

**Clinical trial results:**

**Immunogenicity and Safety of the sanofi pasteur's DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) versus sanofi pasteur's DTacP-IPV Combined Vaccine (TETRAXIM™) given simultaneously at separate sites with PRP~T conjugate Vaccine (ActHIB™) as a three-dose primary vaccination at 2, 4 and 6 Months of Age in South Korean Infants**

**Summary**

EudraCT number	2015-005293-38
Trial protocol	Outside EU/EEA
Global end of trial date	02 March 2012

**Results information**

Result version number	v1 (current)
This version publication date	09 June 2016
First version publication date	09 June 2016

**Trial information****Trial identification**

Sponsor protocol code	E2I49
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01214889
WHO universal trial number (UTN)	U1111-1115-6381

Notes:

**Sponsors**

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
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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 2012
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 March 2012
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority in terms of seroprotection rates (Diphtheria, Tetanus, Polio types 1, 2 and 3, PRP) and vaccine response rates to acellular Pertussis antigens (PT, FHA) of Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine versus sanofi pasteur's DTacP-IPV (TETRAXIM™) and PRP~T (Act-HIB™) vaccines, one month after the three-dose primary vaccination.

Protection of trial subjects:

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

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	28 September 2010
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	Korea, Republic of: 418
Worldwide total number of subjects	418
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)	418
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 28 September 2010 to 26 September 2011 at 13 clinic centers in South Korea.

### Pre-assignment

Screening details:

A total of 418 infants who met all inclusion and none of the exclusion criteria were enrolled in the study; 414 were randomized.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	DTaP-IPV//PRP-T
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Arm description:

Healthy infants received the investigational vaccine (DTaP-IPV//PRP-T) at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	DTaP-IPV//PRP-T combined vaccine (PENTAXIM™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the anterolateral aspect of the right thigh, 1 injection each at 2, 4, and 6 months of age.

<b>Arm title</b>	DTaP-IPV+PRP-T
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Arm description:

Healthy infants received a control vaccine DTaP-IPV combined vaccine (TETRAXIM™) and PRP-T (Act-HIB™) at 2, 4, and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	DTaP-IPV combined vaccine (TETRAXIM™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection into the anterolateral aspect of the right thigh, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	PRP-Tetanus conjugate vaccine (Act-HIB™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

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Dosage and administration details:

0.5 mL, intramuscular into the anterolateral aspect of the left thigh, 1 injection each at 2, 4, and 6 months of age.

<b>Number of subjects in period 1<sup>[1]</sup></b>	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T
Started	208	206
Completed	207	202
Not completed	1	4
Serious adverse event	-	1
Protocol deviation	1	3

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Notes:

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

Justification: A total of 418 subjects were enrolled in the study; 414 were randomized.

## Baseline characteristics

### Reporting groups

Reporting group title	DTaP-IPV//PRP-T
Reporting group description: Healthy infants received the investigational vaccine (DTaP-IPV//PRP-T) at 2, 4, and 6 months of age.	
Reporting group title	DTaP-IPV+PRP-T
Reporting group description: Healthy infants received a control vaccine DTaP-IPV combined vaccine (TETRAXIM™) and PRP-T (Act-HIB™) at 2, 4, and 6 months of age.	

Reporting group values	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T	Total
Number of subjects	208	206	414
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)	208	206	414
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: months			
arithmetic mean	2.04	2.06	-
standard deviation	± 0.112	± 0.12	-
Gender categorical			
Units: Subjects			
Female	90	95	185
Male	118	111	229

## End points

### End points reporting groups

Reporting group title	DTaP-IPV//PRP-T
Reporting group description:	
Healthy infants received the investigational vaccine (DTaP-IPV//PRP-T) at 2, 4, and 6 months of age.	
Reporting group title	DTaP-IPV+PRP-T
Reporting group description:	
Healthy infants received a control vaccine DTaP-IPV combined vaccine (TETRAXIM™) and PRP-T (ActHIB™) at 2, 4, and 6 months of age.	

### Primary: Percentage of Subjects with Seroprotection/Vaccine Response One Month after Primary Vaccination Series with DTaP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP~T Conjugate Vaccine (ActHIB)

End point title	Percentage of Subjects with Seroprotection/Vaccine Response One Month after Primary Vaccination Series with DTaP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP~T Conjugate Vaccine (ActHIB)
End point description:	
Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization. Anti-Polyribosyl Ribitol Phosphate (PRP) was measured using a radioimmunity assay. Seroprotection for Anti-Diphtheria was defined as antibody titers $\geq 0.01$ IU/mL, for Anti-Tetanus $\geq 0.1$ IU/mL, for Anti-Poliovirus types 1, 2, and 3 antibody titers $\geq 8$ (1/dil). Vaccine response for Anti-PT and Anti-FHA was defined as $\geq 4$ -fold increase.	
End point type	Primary
End point timeframe:	
1 month post-primary vaccination	

End point values	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	181		
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria	100	100		
Anti-Tetanus	100	100		
Anti-Polio 1	100	100		
Anti-Polio 2	100	100		
Anti-Polio 3	100	100		
Anti-PRP	100	100		
Anti-PT	99	98.9		
Anti-FHA	97.5	98.9		

## Statistical analyses

<b>Statistical analysis title</b>	Non-inferiority; Anti-Diphtheria
Statistical analysis description: Non-inferiority analysis of Anti-Diphtheria in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[1] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-Tetanus
Statistical analysis description: Non-inferiority analysis of Anti-Tetanus in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[2] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-Polio 1
Statistical analysis description: Non-inferiority analysis of Anti-Polio 1 in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[3] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-Polio 2
Statistical analysis description: Non-inferiority analysis of Anti-Polio 2 in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[4] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-Polio 3
Statistical analysis description: Non-inferiority analysis of Anti-Polio 3 in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[5]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[5] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-PRP
Statistical analysis description: Non-inferiority analysis of Anti-PRP in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[6]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	2.08

Notes:

[6] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-PT
Statistical analysis description: Non-inferiority analysis of Anti-PT in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV+PRP-T v DTaP-IPV//PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[7]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.68
upper limit	3.01

Notes:

[7] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

<b>Statistical analysis title</b>	Non-inferiority; Anti-FHA
Statistical analysis description: Non-inferiority analysis of Anti-FHA in DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T.	
Comparison groups	DTaP-IPV//PRP-T v DTaP-IPV+PRP-T
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[8]</sup>
Parameter estimate	DTaP-IPV//PRP-T minus DTaP-IPV+PRP-T
Point estimate	-1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.79
upper limit	1.75

Notes:

[8] - The non-inferiority was demonstrated if the lower limit of all the 95% confidence intervals of the difference was greater than -10%. DTaP-IPV//PRP-T was non-inferior to DTaP-IPV+PRP-T.

**Primary: Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and After A Primary Vaccination Series with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP~T Vaccine (ActHIB)**

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and After A Primary Vaccination Series with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP~T Vaccine (ActHIB) <sup>[9]</sup>
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End point description:

Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliiovirus types 1, 2, 3 antibody titers were measured using seroneutralization. Anti-Polyribosyl Ribitol Phosphate (PRP) was measured using a radioimmunology assay.

End point type Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 150 post-primary vaccination

Notes:

[9] - 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.

<b>End point values</b>	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	181		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Pre-vaccination	0.008 (0.007 to 0.01)	0.008 (0.007 to 0.01)		
Anti-Diphtheria; Post-vaccination	1.38 (1.21 to 1.58)	1.2 (1.06 to 1.37)		
Anti-Tetanus; Pre-vaccination	0.029 (0.024 to 0.036)	0.03 (0.024 to 0.038)		
Anti-Tetanus; Post-vaccination	2.87 (2.66 to 3.1)	3.55 (3.18 to 3.95)		
Anti-Polio 1; Pre-vaccination	4.26 (3.74 to 4.87)	4.8 (4.14 to 5.56)		
Anti-Polio 1; Post-vaccination	1237 (1072 to 1428)	1042 (908 to 1196)		
Anti-Polio 2; Pre-vaccination	7.77 (6.65 to 9.09)	8.9 (7.47 to 10.6)		
Anti-Polio 2; Post-vaccination	2081 (1776 to 2439)	1781 (1525 to 2080)		
Anti-Polio 3; Pre-vaccination	4.34 (3.85 to 4.88)	4.48 (3.93 to 5.1)		
Anti-Polio 3; Post-vaccination	1868 (1587 to 2199)	1557 (1313 to 1848)		
Anti-PRP; Pre-vaccination	0.083 (0.069 to 0.1)	0.087 (0.071 to 0.105)		
Anti-PRP; Post-vaccination	11 (9.42 to 12.8)	23.9 (20.4 to 27.9)		
Anti-PT; Pre-vaccination	2.23 (1.94 to 2.56)	2.15 (1.87 to 2.47)		
Anti-PT; Post-vaccination	223 (205 to 241)	247 (228 to 269)		
Anti-FHA; Pre-vaccination	3.7 (3.25 to 4.21)	3.54 (3.1 to 4.04)		
Anti-FHA; Post-vaccination	225 (206 to 246)	259 (238 to 282)		

## Statistical analyses

No statistical analyses for this end point

**Primary: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens After A Primary Vaccination Series with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP-T Conjugate Vaccine (ActHIB)**

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens After A Primary Vaccination Series with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP-T Conjugate Vaccine (ActHIB) <sup>[10]</sup>
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End point description:

Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization. Anti-Polyribosyl Ribitol Phosphate (PRP) was measured using a radioimmunology assay. The geometric mean titer ratios of post-dose 3 (Day 150)/pre-dose 1 (Day 0) are reported.

End point type	Primary
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End point timeframe:

Day 0 (pre-vaccination) and Day 150 post-primary vaccination

Notes:

[10] - 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//PRP-T	DTaP-IPV+PRP-T		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	181		
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	170 (135 to 214)	145 (113 to 187)		
Anti-Tetanus	98.5 (76.7 to 127)	118 (87.9 to 160)		
Anti-Polio 1	289 (235 to 356)	217 (175 to 269)		
Anti-Polio 2	268 (211 to 342)	200 (156 to 257)		
Anti-Polio 3	429 (355 to 518)	348 (277 to 437)		
Anti-PRP	136 (107 to 173)	276 (210 to 363)		
Anti-PT	99.9 (83.8 to 119)	115 (96 to 138)		
Anti-FHA	60.9 (51.2 to 72.5)	73.1 (62 to 86.3)		

**Statistical analyses**

No statistical analyses for this end point

**Primary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions After Any and Each Vaccination with DTacP-IPV//PRP~T Combined**

## Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP-T Vaccine (ActHIB)

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions After Any and Each Vaccination with DTaP-IPV//PRP-T Combined Vaccine (PENTAXIM) or DTaP-IPV Combined Vaccine (TETRAXIM) Given at Separate Sites with PRP-T Vaccine (ActHIB) <sup>[11]</sup>
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End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability.

Grade 3 Solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced. Erythema and Swelling,  $\geq 5$  cm. Fever,  $> 39.5^{\circ}\text{C}$ ; Vomiting,  $\geq 6$  episodes per 24 hours or requiring parenteral hydration; Crying abnormal,  $>3$  hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, refuses  $\geq 3$  feeds/meals or refuses most feeds/meals; Irritability, Inconsolable.

Solicited injection site and systemic reactions are reported for each arm. In the DTaP-IPV+PRP-T arm, solicited injection site reactions post-each arm are also reported by separate vaccines DTaP-IPV, and PRP-T.

End point type	Primary
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End point timeframe:

Day 0 up to Day 7 post-any and each primary vaccination

Notes:

[11] - 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//PRP-T	DTaP-IPV+PRP-T		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207 <sup>[12]</sup>	203		
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness; Post-Any injection	61.2	58.2		
Grade 3 Injection site Tenderness; Post-Any inj.	1.4	1		
Injection site Erythema; Post-Any injection	56.9	48.8		
Grade 3 Injection site Erythema; Post-Any inj.	2.9	1		
Injection site Swelling; Post-Any injection	35.9	33.5		
Grade 3 Injection site Swelling; Post-Any inj.	1.9	1.5		
Injection site Tenderness; Post-injection 1	44	44.8		
Grade 3 Injection site Tenderness; Post-inj. 1	1	0		
Injection site Tenderness; Post-inj. 1; DTaP-IPV	0	36.3		
Grade 3 Inj. site Tenderness; Post-inj. 1;DTaP-IPV	0	0		
Injection site Tenderness; Post-injection 1; PRP-T	0	40.3		
Grade 3 Inj. site Tenderness; Post-inj. 1; PRP-T	0	0		
Injection site Erythema; Post-injection 1	38.3	20.9		

Grade 3 Injection site Erythema; Post-injection 1	0.5	0.5		
Injection site Erythema; Post-inj. 1; DTaP-IPV	0	17.9		
Grade 3 Inj. site Erythema; Post-inj. 1; DTaP-IPV	0	0		
Injection site Erythema; Post-inj. 1; PRP-T	0	11.9		
Grade 3 Inj. site Erythema; Post-inj. 1; PRP-T	0	0.5		
Injection site Swelling; Post-injection 1	12.9	11		
Grade 3 Injection site Swelling; Post-injection 1	0	0		
Injection site Swelling; Post-inj. 1; DTaP-IPV	0	10		
Grade 3 Inj. site Swelling; Post-inj. 1; DTaP-IPV	0	0		
Injection site Swelling; Post-inj. 1; PRP-T	0	5		
Grade 3 Inj. site Swelling; Post-inj. 1; PRP-T	0	0		
Injection site Tenderness; Post-injection 2	36.7	36.1		
Grade 3 Injection site Tenderness; Post-inj. 2	0.5	0.5		
Injection site Tenderness; Post-inj. 2; DTaP-IPV	0	34.2		
Grade 3 Inj. site Tenderness; Post-inj. 2;DTaP-IPV	0	0.5		
Injection site Tenderness; Post-inj. 2; PRP-T	0	29.7		
Grade 3 Inj. site Tenderness; Post-inj. 2; PRP-T	0	0.5		
Injection site Erythema; Post-injection 2	40.6	29.2		
Grade 3 Injection site Erythema; Post-injection 2	1	0.5		
Injection site Erythema; Post-inj. 2; DTaP-IPV	0	27.7		
Grade 3 Inj. site Erythema; Post-inj. 2; DTaP-IPV	0	0		
Injection site Erythema; Post-inj. 2; PRP-T	0	14.9		
Grade 3 Inj. site Erythema; Post-inj. 2; PRP-T	0	0.5		
Injection site Swelling; Post-injection 2	22.7	19.8		
Grade 3 Injection site Swelling; Post-injection 2	1	0.5		
Injection site Swelling; Post-inj. 2; DTaP-IPV	0	18.8		
Grade 3 Inj. site Swelling; Post-inj. 2; DTaP-IPV	0	0		
Injection site Swelling; Post-inj. 2; PRP-T	0	8.9		
Grade 3 Inj. site Swelling; Post-inj. 2; PRP-T	0	0.5		
Injection site Tenderness; Post-injection 3	31.4	32.7		
Grade 3 Injection site Tenderness; Post-inj. 3	0	0.5		
Injection site Tenderness; Post-inj. 3; DTaP-IPV	0	31.7		

Grade 3 Inj. site Tenderness; Post-inj. 3;DTaP-IPV	0	0.5		
Injection site Tenderness; Post-inj. 3; PRP-T	0	25.2		
Grade 3 Inj. site Tenderness; Post-inj. 3; PRP-T	0	0		
Injection site Erythema; Post-injection 3	39.1	34.2		
Grade 3 Injection site Erythema; Post-injection 3	1.9	0.5		
Injection site Erythema; Post-inj. 3; DTaP-IPV	0	32.7		
Grade 3 Inj. site Erythema; Post-inj. 3; DTaP-IPV	0	0.5		
Injection site Erythema; Post-inj. 3; PRP-T	0	18.3		
Grade 3 Inj. site Erythema; Post-inj. 3; PRP-T	0	0		
Injection site Swelling; Post-injection 3	24.6	23.3		
Grade 3 Injection site Swelling; Post-injection 3	1	1		
Injection site Swelling; Post-inj. 3; DTaP-IPV	0	22.3		
Grade 3 Inj. site Swelling; Post-inj. 3; DTaP-IPV	0	1		
Injection site Swelling; Post-inj. 3; PRP-T	0	11.4		
Grade 3 Inj. site Swelling; Post-inj. 3; PRP-T	0	0		
Fever; Post-Any injection	15.9	11.4		
Grade 3 Fever; Post-Any injection	0	0		
Vomiting; Post-Any injection	34.9	38.3		
Grade 3 Vomiting; Post-Any injection	1.4	0.5		
Crying abnormal; Post-Any injection	48.3	54.7		
Grade 3 Crying abnormal; Post-Any injection	4.3	1		
Drowsiness; Post-Any injection	49.3	50.7		
Grade 3 Drowsiness; Post-Any injection	1.9	2		
Appetite lost; Post-Any injection	41.1	44.8		
Grade 3 Appetite lost; Post-Any injection	1	2		
Irritability; Post-Any injection	51.2	53.7		
Grade 3 Irritability; Post-Any injection	4.8	4		
Fever; Post-injection 1	6.3	2.5		
Grade 3 Fever; Post-injection 1	0	0		
Vomiting; Post-injection 1	26.8	26.9		
Grade 3 Vomiting; Post-injection 1	0.5	0.5		
Crying abnormal; Post-injection 1	30.1	38.3		
Grade 3 Crying abnormal; Post-injection 1	1.4	0.5		
Drowsiness; Post-injection 1	37.3	39.3		
Grade 3 Drowsiness; Post-injection 1	1.4	2		
Appetite lost; Post-injection 1	25.4	26.9		
Grade 3 Appetite lost; Post-injection 1	0.5	0.5		
Irritability; Post-injection 1	33.5	39.8		
Grade 3 Irritability; Post-injection 1	2.9	2		
Fever; Post-injection 2	3.9	5		
Grade 3 Fever; Post-injection 2	0	0		

Vomiting; Post-injection 2	16.4	19.8		
Grade 3 Vomiting; Post-injection 2	0	0		
Crying abnormal; Post-injection 2	25.6	26.2		
Grade 3 Crying abnormal; Post-injection 2	1.9	0.5		
Drowsiness; Post-injection 2	21.7	27.7		
Grade 3 Drowsiness; Post-injection 2	0.5	0		
Appetite lost; Post-injection 2	18.4	20.8		
Grade 3 Appetite lost; Post-injection 2	0.5	0.5		
Irritability; Post-injection 2	30	30.7		
Grade 3 Irritability; Post-injection 2	2.4	2		
Fever; Post-injection 3	7.3	7		
Grade 3 Fever; Post-injection 3	0	0		
Vomiting; Post-injection 3	12.6	13.9		
Grade 3 Vomiting; Post-injection 3	1	0		
Crying abnormal; Post-injection 3	21.3	18.3		
Grade 3 Crying abnormal; Post-injection 3	1.4	0		
Drowsiness; Post-injection 3	16.9	17.8		
Grade 3 Drowsiness; Post-injection 3	0	0		
Appetite lost; Post-injection 3	13.5	19.3		
Grade 3 Appetite lost; Post-injection 3	0	1		
Irritability; Post-injection 3	19.3	23.3		
Grade 3 Irritability; Post-injection 3	0	0		

Notes:

[12] - 2 subjects in the DTaP-IPV+PRP-T arm received DTaP-IPV//PRP-T and were included for a total of N=209

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 150 of the primary vaccination series.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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### Reporting groups

Reporting group title	DTaP-IPV//PRP-T
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Reporting group description:

Healthy infants received the investigational vaccine (DTaP-IPV//PRP-T) at 2, 4, and 6 months of age.

Reporting group title	DTaP-IPV+PRP-T
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Reporting group description:

Healthy infants received a control vaccine DTaP-IPV combined vaccine (TETRAXIM™) and PRP-T (Act-HIB™) at 2, 4, and 6 months of age.

<b>Serious adverse events</b>	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 209 (7.18%)	8 / 203 (3.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Hypotonia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 203 (0.49%)	
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			
Hypothermia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Gastro-esophageal reflux disease subjects affected / exposed	1 / 209 (0.48%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
<b>Bronchiolitis</b>			
subjects affected / exposed	5 / 209 (2.39%)	2 / 203 (0.99%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bronchitis</b>			
subjects affected / exposed	1 / 209 (0.48%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bronchopneumonia</b>			
subjects affected / exposed	0 / 209 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Croup infectious</b>			
subjects affected / exposed	1 / 209 (0.48%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastroenteritis</b>			
subjects affected / exposed	2 / 209 (0.96%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Kawasaki's disease</b>			
subjects affected / exposed	0 / 209 (0.00%)	1 / 203 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Meningitis</b>			
subjects affected / exposed	1 / 209 (0.48%)	0 / 203 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Meningitis viral</b>			

subjects affected / exposed	1 / 209 (0.48%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pneumonia</b>		
subjects affected / exposed	3 / 209 (1.44%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Respiratory syncytial virus bronchiolitis</b>		
subjects affected / exposed	3 / 209 (1.44%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	DTaP-IPV//PRP-T	DTaP-IPV+PRP-T
<b>Total subjects affected by non-serious adverse events</b>		
subjects affected / exposed	128 / 209 (61.24%)	117 / 203 (57.64%)
<b>Nervous system disorders</b>		
<b>Drowsiness</b>		
alternative assessment type: Systematic		
subjects affected / exposed	103 / 209 (49.28%)	102 / 203 (50.25%)
occurrences (all)	103	102
<b>General disorders and administration site conditions</b>		
<b>Injection site Tenderness</b>		
alternative assessment type: Systematic		
subjects affected / exposed	128 / 209 (61.24%)	117 / 203 (57.64%)
occurrences (all)	128	117
<b>Injection site Erythema</b>		
alternative assessment type: Systematic		
subjects affected / exposed	119 / 209 (56.94%)	98 / 203 (48.28%)
occurrences (all)	119	98
<b>Injection site Swelling</b>		
alternative assessment type: Systematic		

<p>subjects affected / exposed occurrences (all)</p> <p>Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p>	<p>75 / 209 (35.89%) 75</p> <p>33 / 209 (15.79%) 33</p>	<p>67 / 203 (33.00%) 67</p> <p>23 / 203 (11.33%) 23</p>	
<p>Gastrointestinal disorders Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p>	<p>73 / 209 (34.93%) 73</p>	<p>77 / 203 (37.93%) 77</p>	
<p>Psychiatric disorders Crying abnormal alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p> <p>Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p>	<p>101 / 209 (48.33%) 101</p> <p>107 / 209 (51.20%) 107</p>	<p>110 / 203 (54.19%) 110</p> <p>108 / 203 (53.20%) 108</p>	
<p>Metabolism and nutrition disorders Appetite lost alternative assessment type: Systematic subjects affected / exposed occurrences (all)</p>	<p>86 / 209 (41.15%) 86</p>	<p>90 / 203 (44.33%) 90</p>	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2011	Included administrative changes and details on the recruitment procedures, vaccine batches used for the study, and on the recording of adverse events occurring after Day 30.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported