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 6, 10, and 14 Weeks of Age and Followed by a Booster Dose at 18 to 19 Months of Age in Healthy Infants in South Africa. All Infants Receiving Hepatitis B Monovalent Vaccine at 6, 10 and 14 Weeks of Age.

Summary

EudraCT number	2015-005354-35
Trial protocol	Outside EU/EEA
Global end of trial date	15 February 2008

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	E2I43

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00254969
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
Scientific contact	Medical Team Leader, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com

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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 February 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

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 [PRP]) and seroconversion rates (Pertussis toxoid, Filamentous Hemagglutinin [FHA]) of Sanofi 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 5), prior to the booster dose (at Visit 6) and one month after the booster dose (Visit 7).
-To describe the immunogenicity of the recombinant hepatitis B vaccine antigen one month after the three-dose primary vaccination (Visit 5) and approximately 14 to 15 months later (Visit 6).
Safety:
-To describe the safety after each dose of the study combined vaccine (PENTAXIM™).
-To describe the safety after each dose of recombinant hepatitis B vaccine.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were 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	18 October 2005
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	South Africa: 212
Worldwide total number of subjects	212
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)	212
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 18 October 2005 to 01 July 2006 at 1 clinic center in South Africa.

Pre-assignment

Screening details:

A total of 212 subjects who met all inclusion and none of the exclusion criteria were enrolled and vaccinated in the study.

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	Study group

Arm description:

Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks 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 6, 10, and 14 weeks of age.

Investigational medicinal product name	Hepatitis B vaccine (HEBERBIOVAC HB®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the left anterolateral external aspect of the upper thigh, 1 injection each at 6, 10, and 14 weeks of age.

Number of subjects in period 1	Study group
Started	212
Completed	207
Not completed	5
Serious adverse events	1
Lost to follow-up	1

Protocol deviation	3

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	Study group

Arm description:

Subjects received a booster dose of DTacP-IPV//PRP~T vaccine 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 6, 10, and 14 weeks of age.

Number of subjects in period 2	Study group
Started	207
Completed	179
Not completed	29
Consent withdrawn by subject	9
Serious adverse events	2
Lost to follow-up	15
Protocol deviation	3
Joined	1
Withdrawn from study and re-included for booster	1

Baseline characteristics

Reporting groups	
Reporting group title	Study group
Reporting group description:	
Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age.	

Reporting group values	Study group	Total	
Number of subjects	212	212	
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)	212	212	
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			
The Study group and Immunogenicity Analysis Set age is reported in days (standard deviation) whereas the Immunogenicity Analysis Set Pre-Booster and Immunogenicity Analysis Set Post-Booster age is reported in months (standard deviation).			
Units: days			
arithmetic mean	43.2		
standard deviation	± 1.6	-	
Gender categorical Units: Subjects			
Female	105	105	
Male	107	107	

Subject analysis sets	
Subject analysis set title	Immunogenicity Analysis Set Post-dose 3
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Immunogenicity Analysis Set was defined as all infants who received DTacP-IPV//PRP~T at Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98) without any delays, had a blood sample performed at Visit 05 (Day 126; blood sample 02) without any delays, and had an antibody titration available in blood sample 02.	
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 received the DTacP-IPV//PRP-T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98), had a blood sample performed on Visit 06 (Visit 05 + 14-15 months; blood sample 03), age at blood sample on Visit 06 (blood sample 03) less than 17 months (no older than 20 months), and had an antibody titer available for blood sample 03.	

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 received the vaccination with DTacP-IPV//PRP~T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), Visit 04 (Day 98) or Visit 06 (Visit 05 + 14-15 months) who were < 17 months (no older than 20 months) on Visit 06, had a blood sample performed on Visit 07 (Visit 06 + 28-42 days) without any delays, and had an antibody titer available for blood sample 04.

Reporting group values	Immunogenicity Analysis Set Post-dose 3	Immunogenicity Analysis Set Pre-Booster	Immunogenicity Analysis Set Post-Booster
Number of subjects	206	180	176
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)	206	180	176
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			
The Study group and Immunogenicity Analysis Set age is reported in days (standard deviation) whereas the Immunogenicity Analysis Set Pre-Booster and Immunogenicity Analysis Set Post-Booster age is reported in months (standard deviation).			
Units: days			
arithmetic mean	43.2	18.3	18.3
standard deviation	± 1.6	± 0.4	± 0.4
Gender categorical Units: Subjects			
Female	99	86	83
Male	107	94	93

End points

End points reporting groups

Reporting group title	Study group
Reporting group description:	
Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age.	

Reporting group title	Study group
Reporting group description:	
Subjects received a booster dose of DTacP-IPV//PRP~T vaccine 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:	
The Immunogenicity Analysis Set was defined as all infants who received DTacP-IPV//PRP~T at Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98) without any delays, had a blood sample performed at Visit 05 (Day 126; blood sample 02) without any delays, and had an antibody titration available in blood sample 02.	

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 received the DTacP-IPV//PRP-T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98), had a blood sample performed on Visit 06 (Visit 05 + 14-15 months; blood sample 03), age at blood sample on Visit 06 (blood sample 03) less than 17 months (no older than 20 months), and had an antibody titer available for blood sample 03.	

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 received the vaccination with DTacP-IPV//PRP~T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), Visit 04 (Day 98) or Visit 06 (Visit 05 + 14-15 months) who were < 17 months (no older than 20 months) on Visit 06, had a blood sample performed on Visit 07 (Visit 06 + 28-42 days) without any delays, and had an antibody titer available for blood sample 04.	

Primary: Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

End point title	Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)[1]
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 ≥ 2-fold and ≥ 4-fold increase EU/mL.	
End point type	Primary
End point timeframe:	
1 month post-dose 3 of primary vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study group and the study vaccine administered for this outcome.

End point values	Study group			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria	100			
Anti-Tetanus	100			
Anti-Polio 1	100			
Anti-Polio 2	100			
Anti-Polio 3	100			
Anti-PRP	94.6			
Anti-Pertussis toxoid; ≥ 2-fold increase	99			
Anti-Pertussis toxoid; ≥ 4-fold increase	97.5			
Anti-FHA; ≥ 2-fold increase	94.6			
Anti-FHA; ≥ 4-fold increase	83.9			
Anti-Hepatitis B	100			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Antibodies Against Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

End point description:

Anti-Diphtheria was assessed by ELISA and seroneutralization. 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.

End point type	Other pre-specified

End point timeframe:

1 month post-dose 3 of primary vaccination

End point values	Immunogenicity Analysis Set Post-dose 3			
Subject group type	Subject analysis set			
Number of subjects analysed	206			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria (ELISA)	0.9 (0.82 to 0.99)			
Anti-Diphtheria (seroneutralization)	0.05 (0.04 to 0.06)			
Anti-Tetanus	0.78 (0.71 to 0.85)			
Anti-Pertussis toxoid	382.61 (353.13 to 414.55)			
Anti-FHA	161 (145.94 to 177.61)			
Anti-Polio 1	1453.05 (1235.9 to 1708.35)			
Anti-Polio 2	1699.14 (1410.88 to 2046.29)			
Anti-Polio 3	2398.17 (1979.8 to 2904.96)			
Anti-PRP	1.97 (1.55 to 2.51)			
Anti-Hepatitis B	929.21 (786.39 to 1097.97)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

End point title	Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

End point description:

Anti-Diphtheria was assessed by ELISA and seroneutralization. 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 ≥ 2-fold and ≥ 4-fold increase EU/mL.

End point type	Other pre-specified

End point timeframe:

Post-booster vaccination

End point values	Immunogenicity Analysis Set Post-Booster			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria (ELISA)	100			
Anti-Diphtheria (Seroneutralization)	100			
Anti-Tetanus	100			
Anti-Polio 1	100			
Anti-Polio 2	100			
Anti-Polio 3	100			
Anti-PRP	100			
Anti-Pertussis toxoid; ≥ 2-fold increase	100			
Anti-Pertussis toxoid; ≥ 4-fold increase	98.4			
Anti-FHA; ≥ 2-fold increase	98.6			
Anti-FHA; ≥ 4-fold increase	95.7			
Anti-Hepatitis (Pre-booster)	99.4			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

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

End point timeframe:

1 month post-booster vaccination

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	176	175	176	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	0.9 (0.82 to 1)	0.04 (0.03 to 0.05)	3.72 (3.18 to 4.35)	
Anti-Tetanus	0.79 (0.72 to 0.86)	0.17 (0.15 to 0.2)	9.23 (8.1 to 10.51)	
Anti-Pertussis toxoid	390.62 (359.03 to 424.97)	11.21 (9.64 to 13.05)	465.51 (419.47 to 516.61)	
Anti-FHA	160.18 (143.55 to 178.74)	12.89 (10.41 to 15.96)	520.35 (465.28 to 581.95)	
Anti-Polio 1	1459.62 (1219.02 to 1747.7)	233.85 (166.86 to 327.73)	8928.86 (7639.93 to 10435.25)	
Anti-Polio 2	1634.12 (1343.97 to 1986.91)	302.95 (217.92 to 421.16)	6608.29 (5633.61 to 7751.59)	
Anti-Polio 3	2328.15 (1882.84 to 2878.77)	360.1 (254.69 to 509.15)	12119.89 (10247.37 to 14334.58)	
Anti-PRP	2.26 (1.79 to 2.86)	0.35 (0.26 to 0.46)	47.01 (37.7 to 58.62)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

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.

Geometric mean titer ratios are only reported for Anti-Pertussis toxoid and Anti-FHA for the Immunogenicity Analysis Set Post-dose 3.

End point type	Other pre-specified

End point timeframe:

Visit 06 (Visit 05 + 14-15 months, where Visit 05 is Day 126) and Visit 07 (Visit 06 + 28-42 days)

End point values	Immunogenicity Analysis Set Post-dose 3	Immunogenicity Analysis Set Post-Booster		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	175	175		
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	0 (0 to 0)	101.1 (85.58 to 119.45)		
Anti-Tetanus	0 (0 to 0)	56.16 (47.92 to 65.8)		
Anti-Pertussis toxoid	53 (42.65 to 65.85)	39.4 (33.18 to 46.77)		
Anti-FHA	16.17 (13.04 to 20.04)	40.74 (33.88 to 48.98)		
Anti-Polio 1	0 (0 to 0)	35.34 (24.13 to 51.78)		
Anti-Polio 2	0 (0 to 0)	22.24 (15.25 to 32.42)		
Anti-Polio 3	0 (0 to 0)	33.07 (22.27 to 49.12)		
Anti-PRP	0 (0 to 0)	134.12 (100.66 to 178.7)		

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 Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

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

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-any primary vaccination

End point values	Study group			
Subject group type	Reporting group			
Number of subjects analysed	212			
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness	70.3			
Injection site Erythema	47.2			

Injection site Swelling	45.3			
Fever	35.8			
Vomiting	42.9			
Crying abnormal	64.6			
Drowsiness	48.1			
Appetite lost	35.8			
Irritability	55.7			

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 Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

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

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, ≥ 5 cm. Grade 3 systemic reactions: Fever, ≥ 39.0°C; Vomiting, ≥ 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 ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Other pre-specified

End point timeframe:

Day 0 up to Day 8 post-any and each vaccination and per injected dose

End point values	Study group			
Subject group type	Reporting group			
Number of subjects analysed	212			
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; Post-Any; PENTAXIM	68.4			
Grade 3 Inj. site Tenderness; Post-Any; PENTAXIM	0			
Any Inj. site Tenderness; Post-Any; HEBERBIOVAC	65.6			
Grade 3 Inj. site Tenderness; Post-Any;HEBERBIOVAC	0			
Any Inj. site Tenderness; Post-dose 1; PENTAXIM	54			
Grade 3 Inj. site Tenderness; Post-dose 1;PENTAXIM	0			
Any Inj. site Tenderness; Post-dose 1; HEBERBIOVAC	49.3			

Gr 3 Inj. site Tenderness;Post-dose 1;HEBERBIOVAC	0.5			
Any Inj. site Tenderness; Post-dose 2; PENTAXIM	49			
Grade 3 Inj. site Tenderness; Post-dose 2;PENTAXIM	1.4			
Any Inj. site Tenderness; Post-dose 2; HEBERBIOVAC	44.8			
Gr 3 Inj. site Tenderness;Post-dose 2;HEBERBIOVAC	1.4			
Any Inj. site Tenderness; Post-dose 3; PENTAXIM	41.5			
Grade 3 Inj. site Tenderness; Post-dose 3;PENTAXIM	0.5			
Any Inj. site Tenderness; Post-dose 3; HEBERBIOVAC	36.7			
Gr 3 Inj. site Tenderness;Post-dose 3;HEBERBIOVAC	0			
Any Inj. site Erythema; Post-Any; PENTAXIM	45.3			
Grade 3 Inj. site Erythema; Post-Any; PENTAXIM	0			
Any Inj. site Erythema; Post-Any; HEBERBIOVAC	36.8			
Grade 3 Inj. site Erythema; Post-Any; HEBERBIOVAC	0			
Any Inj. site Erythema; Post-dose 1; PENTAXIM	30.3			
Grade 3 Inj. site Erythema; Post-dose 1; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 1; HEBERBIOVAC	25.6			
Grade 3 Inj. site Erythema;Post-dose 1;HEBERBIOVAC	0			
Any Inj. site Erythema; Post-dose 2; PENTAXIM	26.2			
Grade 3 Inj. site Erythema; Post-dose 2; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 2; HEBERBIOVAC	20			
Grade 3 Inj. site Erythema;Post-dose 2;HEBERBIOVAC	0			
Any Inj. site Erythema; Post-dose 3; PENTAXIM	26.1			
Grade 3 Inj. site Erythema; Post-dose 3; PENTAXIM	0			
Any Inj. site Erythema; Post-dose 3; HEBERBIOVAC	18.8			
Grade 3 Inj. site Erythema;Post-dose 3;HEBERBIOVAC	0			
Any Inj. site Swelling; Post-Any; PENTAXIM	42			
Grade 3 Inj. site Swelling; Post-Any; PENTAXIM	0			
Any Inj. site Swelling; Post-Any; HEBERBIOVAC	37.7			
Grade 3 Inj. site Swelling; Post-Any; HEBERBIOVAC	0			
Any Inj. site Swelling; Post-dose 1; PENTAXIM	23.7			
Grade 3 Inj. site Swelling; Post-dose 1; PENTAXIM	0			

Any Inj. site Swelling; Post-dose 1; HEBERBIOVAC	20.4			
Grade 3 Inj. site Swelling;Post-dose 1;HEBERBIOVAC	0			
Any Inj. site Swelling; Post-dose 2; PENTAXIM	25.2			
Grade 3 Inj. site Swelling; Post-dose 2; PENTAXIM	0			
Any Inj. site Swelling; Post-dose 2; HEBERBIOVAC	19			
Grade 3 Inj. site Swelling;Post-dose 2;HEBERBIOVAC	0			
Any Inj. site Swelling; Post-dose 3; PENTAXIM	28.5			
Grade 3 Inj. site Swelling; Post-dose 3; PENTAXIM	0			
Any Inj. site Swelling; Post-dose 3; HEBERBIOVAC	23.7			
Grade 3 Inj. site Swelling;Post-dose 3;HEBERBIOVAC	0			
Any Fever; Post-Any injection	35.8			
Grade 3 Fever; Post-Any injection	0			
Any Fever; Post-dose 1	17.6			
Grade 3 Fever; Post-dose 1	1.4			
Any Fever; Post-dose 2	12.4			
Grade 3 Fever; Post-dose 2	0.5			
Any Fever; Post-dose 3	14			
Grade 3 Fever; Post-dose 3	0			
Any Vomiting; Post-Any injection	42.9			
Grade 3 Vomiting; Post-Any injection	0			
Any Vomiting; Post-dose 1	29.4			
Grade 3 Vomiting; Post-dose 1	0.5			
Any Vomiting; Post-dose 2	18.1			
Grade 3 Vomiting; Post-dose 2	0.5			
Any Vomiting; Post-dose 3	17.9			
Grade 3 Vomiting; Post-dose 3	0.5			
Any Crying abnormal; Post-Any injection	64.6			
Grade 3 Crying abnormal; Post-Any injection	0			
Any Crying abnormal; Post-dose 1	48.3			
Grade 3 Crying abnormal; Post-dose 1	1.4			
Any Crying abnormal; Post-dose 2	36.7			
Grade 3 Crying abnormal; Post-dose 2	1.4			
Any Crying abnormal; Post-dose 3	29			
Grade 3 Crying abnormal; Post-dose 3	1			
Any Drowsiness; Post-Any injection	48.1			
Grade 3 Drowsiness; Post-Any injection	0			
Any Drowsiness; Post-dose 1	33.2			
Grade 3 Drowsiness; Post-dose 1	0.5			
Any Drowsiness; Post-dose 2	25.2			
Grade 3 Drowsiness; Post-dose 2	0.5			
Any Drowsiness; Post-dose 3	18.4			
Grade 3 Drowsiness; Post-dose 3	0.5			
Any Appetite lost; Post-Any injection	35.8			
Grade 3 Appetite lost; Post-Any injection	0			

Any Appetite lost; Post-dose 1	20.9			
Grade 3 Appetite lost; Post-dose 1	0.5			
Any Appetite lost; Post-dose 2	17.1			
Grade 3 Appetite lost; Post-dose 2	0.5			
Any Appetite lost; Post-dose 3	19.3			
Grade 3 Appetite lost; Post-dose 3	1			
Any Irritability; Post-Any injection	55.7			
Grade 3 Irritability; Post-Any injection	0			
Any Irritability; Post-dose 1	46			
Grade 3 Irritability; Post-dose 1	0.5			
Any Irritability; Post-dose 2	30.5			
Grade 3 Irritability; Post-dose 2	1			
Any Irritability; Post-dose 3	26.1			
Grade 3 Irritability; Post-dose 3	1.4			

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 with DTacP-IPV//PRP~T Vaccine (PENTAXIM) After a Primary Series with DTacP-IPV//PRP~T Vaccine (PENTAXIM) Concomitantly with Hepatitis B (HEBERBIOVAC)

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster with DTacP-IPV//PRP~T Vaccine (PENTAXIM) After a Primary Series with DTacP-IPV//PRP~T Vaccine (PENTAXIM) Concomitantly with Hepatitis B (HEBERBIOVAC)

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, ≥ 5 cm. Grade 3 systemic reactions: Fever, ≥ 39.0°C; Vomiting, ≥ 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 ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Other pre-specified

End point timeframe:

Post-booster vaccination

End point values	Study group			
Subject group type	Reporting group			
Number of subjects analysed	180			
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness	60.6			
Grade 3 Injection site Tenderness	7.2			
Any Injection site Erythema	39.4			

Grade 3 Injection site Erythema	3.3			
Any Injection site Swelling	39.4			
Grade 3 Injection site Swelling	3.9			
Any Fever	29.4			
Grade 3 Fever	1.7			
Any Vomiting	11.7			
Grade 3 Vomiting	1.1			
Any Crying abnormal	36.1			
Grade 3 Crying abnormal	1.7			
Any Drowsiness	26.1			
Grade 3 Drowsiness	1.1			
Any Appetite lost	32.8			
Grade 3 Appetite lost	3.3			
Any Irritability	31.7			
Grade 3 Irritability	1.1			

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 post-vaccination up to 1 month post-booster vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9

Reporting groups

Reporting group title	Study group

Reporting group description:

Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age.

Serious adverse events	Study group		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 212 (11.79%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Dehydration with acidosis herbal intoxication			
subjects affected / exposed	1 / 212 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 212 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux			
subjects affected / exposed	1 / 212 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	6 / 212 (2.83%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 2			
Bronchopneumonia				
subjects affected / exposed	7 / 212 (3.30%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Viral bronchiolitis				
subjects affected / exposed	1 / 212 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	7 / 212 (3.30%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 212 (1.42%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Acute gastroenteritis				
subjects affected / exposed	1 / 212 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bilateral bronchopneumonia				
subjects affected / exposed	1 / 212 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcus viridans septicamia				
subjects affected / exposed	1 / 212 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				

subjects affected / exposed	1 / 212 (0.47%)		
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 %

Non-serious adverse events	Study group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 212 (68.40%)		
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	102 / 212 (48.11%)		
occurrences (all)	102		
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	145 / 212 (68.40%)		
occurrences (all)	145		
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	96 / 212 (45.28%)		
occurrences (all)	96		
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	89 / 212 (41.98%)		
occurrences (all)	89		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	76 / 212 (35.85%)		
occurrences (all)	76		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	14 / 212 (6.60%)		
occurrences (all)	14		

Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	91 / 212 (42.92%)		
occurrences (all)	91		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 212 (9.91%)		
occurrences (all)	21		
Nasal congestion			
subjects affected / exposed	13 / 212 (6.13%)		
occurrences (all)	13		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	15 / 212 (7.08%)		
occurrences (all)	15		
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	137 / 212 (64.62%)		
occurrences (all)	137		
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	118 / 212 (55.66%)		
occurrences (all)	118		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	19 / 212 (8.96%)		
occurrences (all)	19		
Rhinitis			
subjects affected / exposed	27 / 212 (12.74%)		
occurrences (all)	27		
Upper respiratory tract infection			
subjects affected / exposed	81 / 212 (38.21%)		
occurrences (all)	81		
Metabolism and nutrition disorders			

Appetite lost alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 76 / 212 (35.85%) 76		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 January 2006	Informed investigators of the protocol to replace screening failures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported