotarix™.

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:

All subjects participating in the study were to have received Hep B and BCG vaccines between birth and 1 month of life in agreement with the national immunization calendar.

Evidence for comparator:

Infanrix hexa was chosen as the comparator vaccine as it is currently the licensed hexavalent vaccine in Colombia and Costa Rica.

Actual start date of recruitment	03 August 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Costa Rica: 442
Country: Number of subjects enrolled	Colombia: 933
Worldwide total number of subjects	1375
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1375
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 03 August 2010 to 23 November 2010 in 2 clinical centers in Columbia and 1 clinical center in Costa Rica.

Pre-assignment

Screening details:

A total of 1375 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	Subject, Investigator, Assessor

Blinding implementation details:

The investigator (blind observer or assessor) and subject's parents or guardians did not know the vaccine administered. The assessor was in charge of the assessment of safety held in a separate room and away from where the vaccines were prepared. A nurse/vaccinator was in charge of the preparation and administration of the vaccine(s) in another room away from the assessor. When necessary the scratch off emergency decoding procedure described in the study protocol were to be followed.

Arms

Are arms mutually exclusive?	Yes
Arm title	DTap-IPV-Hep B-PRP~T Batch A

Arm description:

Subjects received a 3-dose primary series of vaccinations with Batch A of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine (IPV) adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

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

Dosage and administration details:

0.5 mL, intramuscular, one dose each at 2, 4, and 6 months of age

Arm title	DTaP-IPV-Hep B-PRP~T Batch B

Arm description:

Subjects received a 3-dose primary series of vaccinations with Batch B of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Arm type	Experimental

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

Dosage and administration details:

0.5 mL, intramuscular. One dose each at 2, 4, and 6 months of age.

Arm title	DTaP-IPV-Hep B-PRP~T Batch C

Arm description:

Subjects received a 3-dose primary series of vaccinations with Batch C of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

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

Dosage and administration details:

0.5 mL, intramuscular. One dose each at 2, 4, and 6 months of age.

Arm title	Infanrix Hexa

Arm description:

Subjects received a 3-dose primary series of vaccinations with the licensed Infanrix hexa™, with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	DTaP-HBV-IPV + Hib vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular. One dose each at 2, 4, and 6 months of age.

Number of subjects in period 1	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C
Started	344	344	342
Completed	331	334	333
Not completed	13	10	9
Consent withdrawn by subject	10	6	4
Adverse event, non-fatal	-	-	1
Lost to follow-up	3	4	3
Protocol deviation	-	-	1

Number of subjects in period 1	Infanrix Hexa

Started	345
Completed	338
Not completed	7
Consent withdrawn by subject	6
Adverse event, non-fatal	-
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	DTap-IPV-Hep B-PRP~T Batch A
Reporting group description:	
Subjects received a 3-dose primary series of vaccinations with Batch A of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine (IPV) adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch B
Reporting group description:	
Subjects received a 3-dose primary series of vaccinations with Batch B of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch C
Reporting group description:	
Subjects received a 3-dose primary series of vaccinations with Batch C of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.	
Reporting group title	Infanrix Hexa
Reporting group description:	
Subjects received a 3-dose primary series of vaccinations with the licensed Infanrix hexa™, with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.	

Reporting group values	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C
Number of subjects	344	344	342
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)	344	344	342
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	58.8	58.7	58.5
standard deviation	± 3.49	± 3.25	± 3.16

Gender categorical Units: Subjects			
Female	161	165	152
Male	183	179	190

Reporting group values	Infanrix Hexa	Total	
Number of subjects	345	1375	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	345	1375	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: days			
arithmetic mean	58.7		
standard deviation	± 3.31	-	
Gender categorical Units: Subjects			
Female	156	634	
Male	189	741	

End points

End points reporting groups

Reporting group title	DTap-IPV-Hep B-PRP~T Batch A

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch A of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine (IPV) adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch B

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch B of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch C

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch C of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	Infanrix Hexa

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with the licensed Infanrix hexa™, with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Primary: Geometric Mean Titers (GMTs) of Anti-Hepatitis B Before and After 3 Dose Primary Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa™

End point title	Geometric Mean Titers (GMTs) of Anti-Hepatitis B Before and After 3 Dose Primary Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa™[1]

End point description:

Antibodies against Hepatitis B (Hep B) were measured by chemiluminescence detection.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) Dose 1 and 30 days post-vaccination

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-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C	Infanrix Hexa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	312	310	313	316
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Hep B Pre-dose 1	4.02 (3.5 to 4.61)	4.07 (3.58 to 4.62)	4.93 (4.2 to 5.79)	4.3 (3.68 to 5.03)
Anti-Hep B Post-dose 3	3048 (2672 to 3476)	2801 (2467 to 3181)	3202 (2794 to 3668)	2766 (2466 to 3102)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Seroprotection or Vaccine Response After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine

End point title	Number of Subjects With Seroprotection or Vaccine Response After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine[2]

End point description:

Seroprotection was defined as titers ≥ 0.01 IU/mL for Diphtheria (D) and Tetanus (T); ≥ 10 IU/mL for Hep B; ≥ 0.15 µg/mL for PRP, and ≥ 8 (1/dil) for Poliovirus. Vaccine response for PT and FHA were defined as a titer ≥ lower limit of quantitation (LLOQ) in initially seronegative participants, or at least persistence (post-vaccination titer ≥ pre-vaccination titer) in initially seropositive subjects (titer ≥ LLOQ).

End point type	Primary

End point timeframe:

30 Days 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	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C	Infanrix Hexa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	312	310	313	316
Units: Participants				
number (not applicable)				
Anti-Diphtheria (N = 310, 310, 312, 315)	310	310	312	315
Anti-Tetanus (N = 311, 310, 311, 314)	311	310	311	314
Anti-PT (N = 308, 309, 308, 312)	304	299	299	307
Anti-FHA (N = 306, 306, 304, 311)	306	305	303	309
Anti-Polio 1 (N = 310, 309, 308, 311)	310	309	308	311
Anti-Polio 2 (N = 309, 309, 307, 312)	309	309	307	312
Anti-Polio 3 (N = 310, 309, 307, 312)	310	309	307	311
Anti-Hep B (N = 312, 310, 312, 316)	311	310	310	316
Anti-PRP (N = 312, 310, 312, 316)	299	298	287	303

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine

End point description:

Antibodies were measured by toxin neutralization test for Diphtheria (D); enzyme-linked immunosorbent assay (ELISA) for Tetanus (T), Pertussis toxoid (PT), and Filamentous hemagglutinin (FHA); neutralization assay for Poliovirus types 1, 2, and 3; chemiluminescence detection for Hepatitis B (Hep B), and Farr type radioimmunoassay for Haemophilus influenza type b (PRP).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and 30 days post-dose 3

End point values	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C	Infanrix Hexa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	312[3]	310[4]	313[5]	316[6]
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria Pre-dose 1 (N= 312, 308, 311, 315)	0.599 (0.513 to 0.699)	0.596 (0.505 to 0.703)	0.641 (0.547 to 0.752)	0.63 (0.53 to 0.749)
Anti-Diphtheria Post-dose 3 (N=310, 310, 312, 315)	0.252 (0.224 to 0.285)	0.279 (0.247 to 0.316)	0.228 (0.201 to 0.26)	0.24 (0.214 to 0.269)
Anti-Tetanus Post-dose 3 (N = 311, 310, 311, 314)	1.66 (1.54 to 1.78)	1.55 (1.43 to 1.68)	1.45 (1.33 to 1.59)	1.8 (1.69 to 1.93)
Anti-PT Pre-dose 1 (N = 308, 309, 310, 314)	3.02 (2.65 to 3.45)	3.5 (3.03 to 4.04)	3.54 (3.1 to 4.05)	3.11 (2.7 to 3.59)
Anti-PT Post-dose 3 (N = 312, 310, 311, 314)	102 (96.1 to 108)	103 (95.9 to 110)	102 (95 to 110)	98.9 (92.3 to 106)
Anti-FHA Pre-dose 1(N = 307, 307, 307, 312)	5.36 (4.77 to 6.02)	5.66 (5.01 to 6.39)	5.76 (5.12 to 6.49)	5.13 (4.61 to 5.7)
Anti-FHA Post-dose 3 (N=311, 309, 310, 315)	186 (174 to 199)	175 (163 to 188)	183 (171 to 197)	118 (110 to 127)
Anti-Polio 1 Post-dose 3 (N = 310, 309, 308, 311)	755 (674 to 847)	655 (580 to 739)	636 (561 to 722)	1298 (1151 to 1464)
Anti-Polio 2 Post-dose 3 (N = 309, 309, 307, 312)	1190 (1054 to 1344)	1232 (1101 to 1379)	1120 (994 to 1261)	1981 (1756 to 2234)
Anti-Polio 3 Post-dose 3 (N = 310, 309, 307, 312)	1102 (972 to 1250)	1119 (975 to 1284)	1097 (963 to 1250)	1944 (1680 to 2249)
Anti-PRP Post-dose 3 (N = 312, 310, 312, 316)	3.37 (2.8 to 4.05)	4.02 (3.35 to 4.82)	3.33 (2.72 to 4.07)	2.24 (1.9 to 2.64)

Notes:

[3] - Per Protocol Analysis Set

[4] - Per Protocol Analysis Set

[5] - Per Protocol Analysis Set

[6] - Per Protocol Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting at Least One Solicited Injection Site (Study Vaccine) or Systemic Reactions After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine

End point title	Number of Subjects Reporting at Least One Solicited Injection Site (Study Vaccine) or Systemic Reactions After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa Vaccine

End point description:

Solicited Injection Site Reactions: Pain, Erythema, and Swelling. Solicited Systemic Reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia,and Irritability. Grade 3 was defined as: Pain, cries when injected limb is moved or movement of the limb is reduced; Erythema and Swelling, ≥ 5 cm; Pyrexia, (Temperature) ≥ 39.6°C; Vomiting, ≥ 6 episodes/24 hours or requiring parenteral hydration; Crying, > 3 hours; Somnolence, sleeping most of time or difficult to wake up; Anorexia, refuses ≥ 3 feed/meals or refuses most feeds/meals; and Irritability, inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to 7 after each dose

End point values	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C	Infanrix Hexa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	344[7]	343[8]	342	345
Units: Participants				
number (not applicable)				
Pain Post-dose 1 (N = 338, 341, 340, 344)	199	194	216	185
Pain Post-dose 2 (N = 333, 337, 335, 340)	180	196	203	188
Pain Post-dose 3 (N = 331, 331, 334, 337)	168	163	162	147
Grade 3 Pain Post Dose 1 (N = 338, 341, 344, 344)	21	22	22	7
Grade 3 Pain Post Dose 3 (N=331, 331, 334, 338)	10	9	8	8
Erythema Post-dose 1 (N = 338, 341, 340, 344)	72	63	82	52
Erythema Post-dose 2 (N = 333, 337, 335, 340)	87	78	80	67
Erythema Post-dose 3 (N = 331, 331, 334, 337)	85	79	96	68
Grade 3 Erythema Post-dose 1(N=338, 341, 340, 344)	2	3	2	0
Grade 3 Erythema Post-dose 3(N=331, 331, 334, 337)	0	0	1	0

Swelling Post dose 1 (N = 338, 341, 340, 344)	47	30	47	33
Swelling Post dose 2 (N = 333, 337, 335, 340)	44	35	45	44
Swelling Post dose 3 (N = 331, 331, 334, 337)	43	34	48	42
Grade 3 Swelling Post-dose 1(N=338, 341, 340, 344)	2	3	2	0
Grade 3 Swelling post-dose 3(N=331, 331, 340, 338)	0	0	0	0
Pyrexia Post dose 1 (N = 338, 341, 340, 344)	46	42	68	46
Pyrexia Post dose 2 (N = 333, 337, 335, 340)	70	68	68	70
Pyrexia Post dose 3 (N = 331, 331, 333, 337)	67	63	72	65
Grade 3 Pyrexia Post-dose 1 (N=338, 341, 340, 344)	2	0	0	0
Grade 3 Pyrexia Post-dose 3 (N=331, 331, 333, 337)	4	1	1	2
Vomiting Post dose 1 (N = 338, 341, 340, 344)	85	90	86	94
Vomiting Post dose 2 (N = 333, 337, 335, 340)	58	80	64	62
Vomiting Post dose 3 (N = 331, 331, 334, 337)	32	58	46	39
Grade 3 Vomiting Post-dose 1(N=338, 341, 340, 344)	4	5	6	5
Grade 3 Vomiting post-dose 3(N=331, 331, 334, 337)	3	1	2	2
Crying Post dose 1 (N = 338, 341, 340, 344)	198	186	189	161
Crying Post dose 2 (N = 333, 337, 335, 340)	163	179	169	161
Crying Post dose 3 (N = 331, 331, 334, 337)	141	145	142	120
Grade 3 Crying Post-dose 1 (N =338, 341, 340, 344)	15	10	23	9
Grade 3 Crying Post-dose 3 (N =331, 331, 334, 337)	8	6	10	6
Somnolence Post dose 1 (N = 338, 341, 341, 344)	159	146	160	147
Somnolence Post dose 2 (N = 333, 337, 335, 340)	109	108	110	111
Somnolence Post dose 3 (N = 331, 331, 334, 337)	85	99	96	81
Grad 3 Somnolence Post-dose 1 N=338, 341, 341, 344	3	14	19	9
Grad 3 Somnolence Post-dose 3 N=331, 331, 334, 337	5	2	4	4
Anorexia Post dose 1 (N = 338, 341, 341, 344)	78	97	96	75
Anorexia Post dose 2 (N = 333, 337, 335, 340)	75	93	86	74
Anorexia Post dose 3 (N = 331, 331, 334, 337)	63	64	60	54
Grade 3 Anorexia Post-dose 1(N=338, 341, 341, 344)	3	4	8	3
Grade 3 Anorexia Post-dose 3(N=331, 331, 334, 337)	4	7	4	3
Irritability Post dose 1 (N = 338, 341, 341, 344)	208	206	208	180

Irritability Post dose 2 (N = 333, 337, 335, 340)	193	199	191	193
Irritability Post dose 3 (N = 331, 332, 334, 337)	155	161	154	144
Grd 3 Irritability Post-dose 1N=338, 341, 341, 344	15	17	20	8
Grd 3 Irritability Post-dose 3N=331, 332, 334, 337	11	13	12	5

Notes:

[7] - A participant randomized to Batch B got the Batch A vaccine.

[8] - A participant randomized to Batch B got the Batch A vaccine.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting at Least One Solicited Injection Site Reaction at the Prevenar Injection Site After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa™ Vaccine

End point title	Number of Subjects Reporting at Least One Solicited Injection Site Reaction at the Prevenar Injection Site After Vaccination With DTaP-IPV-Hep B-PRP~T Batch A, B, or C, or Infanrix Hexa™ Vaccine

End point description:

Solicited Injection Site Reactions: Pain, Erythema, and Swelling. Grade 3 was defined as: Pain, cries when injected limb is moved or movement of the limb is reduced; Erythema and Swelling, ≥ 5 cm.

End point type	Secondary

End point timeframe:

Day 0 up to 7 post each vaccination

End point values	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C	Infanrix Hexa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	344[9]	341[10]	342	345
Units: Participants				
number (not applicable)				
Pain Post-dose 1 (N = 338, 341, 340, 344)	171	173	184	169
Grade 3 Pain Post-dose 1 (N = 338, 341, 340, 344)	15	15	16	8
Pain Post-dose 2 (N = 333, 337, 335, 340)	160	183	180	174
Grade 3 Pain Post-dose 2 (N = 333, 337, 335, 340)	14	17	16	13
Pain Post-dose 3 (N =331, 331, 334, 337)	146	105	146	125
Grade 3 Pain Post-dose 3 (N = 331, 331, 334, 337)	8	9	10	7
Erythema Post-dose 1 (N = 338, 341, 340, 344)	47	48	55	42
Grade 3 Erythema Post-dose 1 (N=338, 341, 340, 344	0	1	2	0
Erythema Post-dose 2 (N = 333, 337, 335, 340)	65	55	62	53

Grade 3 Erythema Post-dose 2 (N=333, 337, 335, 340	1	0	0	0
Erythema Post-dose 3 (N = 331, 331, 334, 337)	63	57	69	49
Grade 3 Erythema Post-dose 3 (N=331, 331, 334, 337	1	1	0	0
Swelling Post-dose 1 (N = 338, 341, 340, 344)	34	21	33	31
Grade 3 Swelling Post-dose 1 (N=338, 341, 340, 344	0	0	2	1
Swelling Post-dose 2 (N = 333, 337, 335, 340)	32	28	36	32
Grade 3 Swelling Post-dose 2 (N=333, 337, 335, 340	0	0	1	0
Swelling Post-dose 3 (N = 331, 331, 334, 337)	27	29	36	29
Grade 3 Swelling Post-dose 3 (N=331, 331, 334, 337	0	0	0	0

Notes:

[9] - A participant randomized to Batch B got the Batch A vaccine

[10] - A participant randomized to Batch B got the Batch A vaccine

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events data were collected from Day 0 after Dose 1 through up to 6 months after the last dose.

Adverse event reporting additional description:

A participant randomized to Batch B got the Batch A vaccine, safety analyses was according to the actual vaccine administered. Total number reported for each solicited event reflects those with available data for the indicated event.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	DTap-IPV-Hep B-PRP~T Batch A

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch A of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine (IPV) adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch B

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch B of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch C

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with Batch C of diphtheria (D), tetanus (T), pertussis (2-component acellular), recombinant hepatitis B (Hep B) Hansenula polymorpha and poliomyelitis vaccine adsorbed, and Haemophilus influenzae type b (Hib) vaccine [polyribosyl ribitol phosphate (PRP) conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Reporting group title	Infanrix Hexa

Reporting group description:

Subjects received a 3-dose primary series of vaccinations with the licensed Infanrix hexa™, with one dose each at 2, 4, and 6 months of age. Prevenar™ was co-administered with study vaccine at 2, 4, and 6 months of age, and Rotarix™ was co-administered at 2 and 4 months of age.

Serious adverse events	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 345 (2.90%)	14 / 343 (4.08%)	16 / 342 (4.68%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			

Thermal burn			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cerebral Atrophy Congenital			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 345 (0.00%)	2 / 343 (0.58%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	2 / 345 (0.58%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 345 (0.29%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			

subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Abdominal strangulated hernia			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Asthmatic crisis			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body aspiration			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	5 / 345 (1.45%)	6 / 343 (1.75%)	9 / 342 (2.63%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kawasaki's disease			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 345 (1.16%)	5 / 343 (1.46%)	11 / 342 (3.22%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia primary atypical			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	0 / 342 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 345 (0.29%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	3 / 345 (0.87%)	2 / 343 (0.58%)	2 / 342 (0.58%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral diarrhoea			
subjects affected / exposed	0 / 345 (0.00%)	0 / 343 (0.00%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 345 (0.00%)	1 / 343 (0.29%)	1 / 342 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Infanrix Hexa		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 345 (2.90%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Cerebral Atrophy Congenital			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac Failure			

subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden infant death syndrome			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal strangulated hernia			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Enteritis				
subjects affected / exposed	1 / 345 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intussusception				
subjects affected / exposed	1 / 345 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 345 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 345 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	0 / 345 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthmatic crisis				
subjects affected / exposed	0 / 345 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diaphragmatic hernia				
subjects affected / exposed	0 / 345 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foreign body aspiration				
subjects affected / exposed	1 / 345 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	8 / 345 (2.32%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Exanthema subitum			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis bacterial			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Kawasaki's disease			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Otitis media acute			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periorbital cellulitis			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	5 / 345 (1.45%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Pneumonia primary atypical			
subjects affected / exposed	1 / 345 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	3 / 345 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Viral diarrhoea			
subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			

subjects affected / exposed	0 / 345 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DTap-IPV-Hep B-PRP~T Batch A	DTaP-IPV-Hep B-PRP~T Batch B	DTaP-IPV-Hep B-PRP~T Batch C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	208 / 345 (60.29%)	206 / 343 (60.06%)	216 / 342 (63.16%)
Nervous system disorders			
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed[1]	159 / 338 (47.04%)	146 / 341 (42.82%)	160 / 341 (46.92%)
occurrences (all)	159	146	160
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[2]	87 / 338 (25.74%)	79 / 341 (23.17%)	96 / 340 (28.24%)
occurrences (all)	87	79	96
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[3]	199 / 338 (58.88%)	196 / 341 (57.48%)	216 / 340 (63.53%)
occurrences (all)	199	196	216
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	47 / 338 (13.91%)	35 / 341 (10.26%)	48 / 340 (14.12%)
occurrences (all)	47	35	48
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[5]	208 / 338 (61.54%)	206 / 341 (60.41%)	208 / 341 (61.00%)
occurrences (all)	208	206	208
Pyrexia			
alternative assessment type: Systematic			

subjects affected / exposed[6]	70 / 338 (20.71%)	68 / 341 (19.94%)	72 / 340 (21.18%)
occurrences (all)	70	68	72
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[7]	85 / 338 (25.15%)	90 / 341 (26.39%)	86 / 340 (25.29%)
occurrences (all)	85	90	86
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 345 (6.09%)	17 / 343 (4.96%)	23 / 342 (6.73%)
occurrences (all)	24	17	25
Psychiatric disorders			
Crying			
alternative assessment type: Systematic			
subjects affected / exposed[8]	198 / 338 (58.58%)	186 / 341 (54.55%)	189 / 340 (55.59%)
occurrences (all)	198	186	189
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	99 / 345 (28.70%)	96 / 343 (27.99%)	90 / 342 (26.32%)
occurrences (all)	125	132	116
Metabolism and nutrition disorders			
Anorexia			
alternative assessment type: Systematic			
subjects affected / exposed[9]	75 / 338 (22.19%)	97 / 341 (28.45%)	96 / 341 (28.15%)
occurrences (all)	75	97	96

Non-serious adverse events	Infanrix Hexa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	193 / 345 (55.94%)		
Nervous system disorders			
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed[1]	147 / 344 (42.73%)		
occurrences (all)	147		
General disorders and administration site conditions			

Injection site erythema alternative assessment type: Systematic subjects affected / exposed[2] occurrences (all)	68 / 344 (19.77%) 68		
Injection site pain alternative assessment type: Systematic subjects affected / exposed[3] occurrences (all)	188 / 344 (54.65%) 188		
Injection site swelling alternative assessment type: Systematic subjects affected / exposed[4] occurrences (all)	44 / 344 (12.79%) 44		
Irritability alternative assessment type: Systematic subjects affected / exposed[5] occurrences (all)	193 / 344 (56.10%) 193		
Pyrexia alternative assessment type: Systematic subjects affected / exposed[6] occurrences (all)	70 / 344 (20.35%) 70		
Gastrointestinal disorders Vomiting alternative assessment type: Systematic subjects affected / exposed[7] occurrences (all)	94 / 344 (27.33%) 94		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	17 / 345 (4.93%) 18		
Psychiatric disorders Crying alternative assessment type: Systematic subjects affected / exposed[8] occurrences (all)	161 / 344 (46.80%) 161		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	87 / 345 (25.22%) 105		
Metabolism and nutrition disorders Anorexia alternative assessment type: Systematic subjects affected / exposed[9] occurrences (all)	75 / 344 (21.80%) 75		

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 of 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 of 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 of 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 of 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 of 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 of 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 of 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 of 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 of 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
20 October 2009	Protocol was updated with a requirement to collect additional data on the intake of antipyretics (category 1 medication) to perform an observational analysis on the potential impact of antipyretics prophylaxis on the immunogenicity of DTaP-IPV-Hep B-PRP-T.
09 March 2010	A modification in the planned interim analysis for the study.
02 August 2010	A change in the design from a double-blind to an observer blinded study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported