



## Clinical trial results:

**Immunogenicity and Safety of the Aventis Pasteur DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Given as a Three-Dose Primary Vaccination at 2, 4 and 6 Months of Age and Followed by a Booster Dose at 18 to 19 Months of Age in Healthy Infants in Thailand. All Infants Receiving Recombinant Hepatitis B Vaccine at 0, 2 and 6 Months of Age.**

## Summary

EudraCT number	2015-005352-10
Trial protocol	Outside EU/EEA
Global end of trial date	24 September 2007

## 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	E2I34
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00255021
WHO universal trial number (UTN)	-

Notes:

## Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Medical Team Leader, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com
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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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	24 September 2007
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 September 2007
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 assess the seroprotection rates (Diphtheria, Tetanus, polio types 1, 2 and 3, and Polyribosyl Ribitol Phosphate conjugated to Tetanus protein) and seroconversion rates (Pertussis Toxoid, Filamentous Hemagglutinin) of Aventis Pasteur's DTacP-IPV//PRP~T combined vaccine, one month after the three-dose primary vaccination.

To describe the immunogenicity of the study combined vaccine (PENTAXIM™) one month after the three-dose primary vaccination (Visit 4), prior to the booster dose (at Visit 5) and one month after the booster dose (Visit 6).

To describe the immunogenicity of the recombinant hepatitis B vaccine antigen one month after the three-dose primary vaccination (Visit 4) and approximately 11 to 12 months later (Visit 5).

Safety:

To describe the safety after each dose of the study combined vaccine (PENTAXIM™).

To describe the safety after each study dose of recombinant hepatitis B vaccine

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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.

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Background therapy:

Not applicable

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Evidence for comparator:

Not applicable

Actual start date of recruitment	06 December 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

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	Thailand: 186
Worldwide total number of subjects	186
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)	186
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 06 December 2005 to 03 April 2006 at 2 clinic centers in Thailand.

### Pre-assignment

Screening details:

A total of 186 infants who met all inclusion and none of the exclusion criteria were enrolled and vaccinated in the trial.

### Period 1

Period 1 title	Primary Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

### Arms

Arm title	DTacP-IPV//PRP~T vaccine
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Arm description:

All subjects had previously received the first dose of the recombinant 10 µg hepatitis B vaccine at birth according to the National Expanded Program on Immunization (EPI). In this trial, subjects received the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 4, and 6 months of age as well as two subsequent doses of the recombinant 10 µg hepatitis B vaccine at 2 and 6 months of age according to the National EPI. Subjects received a booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.

Arm type	Experimental
Investigational medicinal product name	DTacP-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 right anterolateral external aspect of the upper thigh, 1 injection each at 2, 4, and 6 months of age and a booster dose at 18 to 19 months of age.

Investigational medicinal product name	EUVAX B™ (recombinant hepatitis B vaccine)
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 left anterolateral external aspect of the upper thigh, 1 injection each at birth and at 2 and 6 months of age.

Number of subjects in period 1	DTacP-IPV//PRP~T vaccine
Started	186
Completed	175
Not completed	11
Consent withdrawn by subject	4
Lost to follow-up	3
Protocol deviation	4

## Period 2

Period 2 title	Booster phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: Not applicable	

## Arms

Arm title	DTacP-IPV//PRP~T vaccine
Arm description: Subjects received a booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.	
Arm type	Experimental
Investigational medicinal product name	DTacP-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 right anterolateral external aspect of the upper thigh, booster dose at 18 to 19 months of age.

Number of subjects in period 2	DTacP-IPV//PRP~T vaccine
Started	175
Completed	163
Not completed	12
Lost to follow-up	10
Protocol deviation	2



## Baseline characteristics

### Reporting groups

Reporting group title	DTacP-IPV//PRP~T vaccine
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Reporting group description:

All subjects had previously received the first dose of the recombinant 10 µg hepatitis B vaccine at birth according to the National Expanded Program on Immunization (EPI). In this trial, subjects received the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 4, and 6 months of age as well as two subsequent doses of the recombinant 10 µg hepatitis B vaccine at 2 and 6 months of age according to the National EPI. Subjects received a booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.

Reporting group values	DTacP-IPV//PRP~T vaccine	Total	
Number of subjects	186	186	
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)	186	186	
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	1.9		
standard deviation	± 0.1	-	
Gender categorical			
Units: Subjects			
Female	81	81	
Male	105	105	

### Subject analysis sets

Subject analysis set title	Immunogenicity Analysis Set Post-Dose 3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Immunogenicity Analysis Set Post-Dose 3 was defined as all subjects who had followed the vaccination schedule until Visit 3 (6 months of age) and all subjects for whom injections had been performed and blood samples had been drawn within the tolerated time limits.

Subject analysis set title	Immunogenicity Analysis Set Pre-Booster
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Immunogenicity Analysis Set Pre-Booster was defined as all subjects who had followed the vaccination schedule until Visit 3 (6 months of age) and all subjects for whom a blood sample had been drawn at Visit 5 (blood sample 3), with an age at blood sample on Visit 5 less than 17 months (no older than 20 months), and had an antibody titer available for Visit 5 (blood sample 3).

Subject analysis set title	Immunogenicity Analysis Set Post-Booster
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Immunogenicity Analysis Set Post-Booster was defined as all subjects who had followed the vaccination schedule until Visit 5 (blood sample 3) with an age at blood sample on Visit 5 less than 17 months (no older than 20 months).

<b>Reporting group values</b>	Immunogenicity Analysis Set Post-Dose 3	Immunogenicity Analysis Set Pre-Booster	Immunogenicity Analysis Set Post-Booster
Number of subjects	173	166	161
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)	173	166	161
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	1.9	1.9	1.9
standard deviation	± 0.1	± 0.1	± 0.1
Gender categorical Units: Subjects			
Female	76	73	71
Male	97	93	90



## End points

### End points reporting groups

Reporting group title	DTacP-IPV//PRP~T vaccine
Reporting group description: All subjects had previously received the first dose of the recombinant 10 µg hepatitis B vaccine at birth according to the National Expanded Program on Immunization (EPI). In this trial, subjects received the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 4, and 6 months of age as well as two subsequent doses of the recombinant 10 µg hepatitis B vaccine at 2 and 6 months of age according to the National EPI. Subjects received a booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.	
Reporting group title	DTacP-IPV//PRP~T vaccine
Reporting group description: Subjects received a booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.	
Subject analysis set title	Immunogenicity Analysis Set Post-Dose 3
Subject analysis set type	Sub-group analysis
Subject analysis set description: Immunogenicity Analysis Set Post-Dose 3 was defined as all subjects who had followed the vaccination schedule until Visit 3 (6 months of age) and all subjects for whom injections had been performed and blood samples had been drawn within the tolerated time limits.	
Subject analysis set title	Immunogenicity Analysis Set Pre-Booster
Subject analysis set type	Sub-group analysis
Subject analysis set description: Immunogenicity Analysis Set Pre-Booster was defined as all subjects who had followed the vaccination schedule until Visit 3 (6 months of age) and all subjects for whom a blood sample had been drawn at Visit 5 (blood sample 3), with an age at blood sample on Visit 5 less than 17 months (no older than 20 months), and had an antibody titer available for Visit 5 (blood sample 3).	
Subject analysis set title	Immunogenicity Analysis Set Post-Booster
Subject analysis set type	Sub-group analysis
Subject analysis set description: Immunogenicity Analysis Set Post-Booster was defined as all subjects who had followed the vaccination schedule until Visit 5 (blood sample 3) with an age at blood sample on Visit 5 less than 17 months (no older than 20 months).	

### Primary: Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens One Month after Three Dose Primary Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)

End point title	Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens One Month after Three Dose Primary Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) <sup>[1]</sup>
End point description: Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay. Seroprotection for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers ≥ 0.1 IU/mL, ≥ 8 (dil) for Anti-Polio types 1, 2, and 3, ≥ 0.15 µg/mL for Anti-PRP, and ≥ 10 mIU/mL for Hepatitis B. Seroconversion for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers ≥ 4-fold increase EU/mL.	
End point type	Primary
End point timeframe: 1 month post-dose 3 of primary vaccination (Day 140)	

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 group and the study vaccine administered.

End point values	Immunogenicity Analysis Set Post-Dose 3			
Subject group type	Subject analysis set			
Number of subjects analysed	173			
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria	99.4			
Anti-Tetanus	100			
Anti-Polio 1	100			
Anti-Polio 2	100			
Anti-Polio 3	100			
Anti-PRP	100			
Anti-Pertussis Toxoid	94.1			
Anti-FHA	93			
Anti-Hepatitis B	100			

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects with Seroprotection/Seroconversion Before and After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination

End point title	Percentage of Subjects with Seroprotection/Seroconversion Before and After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination
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End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay. Seroprotection for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers  $\geq 0.1$  IU/mL,  $\geq 8$  (dil) for Anti-Polio types 1, 2, and 3,  $\geq 0.15$   $\mu$ g/mL for Anti-PRP, and  $\geq 10$  mIU/mL for Hepatitis B. Seroconversion for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers  $\geq 4$ -fold increase EU/mL.

Seroconversion rates are not available for Anti-Pertussis toxoid or Anti-FHA pre-booster and for Anti-Hepatitis B post-booster injection.

End point type	Other pre-specified
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End point timeframe:

Day 140 + 11-12 months (Visit 05) pre-booster and Visit 05 + 28-42 days post-booster (Visit 06)

End point values	Immunogenicity Analysis Set Pre-Booster	Immunogenicity Analysis Set Post-Booster		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	166	161		
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria	72.7	100		
Anti-Tetanus	100	100		
Anti-Polio 1	97.5	100		
Anti-Polio 2	99.4	100		
Anti-Polio 3	95	100		
Anti-PRP	94.4	100		
Anti-Pertussis toxoid	0	96.3		
Anti-FHA	0	93.1		
Anti-Hepatitis B	98.2	0		

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Geometric Mean Titers of Antibodies Against Vaccine Antigens Following A Three Dose Primary Vaccination Series, Before and Following A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Following A Three Dose Primary Vaccination Series, Before and Following A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)
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End point description:

Anti-Diphtheria and Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay.

Geometric mean titer data were not available for Anti-Hepatitis B post-booster injection.

End point type	Other pre-specified
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End point timeframe:

1 month post-dose 3 of primary vaccination (Day 140) and Day 140 + 11-12 months (Visit 05) pre-booster and Visit 05 + 28-42 days post-booster (Visit 06)

End point values	Immunogenicity Analysis Set Post-Dose 3	Immunogenicity Analysis Set Pre-Booster	Immunogenicity Analysis Set Post-Booster	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	166	165	161	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				

Anti-Diphtheria	0.12 (0.1 to 0.14)	0.02 (0.02 to 0.03)	2.67 (2.1 to 3.41)	
Anti-Tetanus	1.13 (1.03 to 1.23)	0.3 (0.26 to 0.35)	9.99 (8.97 to 11.13)	
Anti-Pertussis toxoid	181.49 (163.05 to 201.01)	14.01 (11.98 to 16.37)	307.35 (281.01 to 336.16)	
Anti-FHA	119.13 (108.12 to 131.26)	13.94 (11.7 to 16.6)	271.86 (246.91 to 299.32)	
Anti-Polio 1	1267.23 (1033.98 to 1553.09)	166.46 (130.17 to 212.87)	4620.75 (3901.03 to 5473.27)	
Anti-Polio 2	1602.34 (1311.06 to 1958.34)	250.01 (198.31 to 315.18)	6086.64 (5179.62 to 7152.49)	
Anti-Polio 3	3078.57 (2478.53 to 3823.88)	156.07 (121.15 to 201.06)	5596.51 (4598.79 to 6810.69)	
Anti-PRP	9.62 (7.91 to 11.7)	1.21 (0.98 to 1.5)	62.23 (52.81 to 73.33)	
Anti-Hepatitis B	1512.82 (1319 to 1735.12)	180.91 (152.04 to 215.27)	0 (0 to 0)	

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination
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End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay.

End point type	Other pre-specified
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End point timeframe:

Day 140 + 11-12 months (Visit 05) pre-booster and Visit 05 + 28-42 days post-booster (Visit 06)

<b>End point values</b>	Immunogenicity Analysis Set Post-Booster			
Subject group type	Subject analysis set			
Number of subjects analysed	161			
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				

Anti-Diphtheria	128.55 (106.81 to 154.72)			
Anti-Tetanus	33.15 (28.9 to 38.01)			
Anti-Pertussis toxoid	21.95 (18.92 to 25.45)			
Anti-FHA	19.54 (16.8 to 22.71)			
Anti-Polio 1	27.76 (21.39 to 36.02)			
Anti-Polio 2	24.35 (18.78 to 31.57)			
Anti-Polio 3	35.86 (27.71 to 46.41)			
Anti-PRP	51.23 (41.16 to 63.76)			

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Series Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Series Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)
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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.

End point type	Other pre-specified
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End point timeframe:

Day 0 up to Day 7 post-any primary injection

End point values	DTacP-IPV//PRP~T vaccine			
Subject group type	Reporting group			
Number of subjects analysed	186			
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness	48.6			
Injection site Erythema	57			
Injection site Swelling	33.5			
Fever	27			
Vomiting	28.6			
Crying abnormal	55.1			
Drowsiness	25.9			
Appetite lost	28.6			

Irritability	51.4			
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## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any and Each of Three-Dose Primary Series Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any and Each of Three-Dose Primary Series Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™)
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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. Grade 3 systemic reactions: Fever,  $\geq 39.0^{\circ}\text{C}$ ; 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 or refuses most feeds; Irritability, Inconsolable.

For solicited injection site reactions, data are reported post-PENTAXIM and post-Hepatitis B. Solicited injection site data were not collected post-dose 2 (Hepatitis B) and severe data were not available for any solicited injection site reaction post-any injection. For solicited systemic reactions, data are reported post-DTAcP-IPV//PRP-T + Hepatitis B.

End point type	Other pre-specified
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End point timeframe:

Day 0 up to Day 8 post-any and each primary injection

End point values	DTacP-IPV//PRP~T vaccine			
Subject group type	Reporting group			
Number of subjects analysed	186			
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; Post-Any; PENTAXIM	44.3			
Grade 3 Inj. site Tenderness; Post-Any; PENTAXIM	0			
Any Inj. site Tenderness; Post-Any; Hepatitis B	41.6			
Grade 3 Inj. site Tenderness; Post-Any; Hepatitis B	0			
Any Inj. site Tenderness; Post-dose 1; PENTAXIM	29.2			
Grade 3 Inj. site Tenderness; Post-dose 1; PENTAXIM	0			
Any Inj. site Tenderness; Post-dose 1; Hepatitis B	32.4			

Grade 3 Inj. site Tenderness;Post-dose1;HepatitisB	0			
Any Inj. site Tenderness; Post-dose 2; PENTAXIM	25.4			
Grade 3 Inj. site Tenderness; Post-dose 2;PENTAXIM	0.6			
Any Inj. site Tenderness; Post-dose 2; Hepatitis B	0			
Grade 3 Inj. site Tenderness;Post-dose2;HepatitisB	0			
Any Inj. site Tenderness; Post-dose 3; PENTAXIM	26.9			
Grade 3 Inj. site Tenderness; Post-dose 3;PENTAXIM	0			
Any Inj. site Tenderness; Post-dose 3; Hepatitis B	26.9			
Grade 3 Inj. site Tenderness;Post-dose3;HepatitisB	0			
Any Inj. site Erythema; Post-Any; PENTAXIM	27.1			
Grade 3 Inj. site Erythema; Post-Any; PENTAXIM	0.2			
Any Inj. site Erythema; Post-Any; Hepatitis B	29.6			
Grade 3 Inj. site Erythema; Post-Any; Hepatitis B	0			
Any Inj. site Erythema; Post-dose 1; PENTAXIM	52.7			
Grade 3 Inj. site Erythema; Post-dose 1; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 1; Hepatitis B	44.6			
Grade 3 Inj. site Erythema; Post-dose 1;HepatitisB	0			
Any Inj. site Erythema; Post-dose 2; PENTAXIM	23.1			
Grade 3 Inj. site Erythema; Post-dose 2; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 2; Hepatitis B	28			
Grade 3 Inj. site Erythema; Post-dose 2;HepatitisB	0			
Any Inj. site Erythema; Post-dose 3; PENTAXIM	32.2			
Grade 3 Inj. site Erythema; Post-dose 3; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 3; Hepatitis B	0			
Grade 3 Inj. site Erythema; Post-dose 3;HepatitisB	0			
Any Inj. site Swelling; Post-Any; PENTAXIM	29.2			
Grade 3 Inj. site Swelling; Post-Any; PENTAXIM	0			
Any Inj. site Swelling; Post-Any; Hepatitis B	29.4			
Grade 3 Inj. site Swelling; Post-Any; Hepatitis B	0			
Any Inj. site Swelling; Post-dose 1; PENTAXIM	30.8			
Grade 3 Inj. site Swelling; Post-dose 1; PENTAXIM	0			

Any Inj. site Swelling; Post-dose 1; Hepatitis B	20			
Grade 3 Inj. site Swelling; Post-dose 1; Hepatitis B	0			
Any Inj. site Swelling; Post-dose 2; PENTAXIM	13			
Grade 3 Inj. site Swelling; Post-dose 2; PENTAXIM	0			
Any Inj. site Swelling; Post-dose 2; Hepatitis B	14.1			
Grade 3 Inj. site Swelling; Post-dose 2; Hepatitis B	0.5			
Any Inj. site Swelling; Post-dose 3; PENTAXIM	12.4			
Grade 3 Inj. site Swelling; Post-dose 3; PENTAXIM	0			
Any Inj. site Swelling; Post-dose 3; Hepatitis B	0			
Grade 3 Inj. site Swelling; Post-dose 3; Hepatitis B	0			
Any Fever; Post-Any injection	13.8			
Grade 3 Any Fever; Post-Any injection	0			
Any Fever; Post-dose 1	11.9			
Grade 3 Fever; Post-dose 1	0.6			
Any Fever; Post-dose 2 (PENTAXIM)	27			
Grade 3 Fever; Post-dose 2 (PENTAXIM)	0			
Any Fever; Post-dose 3	9.2			
Grade 3 Fever; Post-dose 3	0			
Any Vomiting; Post-Any injection	13.7			
Grade 3 Vomiting; Post-Any injection	1.1			
Any Vomiting; Post-dose 1	11.5			
Grade 3 Vomiting; Post-dose 1	0.9			
Any Vomiting; Post-dose 2 (PENTAXIM)	28.6			
Grade 3 Vomiting; Post-dose 2 (PENTAXIM)	0			
Any Vomiting; Post-dose 3	21.6			
Grade 3 Vomiting; Post-dose 3	0			
Any Crying abnormal; Post-Any injection	10.9			
Grade 3 Crying abnormal; Post-Any injection	0			
Any Crying abnormal; Post-dose 1	14.7			
Grade 3 Crying abnormal; Post-dose 1	0			
Any Crying abnormal; Post-dose 2 (PENTAXIM)	55.1			
Grade 3 Crying abnormal; Post-dose 2 (PENTAXIM)	0			
Any Crying abnormal; Post-dose 3	39.5			
Grade 3 Crying abnormal; Post-dose 3	0			
Any Drowsiness; Post-Any injection	29.1			
Grade 3 Drowsiness; Post-Any injection	0.6			
Any Drowsiness; Post-dose 1	34.9			
Grade 3 Drowsiness; Post-dose 1	0.2			
Any Drowsiness; Post-dose 2 (PENTAXIM)	25.9			
Grade 3 Drowsiness; Post-dose 2 (PENTAXIM)	0			
Any Drowsiness; Post-dose 3	16.2			



Grade 3 Drowsiness; Post-dose 3	0			
Any Appetite lost; Post-Any injection	10.9			
Grade 3 Appetite lost; Post-Any injection	0			
Any Appetite lost; Post-dose 1	13.2			
Grade 3 Appetite lost; Post-dose 1	0			
Any Appetite lost; Post-dose 2 (PENTAXIM)	28.6			
Grade 3 Appetite lost; Post-dose 2 (PENTAXIM)	0			
Any Appetite lost; Post-dose 3	13			
Grade 3 Appetite lost; Post-dose 3	0			
Any Irritability; Post-Any injection	14.3			
Grade 3 Irritability; Post-Any injection	0			
Any Irritability; Post-dose 1	13.6			
Grade 3 Irritability; Post-dose 1	0.2			
Any Irritability; Post-dose 2 (PENTAXIM)	51.4			
Grade 3 Irritability; Post-dose 2 (PENTAXIM)	0			
Any Irritability; Post-dose 3	36.2			
Grade 3 Irritability; Post-dose 3	0			

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster Injection with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Following A Three Dose Primary Vaccination			
End point description:	Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability.			
End point type	Other pre-specified			
End point timeframe:	Post-booster injection (Visit 05 + 28-42 days post-booster [Visit 06], where Visit 05 was Day 140 + 11-12 months)			

End point values	DTacP-IPV//PRP~T vaccine			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness	55.5			
Injection site Erythema	36.6			

Injection site Swelling	22			
Fever	25.6			
Vomiting	14			
Crying abnormal	34.1			
Drowsiness	14.6			
Appetite lost	22			
Irritability	29.3			

### Statistical analyses

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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 pre-vaccination up to post-booster vaccination (Visit 05 + 28-42 days post-booster [Visit 06], where Visit 05 was Day 140 + 11-12 months).

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	9
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### Reporting groups

Reporting group title	DTacP-IPV//PRP~T vaccine
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Reporting group description:

All subjects had previously received the first dose of the recombinant 10 µg hepatitis B vaccine at birth according to the National Expanded Program on Immunization (EPI). In this trial, subjects received the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 4, and 6 months of age as well as two subsequent doses of the recombinant 10 µg hepatitis B vaccine at 2 and 6 months of age according to the National EPI. Subjects received the booster dose of the DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 19 months of age.

Serious adverse events	DTacP-IPV//PRP~T vaccine		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 186 (5.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	2 / 186 (1.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pharyngeal ulcers			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Infective diarrhea			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Asthmatic attack			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Difficult urination			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute gastroenteritis			
subjects affected / exposed	6 / 186 (3.23%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 186 (1.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Acute tonsillitis			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 186 (1.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute bronchitis			

subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 186 (1.61%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bacterial pneumonia				
subjects affected / exposed	2 / 186 (1.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suspected viral myocarditis				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral croup				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpetic gingivostomatitis				
subjects affected / exposed	1 / 186 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral pneumonia				
subjects affected / exposed	3 / 186 (1.61%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Viral gastroenteritis				

subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute bronchiolitis			
subjects affected / exposed	1 / 186 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	DTacP-IPV//PRP~T vaccine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 186 (56.99%)		
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	48 / 186 (25.81%)		
occurrences (all)	48		
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	91 / 186 (48.92%)		
occurrences (all)	91		
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	106 / 186 (56.99%)		
occurrences (all)	106		
Injection site Swelling			
alternative assessment type: Systematic			

<p>subjects affected / exposed</p> <p>62 / 186 (33.33%)</p> <p>occurrences (all)</p> <p>62</p> <p>Fever</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>50 / 186 (26.88%)</p> <p>occurrences (all)</p> <p>50</p>			
<p>Gastrointestinal disorders</p> <p>Vomiting</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>53 / 186 (28.49%)</p> <p>occurrences (all)</p> <p>53</p>			
<p>Psychiatric disorders</p> <p>Crying abnormal</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>102 / 186 (54.84%)</p> <p>occurrences (all)</p> <p>102</p> <p>Irritability</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>95 / 186 (51.08%)</p> <p>occurrences (all)</p> <p>95</p>			
<p>Infections and infestations</p> <p>Pharyngitis</p> <p>subjects affected / exposed</p> <p>11 / 186 (5.91%)</p> <p>occurrences (all)</p> <p>11</p> <p>Upper respiratory tract infection</p> <p>subjects affected / exposed</p> <p>30 / 186 (16.13%)</p> <p>occurrences (all)</p> <p>30</p>			
<p>Metabolism and nutrition disorders</p> <p>Appetite lost</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>53 / 186 (28.49%)</p> <p>occurrences (all)</p> <p>53</p>			

## **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