



## Clinical trial results:

### Immunogenicity Study of the Antibody Persistence and Booster Effect of the DTaP-IPV-Hep B-PRP-T Combined Vaccine at 15 to 18 Months of Age Following a Primary Series of DTaP-IPV-Hep B-PRP-T or Infanrix hexa™ Administered at 2, 4, and 6 Months of Age in Healthy Mexican Infants

#### Summary

EudraCT number	2011-004456-19
Trial protocol	Outside EU/EEA
Global end of trial date	28 May 2009

#### Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	27 September 2014

#### Trial information

##### Trial identification

Sponsor protocol code	A3L21
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00654901
WHO universal trial number (UTN)	-

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 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com
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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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	29 January 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 May 2009
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

Immunogenicity

-To describe the antibody (Ab) persistence at 15 to 18 months of age for all valences following a three-dose primary series vaccination of either DTaP-IPV-Hep B-PRP-T or Infanrix hexa™ at 2, 4 and 6 months of age in a subset of subjects,

-To describe the immunogenicity of a booster dose of DTaP-IPV-Hep B-PRP-T given at 15 to 18 months of age in a subset of subjects.

Safety

- To describe the safety profile after a booster dose of DTaP-IPV-Hep B-PRP-T given at 15 to 18 months of age.

Protection of trial subjects:

Only subjects that met all of 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 were previously vaccinated at 2, 4, and 6 months of age with DTaP-IPV-Hep B-PRP-T (Group 1 [batch A], Group 2 [batch B] and Group 3 [batch C]) or Infanrix hexa™ (Group 4) and all were to receive one dose of DTaP-IPV-Hep B-PRP-T at 15 to 18 months of age in the current study.

Evidence for comparator:

A fourth treatment group was added in order to provide an estimate of the immunogenicity and safety profile of a reference vaccine. Infanrix hexa™ was chosen as this vaccine is one of the standards of care in Mexico.

Actual start date of recruitment	26 March 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Mexico: 881
Worldwide total number of subjects	881
EEA total number of subjects	0

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	881
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:

Participants were enrolled from 25 March 2008 to 28 November 2008 at 5 clinical centers in Mexico.

### Pre-assignment

Screening details:

A total of 881 participants who met the inclusion but 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	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	DTaP-IPV-Hep B-PRP~T Batch 1

Arm description:

Subjects had received 3 primary doses of Batch 1 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

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 15 and 18 months of age.

<b>Arm title</b>	DTaP-IPV-Hep B-PRP~T Batch 2
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Arm description:

Subjects had received 3 primary doses of Batch 2 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

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 15 and 18 months of age.

<b>Arm title</b>	DTaP-IPV-Hep B-PRP~T Batch 3
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Arm description:

Subjects had received 3 primary doses of Batch 3 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study

A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

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 15 and 18 months of age.	
<b>Arm title</b>	Infanrix Hexa™

Arm description:

Subjects had received 3 primary doses of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), (Infanrix hexa™), plus Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed in Study A3L11 and received a booster dose of DTaP-IPV-Hep B-PRP~T at Day 0 in the present study.

Arm type	Active comparator
Investigational medicinal product name	Infanrix Hexa™
Investigational medicinal product code	DTaP-HBV-IPV 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 15 and 18 months of age.

<b>Number of subjects in period 1</b>	DTaP-IPV-Hep B-PRP~T Batch 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3
Started	254	262	252
Completed	250	262	250
Not completed	4	0	2
Consent withdrawn by subject	3	-	1
Lost to follow-up	1	-	1

<b>Number of subjects in period 1</b>	Infanrix Hexa™
Started	113
Completed	113
Not completed	0
Consent withdrawn by subject	-
Lost to follow-up	-

## Baseline characteristics

### Reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 1
Reporting group description:	
Subjects had received 3 primary doses of Batch 1 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 2
Reporting group description:	
Subjects had received 3 primary doses of Batch 2 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 3
Reporting group description:	
Subjects had received 3 primary doses of Batch 3 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	Infanrix Hexa™
Reporting group description:	
Subjects had received 3 primary doses of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), (Infanrix hexa™), plus Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed in Study A3L11 and received a booster dose of DTaP-IPV-Hep B-PRP~T at Day 0 in the present study.	

Reporting group values	DTaP-IPV-Hep B-PRP~T Batch 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3
Number of subjects	254	262	252
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)	254	262	252
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: months			
arithmetic mean	17.3	17.2	17.4
standard deviation	± 1.51	± 1.47	± 1.42
Gender categorical			
Units: Subjects			
Female	125	125	130
Male	129	137	122
Reporting group values	Infanrix Hexa™	Total	

Number of subjects	113	881	
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)	113	881	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: months			
arithmetic mean	17.1		
standard deviation	± 1.51	-	
Gender categorical			
Units: Subjects			
Female	58	438	
Male	55	443	

## End points

### End points reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 1
Reporting group description: Subjects had received 3 primary doses of Batch 1 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 2
Reporting group description: Subjects had received 3 primary doses of Batch 2 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 3
Reporting group description: Subjects had received 3 primary doses of Batch 3 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.	
Reporting group title	Infanrix Hexa™
Reporting group description: Subjects had received 3 primary doses of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), (Infanrix hexa™), plus Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed in Study A3L11 and received a booster dose of DTaP-IPV-Hep B-PRP~T at Day 0 in the present study.	

### Primary: Geometric Mean Titers of Antibodies Before and After Booster Vaccination With DTaP-IPV-Hep B-PRP~T

End point title	Geometric Mean Titers of Antibodies Before and After Booster Vaccination With DTaP-IPV-Hep B-PRP~T <sup>[1]</sup>
End point description: Antibody titers were measured for hepatitis B (Hep B) by enhanced chemiluminescence detection, for Haemophilus influenzae type b (PRP) by Farr type radioimmunoassay, for diphtheria by toxin neutralization test, and for tetanus by enzyme linked immunosorbent assay (ELISA). Antibody titers were measured for poliovirus types 1, 2, and 3 by neutralization assay. Antibody titers were measured for pertussis toxoid (PT) and filamentous hemagglutinin (FHA) by ELISA.	
End point type	Primary
End point timeframe: Day 0 (pre-booster) and Day 30 (one month post-booster)	

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 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3	Infanrix Hexa™
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	58	65
Units: Titers				
geometric mean (confidence interval 95%)				



Anti Hep B Pre-booster	91.1 (56.8 to 146)	127 (83.9 to 193)	69.2 (42.3 to 113)	127 (86.2 to 186)
Anti Hep B Post-booster	2167 (1314 to 3573)	3998 (2510 to 6368)	1877 (1152 to 3058)	4757 (3124 to 7243)
Anti PRP Pre-booster	1.09 (0.644 to 1.86)	1.32 (0.937 to 1.87)	0.88 (0.51 to 1.52)	1.33 (0.839 to 2.1)
Anti PRP Post-booster	64 (47.4 to 86.6)	94.8 (71.6 to 125)	49.7 (30.6 to 80.6)	102 (72.8 to 144)
Anti Diphtheria Pre-booster	0.116 (0.072 to 0.187)	0.19 (0.126 to 0.287)	0.101 (0.062 to 0.164)	0.081 (0.055 to 0.119)
Anti Diphtheria Post-booster	7.78 (4.88 to 12.4)	15.2 (10.1 to 23.1)	9.31 (5.8 to 14.9)	6.01 (3.99 to 9.06)
Anti Tetanus Pre-booster	0.33 (0.236 to 0.462)	0.331 (0.256 to 0.427)	0.231 (0.167 to 0.318)	0.297 (0.229 to 0.385)
Anti Tetanus Post-booster	5.26 (3.97 to 6.96)	8.49 (6.5 to 11.1)	5.55 (4.2 to 7.33)	6.98 (5.26 to 9.26)
Anti Polio 1 Pre-booster	614 (382 to 988)	663 (458 to 959)	551 (356 to 853)	887 (571 to 1378)
Anti Polio 1 Post-booster	7037 (4977 to 9949)	9938 (7418 to 13313)	8907 (6474 to 12254)	10173 (7909 to 13086)
Anti Polio 2 Pre-booster	936 (584 to 1501)	839 (530 to 1326)	531 (309 to 913)	1267 (747 to 2152)
Anti Polio 2 Post-booster	10756 (7636 to 15151)	10224 (7476 to 13981)	9232 (6549 to 13014)	13482 (10245 to 17742)
Anti Polio 3 Pre-booster	428 (255 to 719)	373 (224 to 619)	241 (130 to 446)	896 (508 to 1580)
Anti Polio 3 Post-booster	6597 (4281 to 10164)	9575 (6859 to 13365)	5296 (3503 to 8007)	13337 (9619 to 18491)
Anti PT Pre-booster	15.6 (11.6 to 20.9)	14.7 (11.8 to 18.4)	14.5 (11.3 to 18.6)	15.3 (11.6 to 20.2)
Anti PT Post-booster	186 (151 to 230)	200 (166 to 241)	171 (137 to 212)	162 (131 to 200)
Anti FHA Pre-booster	42.1 (30.6 to 57.9)	33.7 (26 to 43.8)	28.3 (21.5 to 37.3)	25.9 (19.6 to 34.2)
Anti FHA Post-booster	410 (336 to 499)	455 (387 to 536)	346 (284 to 421)	291 (242 to 349)

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Antibody Persistence Before and Immunogenicity Response After Booster Vaccination With DTaP-IPV-Hep B-PRP~T Vaccine

End point title	Number of Subjects With Antibody Persistence Before and Immunogenicity Response After Booster Vaccination With DTaP-IPV-Hep B-PRP~T Vaccine <sup>[2]</sup>
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End point description:

Antibody persistence and immunogenicity response:

Level 1:  $\geq 10$  mIU/mL for hepatitis B (Hep B),  $\geq 0.15$   $\mu$ g/mL for Haemophilus influenzae type b (PRP), and  $\geq 0.01$  IU/mL for diphtheria (D) and tetanus (T). Level 2:  $\geq 100$  mIU/mL (Hep B),  $\geq 1.0$   $\mu$ g/mL (PRP), and  $\geq 0.1$  IU/mL (D and T). Level 3,  $\geq 1.0$  IU/mL (D and T). Anti-polio titers were defined as  $\geq 8$  (1.dil), and pertussis toxoid (PT) and filamentous hemagglutinin (FHA) by a 4 fold increase from Day 0.

End point type	Primary
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End point timeframe:

Day 0 (pre-booster) and Day 30 (one month post-booster)

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 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3	Infanrix Hexa™
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	58	65
Units: Subjects				
number (not applicable)				
Anti-Hep B Level 1 Pre-booster	51	56	51	62
Anti-Hep B Level 2 Pre-booster	29	39	25	38
Anti-Hep B Level 1 Post-booster	58	61	57	65
Anti-Hep B Level 2 Post-booster	52	58	55	63
Anti-PRP Level 1 Pre-booster	51	54	47	60
Anti-PRP Level 2 Pre-booster	27	36	25	32
Anti-PRP Level 1 Post-booster	58	61	58	65
Anti-PRP Level 2 Post booster	58	61	55	64
Anti-D Level 1 Pre-booster	51	59	51	62
Anti-D Level 2 Pre-booster	31	39	29	32
Anti-D Level 1 Post-booster	58	60	58	64
Anti-D Level 2 Post-booster	56	60	56	63
Anti-D Level 3 Post-booster	53	59	53	60
Anti-T Level 1 Pre-booster	58	60	57	65
Anti-T Level 2 Pre-booster	48	52	41	54
Anti-T Level 1 Post-booster	58	61	58	65
Anti-T Level 2 Post-booster	58	61	58	64
Anti-T Level 3 Post-booster	52	58	55	62
Anti-Polio 1 Pre-booster	57	59	57	65
Anti-Polio 1 Post-booster	57	61	58	64
Anti-Polio 2 Pre-booster	58	59	56	65
Anti-Polio 2 Post-booster	56	61	58	64
Anti-Polio 3 Pre-booster	57	57	53	64
Anti-Polio 3 Post-booster	56	60	58	64
Anti-PT Post-booster	48	57	52	51
Anti-FHA Post-booster	48	50	52	57

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Solicited Injection Site or Systemic Reactions After Vaccination With DTaP-IPV-Hep B-PRP~T Vaccine

End point title	Number of Subjects With Solicited Injection Site or Systemic Reactions After Vaccination With DTaP-IPV-Hep B-PRP~T Vaccine <sup>[3]</sup>
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End point description:

Solicited Injection Site Reactions: Pain, Erythema, Swelling, Extensive Swelling of Vaccinated Limb.  
Solicited Systemic Reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia,

Irritability.

Grade 3 reactions were defined as: Pain, cries when injected limb is moved or movement of injected limb reduced; Erythema and swelling,  $\geq 5\text{cm}$ ; Extensive swelling of limb; Pyrexia,  $\geq 39.6^{\circ}\text{C}$ ; Vomiting  $\geq 6$  episodes/24 hours or requiring parenteral hydration; Somnolence, sleeping most of time or difficult to wake up; Anorexia, refuses  $\geq$  feeds or most feeds; Irritability, inconsolable.

End point type	Primary
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End point timeframe:

Days 0 up to 7 after any injection

Notes:

[3] - 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 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3	Infanrix Hexa™
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	254	262	252	113
Units: Subjects				
number (not applicable)				
Injection site Pain	174	193	177	80
Grade 3 injection site Pain	8	11	14	6
Injection site Erythema	135	127	135	63
Grade 3 injection site Erythema	3	4	5	1
Injection site Swelling	51	69	58	35
Grade 3 injection site Swelling	2	3	3	1
Extensive Swelling of Vaccinated Limb	0	1	0	0
Grade 3 Extensive Swelling of Vaccinated Limb	0	1	0	0
Pyrexia	25	35	28	22
Grade 3 Pyrexia	2	0	2	1
Vomiting	44	49	36	19
Grade 3 Vomiting	0	1	0	1
Crying	91	91	87	42
Grade 3 Crying	1	2	2	2
Somnolence	55	66	54	33
Grade 3 Somnolence	5	2	0	0
Anorexia	95	101	87	42
Grade 3 Anorexia	6	5	3	3
Irritability	145	166	166	75
Grade 3 Irritability	8	3	3	2

## 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 the booster injection to up to 6 months post-booster injection.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

### Reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 1
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Reporting group description:

Subjects had received 3 primary doses of Batch 1 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 2
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Reporting group description:

Subjects had received 3 primary doses of Batch 2 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

Reporting group title	DTaP-IPV-Hep B-PRP~T Batch 3
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Reporting group description:

Subjects had received 3 primary doses of Batch 3 of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) in Study A3L11 and received a booster dose of (DTaP-IPV-Hep B-PRP~T) at Day 0 in the present study.

Reporting group title	Infanrix Hexa™
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Reporting group description:

Subjects had received 3 primary doses of Diphtheria (D), Tetanus (T), Pertussis (acellular, component [aP]), Hepatitis B (Hep B, [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), (Infanrix hexa™), plus Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed in Study A3L11 and received a booster dose of DTaP-IPV-Hep B-PRP~T at Day 0 in the present study.

Serious adverse events	DTaP-IPV-Hep B-PRP~T Batch 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 254 (0.39%)	1 / 262 (0.38%)	1 / 252 (0.40%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 262 (0.00%)	0 / 252 (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
Pharyngitis			

subjects affected / exposed	0 / 254 (0.00%)	0 / 262 (0.00%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 262 (0.38%)	0 / 252 (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

<b>Serious adverse events</b>	Infanrix Hexa™		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 113 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 113 (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 %

<b>Non-serious adverse events</b>	DTaP-IPV-Hep B-PRP~T Batch 1	DTaP-IPV-Hep B-PRP~T Batch 2	DTaP-IPV-Hep B-PRP~T Batch 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	188 / 254 (74.02%)	207 / 262 (79.01%)	197 / 252 (78.17%)
Nervous system disorders			
Somnolence			
alternative assessment type: Systematic			

subjects affected / exposed <sup>[1]</sup> occurrences (all)	55 / 252 (21.83%) 55	66 / 262 (25.19%) 66	54 / 251 (21.51%) 54
General disorders and administration site conditions Solicited Injection Site Erythema alternative assessment type: Systematic subjects affected / exposed <sup>[2]</sup> occurrences (all)	135 / 252 (53.57%) 135	127 / 262 (48.47%) 127	135 / 251 (53.78%) 135
Solicited Injection Site Pain alternative assessment type: Systematic subjects affected / exposed <sup>[3]</sup> occurrences (all)	174 / 252 (69.05%) 174	193 / 262 (73.66%) 193	177 / 251 (70.52%) 177
Solicited Injection Site Swelling alternative assessment type: Systematic subjects affected / exposed <sup>[4]</sup> occurrences (all)	51 / 252 (20.24%) 51	69 / 262 (26.34%) 69	58 / 251 (23.11%) 58
Pyrexia alternative assessment type: Systematic subjects affected / exposed <sup>[5]</sup> occurrences (all)	25 / 252 (9.92%) 25	35 / 262 (13.36%) 35	28 / 251 (11.16%) 28
Gastrointestinal disorders Vomiting alternative assessment type: Systematic subjects affected / exposed <sup>[6]</sup> occurrences (all)	44 / 252 (17.46%) 44	49 / 262 (18.70%) 49	36 / 251 (14.34%) 36
Psychiatric disorders Irritability alternative assessment type: Systematic subjects affected / exposed <sup>[7]</sup> occurrences (all)	145 / 252 (57.54%) 145	166 / 262 (63.36%) 166	166 / 251 (66.14%) 166
Crying alternative assessment type: Systematic subjects affected / exposed <sup>[8]</sup> occurrences (all)	91 / 252 (36.11%) 91	91 / 262 (34.73%) 91	87 / 251 (34.66%) 87
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	13 / 254 (5.12%) 14	19 / 262 (7.25%) 19	14 / 252 (5.56%) 14
Metabolism and nutrition disorders Anorexia alternative assessment type: Systematic subjects affected / exposed <sup>[9]</sup> occurrences (all)	95 / 252 (37.70%) 95	101 / 262 (38.55%) 101	87 / 251 (34.66%) 87

<b>Non-serious adverse events</b>	Infanrix Hexa™		
Total subjects affected by non-serious adverse events subjects affected / exposed	92 / 113 (81.42%)		
Nervous system disorders Somnolence alternative assessment type: Systematic subjects affected / exposed <sup>[1]</sup> occurrences (all)	33 / 113 (29.20%) 33		
General disorders and administration site conditions Solicited Injection Site Erythema alternative assessment type: Systematic subjects affected / exposed <sup>[2]</sup> occurrences (all)  Solicited Injection Site Pain alternative assessment type: Systematic subjects affected / exposed <sup>[3]</sup> occurrences (all)  Solicited Injection Site Swelling alternative assessment type: Systematic subjects affected / exposed <sup>[4]</sup> occurrences (all)  Pyrexia alternative assessment type: Systematic subjects affected / exposed <sup>[5]</sup> occurrences (all)	63 / 113 (55.75%) 63  80 / 113 (70.80%) 80  35 / 113 (30.97%) 35  22 / 113 (19.47%) 22		
Gastrointestinal disorders			

Vomiting alternative assessment type: Systematic subjects affected / exposed <sup>[6]</sup> occurrences (all)	19 / 113 (16.81%) 19		
Psychiatric disorders Irritability alternative assessment type: Systematic subjects affected / exposed <sup>[7]</sup> occurrences (all)  Crying alternative assessment type: Systematic subjects affected / exposed <sup>[8]</sup> occurrences (all)	75 / 113 (66.37%) 75  42 / 113 (37.17%) 42		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 4		
Metabolism and nutrition disorders Anorexia alternative assessment type: Systematic subjects affected / exposed <sup>[9]</sup> occurrences (all)	42 / 113 (37.17%) 42		

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? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported