Clinical trial results:
Immunogenicity and Safety of Sanofi Pasteur's DTaP-IPV-HB-PRP~T Combined Vaccine Given as a Three-Dose Primary Series at 2, 3, 4 Months of Age and Followed by a Booster Dose Given at 16 to 17 Months of Age in Vietnamese Infants Who Previously Received a Dose of Hepatitis B Vaccine at Birth or within 1 Week after Birth

Summary

EudraCT number	2017-004181-10
Trial protocol	Outside EU/EEA
Global end of trial date	11 January 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2018
First version publication date	13 May 2018

Trial information

Trial identification

Sponsor protocol code	A3L35

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02428491
WHO universal trial number (UTN)	U1111-1143-8177

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	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	31 July 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile after each and all doses of Sanofi Pasteur's DTaP-IPV-HB-PRP~T in Vietnamese infants and toddlers.

Protection of trial subjects:

All subjects that met all the study inclusion and none of the exclusion criteria, including one subject who did not meet an inclusion criterion, were randomized and vaccinated. 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: -

Evidence for comparator: -

Actual start date of recruitment	20 April 2015
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	Vietnam: 354
Worldwide total number of subjects	354
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	354
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 in 1 centre in Vietnam from 20 April 2015 to 23 October 2015.

Pre-assignment

Screening details:

A total of 354 subjects who met all of the inclusion criteria and none of the exclusion criteria, including one subject who did not meet an inclusion criterion were randomized and vaccinated in this study.

Period 1

Period 1 title	DTaP-IPV-HB-PRP~T Vaccine (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	DTaP-IPV-HB-PRP~T Vaccine

Arm description:

Subjects received 3 doses of 0.5 mL DTaP-IPV-HB-PRP~T combined vaccine, intramuscularly, at 2, 3 and 4 months of age (Infant Series), followed by a booster dose approximately 12 months after the completion of the Infant Series (at 16 to 17 months of age).

Arm type	Experimental
Investigational medicinal product name	DTaP-IPV-HB-PRP~T Combined Vaccine
Investigational medicinal product code	
Other name	Hexaxim
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection into the anterolateral area of the right thigh.

Number of subjects in period 1	DTaP-IPV-HB-PRP~T Vaccine
Started	354
Subjects completed the Infant Series	352
Subjects completed Booster vaccination	349
Completed	346
Not completed	8
Consent withdrawn by subject	4
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	DTaP-IPV-HB-PRP~T Vaccine
Reporting group description:	
Subjects received 3 doses of 0.5 mL DTaP-IPV-HB-PRP~T combined vaccine, intramuscularly, at 2, 3 and 4 months of age (Infant Series), followed by a booster dose approximately 12 months after the completion of the Infant Series (at 16 to 17 months of age).	

Reporting group values	DTaP-IPV-HB-PRP~T Vaccine	Total	
Number of subjects	354	354	
Age categorical			
Units: Subjects			
Age continuous			
Units: days			
arithmetic mean	75.4		
standard deviation	± 8.6	-	
Gender categorical			
Units: Subjects			
Female	175	175	
Male	179	179	
Recruitment by cohort			
Subjects in this trial were randomized in a 1:1 ratio in 2 cohorts. All subjects in both cohorts received Sanofi Pasteur's DTaP-IPV-HB-PRP~T combined vaccine in a 3-dose Infant Series. Subjects from Cohort 1 provided blood samples for immunogenicity assessment and were evaluated for safety and immunogenicity. Subjects in Cohort 2 did not provide any blood samples for immunogenicity analysis and were evaluated for safety only.			
Units: Subjects			
Cohort 1	178	178	
Cohort 2	176	176	

End points

End points reporting groups

Reporting group title	DTaP-IPV-HB-PRP~T Vaccine

Reporting group description:

Subjects received 3 doses of 0.5 mL DTaP-IPV-HB-PRP~T combined vaccine, intramuscularly, at 2, 3 and 4 months of age (Infant Series), followed by a booster dose approximately 12 months after the completion of the Infant Series (at 16 to 17 months of age).

Subject analysis set title	Group 3 A3L15
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects from Study A3L15 (NCT01105559 and 2011-004450-26), who had been given DTaP-IPV-HB-PRP~T vaccine at 6, 10, and 14 weeks of age following Hep B vaccination at birth, were included in this group for the non-inferiority analysis.

Primary: Number of Subjects Reporting Solicited Injection Site Reactions (Pain, Erythema, Swelling) After Infant Series

End point title	Number of Subjects Reporting Solicited Injection Site Reactions (Pain, Erythema, Swelling) After Infant Series[1]

End point description:

A solicited reaction was an AE prelisted in the electronic case report from (eCRF) and considered to be related to vaccination. Injection site reactions: pain (Grade 3: Cried when injected limb was moved, or the movement of the injected limb was reduced), erythema and swelling (Grade 3: >= 50 mm). Number of subjects with any solicited injection-site reaction and Grade 3 solicited injection-site reactions were reported. Analysis was performed on safety analysis set after infant series, which included all subjects who received at least 1 dose of infant series vaccine.

End point type	Primary

End point timeframe:

Within 7 days after any 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	354			
Units: subjects				
Any Injection site pain	205			
Grade 3 Injection site pain	2			
Any Injection site erythema	113			
Grade 3 Injection site erythema	6			
Any Injection site swelling	47			
Grade 3 Injection site swelling	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Solicited Systemic Reactions (Pyrexia, Vomiting, Crying, Somnolence, Decreased Appetite, Irritability) After Infant Series

End point title	Number of Subjects Reporting Solicited Systemic Reactions (Pyrexia, Vomiting, Crying, Somnolence, Decreased Appetite, Irritability) After Infant Series[2]

End point description:

A solicited reaction was an AE prelisted in eCRF and considered to be related to vaccination. Systemic reactions: pyrexia (Grade 3: >39.5 degree Celsius), vomiting (Grade 3: >= 6 episodes per 24 hours), crying (Grade 3: >3 hours), somnolence (Grade 3: Sleeping most of the time/difficult to wake up), decreased appetite (Grade 3: Refuses >=3 feeds/meals or most feeds/meals) & irritability (Grade 3: Inconsolable). Number of subjects with any systemic reaction and Grade 3 systemic reactions were reported. Analysis was performed on safety analysis set after infant series. Here, "n" signifies number of subjects with available data for each category.

End point type	Primary

End point timeframe:

Within 7 days after any vaccination

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	354			
Units: subjects				
Any Pyrexia (n=353)	71			
Grade 3 Pyrexia (n=353)	0			
Any Vomiting (n=354)	82			
Grade 3 Vomiting (n=354)	0			
Any Crying (n=354)	158			
Grade 3 Crying (n=354)	3			
Any Somnolence (n=354)	141			
Grade 3 Somnolence (n=354)	0			
Any Decreased appetite (n=354)	108			
Grade 3 Decreased appetite (n=354)	2			
Any Irritability (n=354)	119			
Grade 3 Irritability (n=354)	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Solicited Injection Site Reactions (Pain, Erythema, Swelling, Extensive Swelling of Vaccinated Limb) After Booster Vaccination

End point title	Number of Subjects Reporting Solicited Injection Site Reactions (Pain, Erythema, Swelling, Extensive Swelling of Vaccinated Limb) After Booster Vaccination[3]

End point description:

A solicited reaction was an AE prelisted in the eCRF and considered to be related to vaccination. Injection site reactions: pain (Grade 3: Cried when injected limb was moved, or the movement of the injected limb was reduced), erythema and swelling (Grade 3: >= 50 mm). Number of subjects with any solicited injection-site systemic reaction and Grade 3 solicited injection-site reactions were reported. Analysis was performed on safety analysis set after booster dose, which included all subjects who received booster vaccine.

End point type	Primary

End point timeframe:

Within 7 days after vaccination

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	349			
Units: subjects				
Any Injection site pain	83			
Grade 3 Injection site pain	0			
Any Injection site erythema	37			
Grade 3 Injection site erythema	2			
Any Injection site swelling	29			
Grade 3 Injection site swelling	1			
Any Extensive swelling of vaccinated limb	0			
Grade 3 Extensive swelling of vaccinated limb	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Solicited Systemic Reactions (Pyrexia, Vomiting, Crying, Somnolence, Decreased Appetite, Irritability) After Booster Vaccination

End point title	Number of Subjects Reporting Solicited Systemic Reactions (Pyrexia, Vomiting, Crying, Somnolence, Decreased Appetite, Irritability) After Booster Vaccination[4]

End point description:

A solicited reaction is an AE prelisted in the eCRF and considered to be related to vaccination. Systemic reactions: pyrexia (Grade 3: >39.5 degree Celsius), vomiting (Grade 3: >=6 episodes per 24 hours), crying (Grade 3: >3 hours), somnolence (Grade 3: Sleeping most of the time or difficult to wake up), decreased appetite (Grade 3: Refuses>=3 feeds/meals or most feeds/meals) & irritability (Grade 3: Inconsolable). Number of subjects with any systemic reaction and Grade 3 systemic reactions were reported. Analysis was performed on safety analysis set after booster dose. Here, "n" signifies number of subjects with available data for each category.

End point type	Primary

End point timeframe:

Within 7 days after vaccination

Notes:

[4] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	349			
Units: subjects				
Any Pyrexia (n=348)	36			
Grade 3 Pyrexia (n=348)	0			
Any Vomiting (n=349)	11			
Grade 3 Vomiting (n=349)	1			
Any Crying (n=349)	32			
Grade 3 Crying (n=349)	0			
Any Somnolence (n=349)	25			
Grade 3 Somnolence (n=349)	0			
Any Decreased appetite (n=349)	53			
Grade 3 Decreased appetite (n=349)	1			
Any Irritability (n=349)	45			
Grade 3 Irritability (n=349)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Seroprotection/Seroconversion/Vaccine Response After Infant Series in Cohort 1

End point title	Number of Subjects With Seroprotection/Seroconversion/Vaccine Response After Infant Series in Cohort 1

End point description:

Seroconversion:4fold increase in anti-Pertussis(PT)& anti-Filamentous hemagglutinin(FHA) antibody(Ab) concentrations from pre-vaccination to one month after first dose.Vaccine response:anti-PT/anti-FHA Ab concentrations in Enzyme Linked Immunosorbent Assay(ELISA) units(EU)/mL>=4*Lower Limit of Quantitation(LLOQ) if pre-vaccination concentration <4*LLOQ/>=pre-vaccination concentration if pre-vaccination concentrations>=4*LLOQ. Seroprotection:anti-Diphtheria &anti-Tetanus>=0.01 International Units(IU)/mL&>=0.1 IU/mL;anti-PT &anti-FHA>=2 EU/mL &>=8 EU/mL;anti-Polyribosyl Ribitol Phosphate(PRP)>=0.15 microgram per milliliter(mcg/mL) &>=1.0mcg/mL;anti-Polio types 1,2,&3>=8(1/dilution),anti-Hepatitis B>=10 mili-international units per mililiter(mIU/mL)&>=100 mIU/mL.Analysis performed on per protocol analysis set which included subjects from Cohort 1 who received at least one dose of study vaccine & excluding those who had protocol deviations.n=subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination, only for anti-PT and anti-FHA) and Day 90 (1 month after third dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: subjects				
Anti-Diphtheria; Day 90(>= 0.01 IU/mL) (n= 163)	162			

Anti-Diphtheria; Day 90 (>= 0.1 IU/mL) (n= 163)	59			
Anti-Tetanus; Day 90 (>= 0.01 IU/mL) (n= 166)	166			
Anti-Tetanus; Day 90 (>= 0.1 IU/mL) (n= 166)	166			
Anti-PT; Day 0 (>=2 EU/mL) (n= 167)	84			
Anti-PT; Day 0 (>=8 EU/mL) (n= 167)	24			
Anti-PT; Day 0/Day 90 (Vaccine Response) (n= 167)	166			
Anti-PT; Day 0/Day 90(Seroconversion) (n= 167)	160			
Anti-FHA; Day 0 (>=2 EU/mL) (n= 167)	149			
Anti-FHA; Day 0 (>=8 EU/mL) (n= 167)	64			
Anti-FHA; Day 0/Day 90 (Vaccine Response) (n= 167)	167			
Anti-FHA; Day 0/Day 90 (Seroconversion) (n= 167)	161			
Anti-Polio 1; Day 90 (>=8 [1/dil]) (n= 163)	163			
Anti-Polio 2; Day 90 (>=8 [1/dil]) (n= 164)	164			
Anti-Polio 3; Day 90 (>=8 [1/dil]) (n= 166)	166			
Anti- Hep B; Day 90 (>=10 mIU/mL) (n= 167)	164			
Anti- Hep B; Day 90 (>=100 mIU/mL) (n= 167)	159			
Anti-PRP; Day 90 (>=0.15 mcg/mL) (n= 166)	157			
Anti-PRP; Day 90 (>=1.0 mcg/mL) (n= 166)	122			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Seroprotection/Seroconversion/Vaccine and Booster Response Before and After Booster Vaccination in Cohort 1

End point title	Number of Subjects With Seroprotection/Seroconversion/Vaccine and Booster Response Before and After Booster Vaccination in Cohort 1

End point description:

Seroconversion:4fold increase in anti-PT & anti-FHA Ab concentrations from pre-booster vaccination to 1 month after booster dose.Vaccine response post-booster vaccination:post-booster Ab concentrations>=4*LLOQ if pre-dose 1 Ab concentrations<4*LLOQ/post-booster Ab concentrations>=pre-dose 1 Ab concentrations if pre-dose 1>=4*LLOQ. Booster response:>=4 fold Ab concentrations increase from pre-dose 4 to one-month post-dose 4 if one-month post-dose 3<4*LLOQ/>=2 fold Ab concentrations increase from pre-dose 4 to one-month post-dose 4 if pre-dose 4>=4*LLOQ.Seroprotection:anti-Diphtheria & anti-Tetanus>=0.01 IU/mL &>=0.1 IU/mL &>=1.0 IU/mL;anti-PRP >=0.15 mcg/mL &>=1.0 mcg/mL;anti-Polio types 1, 2, & 3>=8 (1/dilution),anti-Hepatitis B>=10 mIU/mL &>=100 mIU/mL. Analysis performed on booster per-protocol analysis set which included subjects from Cohort 1 who received booster dose of study vaccine & excluding those who had protocol deviations.n=subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 425 (pre-booster) and Day 455 (1 month after booster dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: subjects				
Anti-Diphtheria; Day 425 (> =0.01 IU/mL) (n=167)	163			
Anti-Diphtheria; Day 425 (>=0.1 IU/mL) (n=167)	57			
Anti-Diphtheria; Day 455 (> =0.01 IU/mL) (n=166)	166			
Anti-Diphtheria; Day 455 (> =0.1 IU/mL) (n=166)	166			
Anti-Diphtheria; Day 455 (> =1.0 IU/mL) (n=166)	158			
Anti-Tetanus; Day 425 (> =0.01 IU/mL) (n=167)	167			
Anti-Tetanus; Day 425 (> =0.1 IU/mL) (n=167)	142			
Anti-Tetanus; Day 455 (> = 0.01 IU/mL) (n=165)	165			
Anti-Tetanus; Day 455 (> =0.1 IU/mL) (n=165)	165			
Anti-Tetanus; Day 455 (> =1.0 IU/mL) (n=165)	164			
Anti-PT; Day 425 (> =2 EU/mL) (n=160)	130			
Anti-PT; Day 425 (> =8 EU/mL) (n=160)	44			
Anti-PT; Day 455/ Day 0 (Vaccine Response) (n=166)	166			
Anti-PT;Day 455/Day 425(Booster Response)(n=160)	157			
Anti-PT; Day 455/Day 425 (Seroconversion) (n=160)	155			
Anti-FHA; Day 425 (> =2 EU/mL) (n=164)	164			
Anti-FHA; Day 425 (> =8 EU/mL) (n=164)	141			
Anti-FHA; Day 455/Day 0 (Vaccine Response) (n=166)	166			
Anti-FHA; Day 455/Day 425(Booster Response)(n=163)	158			
Anti-FHA; Day 455/Day 425 (Seroconversion) (n=163)	147			
Anti-Polio 1; Day 425 (> =8 [1/dil]) (n=167)	161			
Anti-Polio 1; Day 455 (> =8 [1/dil]) (n=164)	164			
Anti-Polio 2; Day 425 (> =8 [1/dil]) (n=167)	165			
Anti-Polio 2; Day 455 (> =8 [1/dil]) (n=163)	163			
Anti-Polio 3; Day 425 (> =8 [1/dil]) (n=167)	159			
Anti-Polio 3; Day 455 (> =8 [1/dil]) (n=164)	164			

Anti-Hep B; Day 425 (> =10 mIU/mL) (n=167)	153			
Anti-Hep B; Day 425 (> =100 mIU/mL) (n=167)	94			
Anti- Hep B; Day 455 (> =10 mIU/mL) (n=167)	164			
Anti- Hep B; Day 455 (> =100 mIU/mL) (n=167)	161			
Anti-PRP; Day 425 (> =0.15 mcg/mL) (n=167)	135			
Anti-PRP; Day 425 (> =1.0 mcg/mL) (n=167)	77			
Anti-PRP; Day 455 (> =0.15 mcg/mL) (n=167)	167			
Anti-PRP; Day 455 (> =1.0 mcg/mL) (n=167)	167			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers or Geometric Mean Concentrations of DTaP-IPV-HB-PRP~T Antibodies Before and After Infant Series in Cohort 1

End point title	Geometric Mean Titers or Geometric Mean Concentrations of DTaP-IPV-HB-PRP~T Antibodies Before and After Infant Series in Cohort 1

End point description:

Anti-diphtheria Ab levels were measured by a toxin neutralization test. Anti-tetanus, anti- pertussis toxin (anti-PT) and anti- filamentous hemagglutinin (anti-FHA) Ab levels were measured by ELISA. Anti-poliovirus types 1, 2, and 3 Ab levels were measured by neutralization assay. Anti-Hep B Ab levels were measured by VITROS ECi/ECiQ Immunodiagnostic system using chemiluminescence detection technology. Anti-PRP Ab levels were measured using a Farr-type radioimmunoassay (RIA). Analysis was performed on per-protocol analysis set which included subjects from Cohort 1 who received at least one dose of study vaccine and excluding those who had protocol deviations. Here, "n" signifies number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination, only for anti-PT and anti-FHA) and Day 90 (1 month after third dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Day 90 (n= 163)	0.080 (0.069 to 0.092)			
Anti-Tetanus; Day 90 (n= 166)	1.16 (1.02 to 1.31)			
Anti-PT; Day 0 (n= 167)	2.35 (2.01 to 2.75)			
Anti-PT; Day 90 (n= 167)	111 (99 to 125)			

Anti-FHA; Day 0 (n= 167)	5.44 (4.69 to 6.31)			
Anti-FHA; Day 90 (n= 167)	208 (190 to 228)			
Anti-Polio 1; Day 90 (n= 163)	283 (237 to 337)			
Anti-Polio 2; Day 90 (n= 164)	582 (476 to 712)			
Anti-Polio 3; Day 90 (n= 166)	735 (582 to 927)			
Anti- Hep B; Day 90 (n= 167)	1383 (1092 to 1752)			
Anti-PRP; Day 90 (n= 163)	2.48 (1.95 to 3.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers or Geometric Mean Concentrations of DTaP-IPV-HB-PRP~T Antibodies Before and After Booster Vaccination in Cohort 1

End point title	Geometric Mean Titers or Geometric Mean Concentrations of DTaP-IPV-HB-PRP~T Antibodies Before and After Booster Vaccination in Cohort 1

End point description:

Anti-diphtheria Ab were measured by a toxin neutralization test. Anti-tetanus, anti-PT and anti-FHA Ab levels were measured by ELISA. Anti-poliovirus types 1, 2, and 3 Ab levels were measured by neutralization assay. Anti-Hep B Ab levels were measured by VITROS ECi/ECiQ Immunodiagnostic system using chemiluminescence detection technology. Anti-PRP Ab levels were measured using a Farr-type RIA. Analysis was performed on booster per-protocol analysis set which included subjects from Cohort 1 who received the booster dose of study vaccine and excluding those who had protocol deviations. Here, "n" signifies number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 425 (pre-booster) and Day 455 (1 month after booster dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Day 425 (n=167)	0.065 (0.054 to 0.078)			
Anti-Diphtheria; Day 455 (n=166)	5.36 (4.56 to 6.30)			
Anti-Tetanus; Day 425 (n=167)	0.242 (0.211 to 0.277)			
Anti-Tetanus; Day 455 (n=165)	10.0 (8.85 to 11.4)			
Anti-PT; Day 425 (n=160)	4.80 (4.00 to 5.75)			

Anti-PT; Day 455 (n=167)	94.9 (84.7 to 106)			
Anti-FHA; Day 425 (n=164)	18.3 (15.7 to 21.4)			
Anti-FHA; Day 455 (n=166)	216 (192 to 242)			
Anti-Polio 1; Day 425 (n=167)	68.1 (55.7 to 83.2)			
Anti-Polio 1; Day 455 (n=164)	2173 (1888 to 2501)			
Anti-Polio 2; Day 425 (n=167)	113 (92.6 to 137)			
Anti-Polio 2; Day 455 (n=163)	3867 (3330 to 4492)			
Anti-Polio 3; Day 425 (n=167)	61.7 (48.7 to 78.1)			
Anti-Polio 3; Day 455 (n=164)	2812 (2411 to 3280)			
Anti-Hep B; Day 425 (n=167)	101 (80.6 to 126)			
Anti-Hep B; Day 455 (n=167)	5554 (4256 to 7247)			
Anti-PRP; Day 425 (n=167)	0.806 (0.619 to 1.05)			
Anti-PRP; Day 455 (n=167)	79.2 (64.9 to 96.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratio of DTaP-IPV-HB-PRP~T Antibodies After Infant Series in Cohort 1 for PT and FHA Antigens

End point title	Geometric Mean Titer Ratio of DTaP-IPV-HB-PRP~T Antibodies After Infant Series in Cohort 1 for PT and FHA Antigens

End point description:

Anti-PT and anti-FHA Ab levels were measured by ELISA. Analysis was performed on per-protocol analysis set which included subjects from Cohort 1 who received at least one dose of study vaccine and excluding those who had protocol deviations.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 90 (1 month after third dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: Ratio				
number (confidence interval 95%)				
Anti-PT; Day 90/Day 0	47.2 (38.4 to 58.1)			
Anti-FHA; Day 90/Day 0	38.2 (32.0 to 45.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration/Titer Ratio of DTaP-IPV-HB-PRP~T Antibodies After Booster Vaccination in Cohort 1

End point title	Geometric Mean Concentration/Titer Ratio of DTaP-IPV-HB-PRP~T Antibodies After Booster Vaccination in Cohort 1

End point description:

Anti-diphtheria Ab were measured by a toxin neutralization test. Anti-tetanus, anti-PT and anti-FHA Ab levels were measured by ELISA. Anti-poliovirus types 1, 2, and 3 Ab levels were measured by neutralization assay. Anti-Hep B Ab levels were measured by VITROS ECi/ECiQ Immunodiagnostic system using chemiluminescence detection technology. Anti-PRP Ab levels were measured using a Farr-type RIA. Analysis was performed on booster per-protocol analysis set which included subjects from Cohort 1 who received the booster dose of study vaccine and excluding those who had protocol deviations. Here, "n" signifies number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 425 (pre-booster) and Day 455 (1 month after booster dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: Ratio				
number (confidence interval 95%)				
Anti-Diphtheria; Day 455/Day 425 (n=166)	82.6 (71.1 to 95.8)			
Anti-Tetanus; Day 455 /Day 425 (n=165)	41.3 (36.9 to 46.2)			
Anti-PT; Day 455 /Day 425 (n=160)	19.9 (17.2 to 23.0)			
Anti-FHA; Day 455 /Day 425 (n=163)	11.9 (10.4 to 13.5)			
Anti-Polio 1; Day 455 /Day 425 (n=164)	32.8 (26.4 to 40.6)			
Anti-Polio 2; Day 455 /Day 425 (n=163)	34.5 (27.6 to 43.0)			
Anti-Polio 3; Day 455 /Day 425 (n=164)	47.1 (37.1 to 59.9)			
Anti-Hep B; Day 455/Day 425 (n=167)	55.1 (46.6 to 65.3)			
Anti-PRP; Day 455 /Day 425 (n=167)	98.2 (78.8 to 122)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Seroprotection/Seroconversion Rates after Infant Series in Cohort 1 and Group 3 of A3L15 (U1111-1111-5789, NCT ID: NCT01105559, EudraCT number: 2011-004433-14)

End point title	Percentage of Subjects With Seroprotection/Seroconversion Rates after Infant Series in Cohort 1 and Group 3 of A3L15 (U1111-1111-5789, NCT ID: NCT01105559, EudraCT number: 2011-004433-14)

End point description:

Seroconversion defined as 4-fold increase in anti-PT & anti-FHA Ab concentrations from pre-vaccination to one month after first dose. Seroprotection defined as following: anti-Diphtheria & anti-Tetanus >=0.01 IU/mL; anti-PT & anti-FHA >=4EU/mL; anti-PRP >=0.15 mcg/mL; anti-Polio types 1, 2, & 3 >=8 (1/dilution), anti-Hepatitis B >=10 mIU/mL. Analysis performed on per protocol analysis set, which included subjects from Cohort 1 who received at least one dose of study vaccine & excluding those who had protocol deviations. Here, "n" signifies number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 90 (1 month after third dose)

End point values	DTaP-IPV-HB-PRP~T Vaccine	Group 3 A3L15		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	167	123		
Units: percentage of subjects				
number (not applicable)				
Anti-Diphtheria; Day 90 (>=0.01 IU/mL) (n=163,122)	99.4	95.1		
Anti-Tetanus; Day 90 (>=0.01 IU/mL) (n=166,122)	100.0	100.0		
Anti-PRP; Day 90 (>=0.15 mcg/mL) (n=166,122)	94.6	97.5		
Anti-PT; Day 90 (>=4-fold rise EU/mL) (n=167,103)	95.8	95.1		
Anti-FHA; Day 90 (>=4-fold rise EU/mL) (n=167,90)	96.4	90.0		
Anti-Polio 1; Day 90 (>=8 [1/dil]) (n=163,104)	100.0	99.0		
Anti-Polio 2; Day 90 (>=8 [1/dil]) (n=164,113)	100.0	98.2		
Anti-Polio 3; Day 90 (>=8 [1/dil]) (n=166,98)	100.0	100.0		
Anti-Hep B; Day 90 (>=10 mIU/mL) (n=167,98)	98.2	99.0		

Statistical analyses

Statistical analysis title	Non-inferiority analysis of anti-D antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days

after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 163).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	99.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.6
upper limit	100

Statistical analysis title	Non-inferiority analysis of anti-T antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 166).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.8
upper limit	100

Statistical analysis title	Non-inferiority analysis of anti-PRP antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 166).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	94.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	90
upper limit	97.5

Statistical analysis title	Non-inferiority analysis of anti-PRP antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 166).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	94.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	90
upper limit	97.5

Statistical analysis title	Non-inferiority analysis of anti-FHA antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 167).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	96.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.3
upper limit	98.7

Statistical analysis title	Non-inferiority analysis of antiPolio-1 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 163).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.8
upper limit	100

Statistical analysis title	Non-inferiority analysis of antiPolio-2 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 164).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.8
upper limit	100

Statistical analysis title	Non-inferiority analysis of antiPolio-3 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 166).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.8
upper limit	100

Statistical analysis title	Non-inferiority analysis of anti-Hep B antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only DTaP-IPV-HB-PRP~T combined vaccine group (number of subject analyzed= 167).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	98.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.8
upper limit	99.6

Statistical analysis title	Non-inferiority analysis of anti-D antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 122).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	95.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	89.6
upper limit	98.2

Statistical analysis title	Non-inferiority analysis of anti-T antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 122).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	97
upper limit	100

Statistical analysis title	Non-inferiority analysis of anti-PRP antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 122).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	97.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	93
upper limit	99.5

Statistical analysis title	Non-inferiority analysis of anti-PT antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 103).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	95.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	89
upper limit	98.4

Statistical analysis title	Non-inferiority analysis of anti-FHA antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 90).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	90
Confidence interval	
level	95 %
sides	2-sided
lower limit	81.9
upper limit	95.3

Statistical analysis title	Non-inferiority analysis of antiPolio-1 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 104).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	99
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.8
upper limit	100

Statistical analysis title	Non-inferiority analysis of antiPolio-2 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 113).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	98.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	93.8
upper limit	99.8

Statistical analysis title	Non-inferiority analysis of antiPolio-3 antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 98).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.3
upper limit	100

Statistical analysis title	Non-inferiority analysis of anti-Hep B antibodies

Statistical analysis description:

Non-inferiority concluded if the lower limit of the two-sided 95% CI for the rates observed 30 days after the third infant series dose in A3L35 lies entirely above the reference value (rates observed 30 days after the third dose in Group 3 of A3L15) minus the clinical acceptable limit of 10%. This statistical data represents data of only group 3 A3L15 (number of subject analyzed= 98).

Comparison groups	DTaP-IPV-HB-PRP~T Vaccine v Group 3 A3L15

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	percentage of subjects
Point estimate	99
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.4
upper limit	100

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited reactions were collected up to Day 7 after each injection, non-serious unsolicited adverse events (AEs) were collected up to Day 30 after each injection, and serious AEs were collected throughout the study period.

Adverse event reporting additional description:

Solicited reaction: AE prelisted in eCRF, considered related to vaccination. A solicited reaction was therefore, an adverse drug reaction observed, reported under conditions (nature and onset) prelisted in the eCRF. Unsolicited AE: an observed AE that does not fulfill conditions prelisted in eCRF in terms of symptom and/or onset post-vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	DTaP-IPV-HB-PRP~T Vaccine: Infant Series

Reporting group description:

Subjects received 3 doses of 0.5 mL DTaP-IPV-HB-PRP~T combined vaccine, intramuscularly, at 2, 3 and 4 months of age.

Reporting group title	DTaP-IPV-HB-PRP~T Vaccine: Booster Vaccination

Reporting group description:

Subjects received a booster dose of 0.5 mL DTaP-IPV-HB-PRP~T combined vaccine, intramuscularly, approximately 12 months after the completion of the Infant Series (at 16 to 17 months of age).

Serious adverse events	DTaP-IPV-HB-PRP~T Vaccine: Infant Series	DTaP-IPV-HB-PRP~T Vaccine: Booster Vaccination	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 354 (4.52%)	4 / 349 (1.15%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Cataract Congenital			
subjects affected / exposed	0 / 354 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza Like Illness			
subjects affected / exposed	1 / 354 (0.28%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	2 / 354 (0.56%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Disorder			
subjects affected / exposed	1 / 354 (0.28%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis Acute			
subjects affected / exposed	0 / 354 (0.00%)	1 / 349 (0.29%)	
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			
Dermatitis			
subjects affected / exposed	1 / 354 (0.28%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	2 / 354 (0.56%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 354 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 354 (0.28%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	2 / 354 (0.56%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 354 (1.69%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	1 / 354 (0.28%)	0 / 349 (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-PRP~T Vaccine: Infant Series	DTaP-IPV-HB-PRP~T Vaccine: Booster Vaccination	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	301 / 354 (85.03%)	137 / 349 (39.26%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	141 / 354 (39.83%)	25 / 349 (7.16%)	
occurrences (all)	202	25	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	158 / 354 (44.63%)	32 / 349 (9.17%)	
occurrences (all)	250	32	
Injection Site Erythema			
subjects affected / exposed	113 / 354 (31.92%)	37 / 349 (10.60%)	
occurrences (all)	181	37	
Injection Site Pain			
subjects affected / exposed	205 / 354 (57.91%)	83 / 349 (23.78%)	
occurrences (all)	360	83	
Injection Site Swelling			
subjects affected / exposed	47 / 354 (13.28%)	29 / 349 (8.31%)	
occurrences (all)	85	29	

Pyrexia			
subjects affected / exposed	87 / 354 (24.58%)	38 / 349 (10.89%)	
occurrences (all)	106	39	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	82 / 354 (23.16%)	13 / 349 (3.72%)	
occurrences (all)	118	13	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 354 (6.21%)	7 / 349 (2.01%)	
occurrences (all)	23	8	
Psychiatric disorders			
Irritability			
subjects affected / exposed	119 / 354 (33.62%)	45 / 349 (12.89%)	
occurrences (all)	200	45	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	108 / 354 (30.51%)	53 / 349 (15.19%)	
occurrences (all)	148	53	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2014	• A brief presentation of the commercialization status of hexavalent vaccines in the world and the advantages of the Sanofi Pasteur's hexavalent vaccine, if any, over other commercialized combined vaccines from Italy or United States was added in the Introduction section. • Since it was possible that the number of enrolled subjects was not achieved, the rule of three could be used in data analyses and this had been briefly explained. • Clarification on the fact that the insurance coverage cases at the end of study involvement for all subjects, with the exception of insurance coverage for subjects who reported an SAE during the trial that was determined to be related to study vaccines by the Investigator (insurance coverage was continued for these subjects until the SAE is resolved).
25 August 2014	• A booster dose was added to evaluate Ab persistence after 1 year. • A non-inferiority test comparing the immune response to all antigens induced by the study vaccine in Vietnam versus the response outside Vietnam was added. • The booster objective was added. • A booster endpoint was added.
16 February 2016	• A new Regional Director Of Medical Affairs was appointed. • The timelines were updated. • Clarification on the fact that reportable medications were to be collected in the CRF from the day of each vaccination up to the end of the safety follow-up, and that there was no collection between V4 and V5. • Restricted use therapies and non-authorized therapies were not to be collected anymore.
07 March 2016	Correction and clarification of the booster endpoints for PT and FHA were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported