



## Clinical trial results:

**Immunogenicity and Safety of the DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Given as a Three-Dose Primary Vaccination at 2, 3 and 4 Months of Age or 3, 4 and 5 Months of Age and followed by a Booster Dose at 18 to 20 Months, as compared to commercially available DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) monovalent vaccines in infants in People's Republic of China**

### Summary

EudraCT number	2015-005353-12
Trial protocol	Outside EU/EEA
Global end of trial date	08 January 2009

### 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	E2I42
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00453570
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
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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	03 August 2009
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 January 2009
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 seroconversion/vaccine response rates to Pertussis antigens (PT, FHA) of sanofi pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) administered at 2, 3 and 4 months of age or administered at 3, 4 and 5 months of age versus commercially available Wuhan's DTacP vaccine and sanofi pasteur's Hib tetanus conjugate (Act-HIB™) and IPV (IMOVAX Polio™) monovalent vaccines, one month after the three-dose primary vaccination of the combined vaccine.

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	16 March 2007
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	China: 792
Worldwide total number of subjects	792
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)	792

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 16 March 2007 to 24 July 2007 at 3 clinic centers in China.

### Pre-assignment

Screening details:

A total of 792 subjects who met all inclusion and none of the exclusion criteria were randomized and vaccinated in the study.

### Period 1

Period 1 title	Primary phase
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
<b>Arm title</b>	Group A

Arm description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 3, and 4 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 anterolateral aspect of the right thigh, 1 injection each at 2, 3, and 4 months of age and a booster at 18 to 20 months of age.

<b>Arm title</b>	Group B
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Arm description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 3, 4, and 5 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 anterolateral aspect of the right thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

<b>Arm title</b>	Group C
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Arm description:

Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) at 3, 4, and 5 months of age.

Arm type	Active comparator
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Investigational medicinal product name	DTacP combined vaccine (Diphtheria, Tetanus and Acellular Pertussis Combined Vaccine, Absorbed)
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 right deltoid, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

Investigational medicinal product name	PRP-Tetanus conjugated vaccine (Act-HIB™)
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 left thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

Investigational medicinal product name	IPV vaccine (IMOVAX Polio™)
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 anterolateral area of the right thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

Number of subjects in period 1	Group A	Group B	Group C
Started	264	264	264
Completed	257	237	237
Not completed	7	27	27
Consent withdrawn by subject	4	21	24
Adverse event, non-fatal	2	1	1
Serious adverse event	-	1	-
Lost to follow-up	1	1	-
Protocol deviation	-	3	2

## Period 2

Period 2 title	Booster phase
Is this the baseline period?	No
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>	Group A
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### Arm description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) booster dose at 18 to 20 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 anterolateral aspect of the right thigh, 1 injection each at 2, 3, and 4 months of age and a booster at 18 to 20 months of age.

<b>Arm title</b>	Group B
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### Arm description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) booster dose at 18 to 20 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 anterolateral aspect of the right thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

<b>Arm title</b>	Group C
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### Arm description:

Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) booster dose at 18 to 20 months of age.

Arm type	Active comparator
Investigational medicinal product name	DTacP combined vaccine (Diphtheria, Tetanus and Acellular Pertussis Combined Vaccine, Absorbed)
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 right deltoid, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

Investigational medicinal product name	PRP-Tetanus conjugated vaccine (Act-HIB™)
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 left thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

Investigational medicinal product name	IPV vaccine (IMOVAX Polio™)
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 anterolateral area of the right thigh, 1 injection each at 3, 4, and 5 months of age and a booster at 18 to 20 months of age.

<b>Number of subjects in period 2</b>	Group A	Group B	Group C
Started	257	237	237
Completed	251	233	228
Not completed	6	4	9
Consent withdrawn by subject	5	2	5
Serious adverse event	-	1	-
Lost to follow-up	-	-	1
Protocol deviation	1	1	3

## Baseline characteristics

### Reporting groups

Reporting group title	Group A
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 3, and 4 months of age.	
Reporting group title	Group B
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 3, 4, and 5 months of age.	
Reporting group title	Group C
Reporting group description: Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) at 3, 4, and 5 months of age.	

Reporting group values	Group A	Group B	Group C
Number of subjects	264	264	264
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)	264	264	264
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	2.2	2.2	2.2
standard deviation	± 0.1	± 0.1	± 0.1
Gender categorical Units: Subjects			
Female	116	133	127
Male	148	131	137

Reporting group values	Total		
Number of subjects	792		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	792		
Children (2-11 years)	0		



Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	376		
Male	416		

## Subject analysis sets

Subject analysis set title	Group A; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a booster dose of DTaP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 20 months of age.

Subject analysis set title	Group B; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a booster dose of DTaP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 20 months of age.

Subject analysis set title	Group C; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a booster dose of Wuhan's DTaP, Sanofi Pasteur's Hib tetanus conjugate (Act-HIB™) and IPV (IMOVAX Polio™) monovalent vaccines at 18 to 20 months of age.

Reporting group values	Group A; Post-Booster Analysis Set	Group B; Post-Booster Analysis Set	Group C; Post-Booster Analysis Set
Number of subjects	250	230	227
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)	250	230	227
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	2.2	2.2	2.2
standard deviation	± 0.1	± 0.1	± 0.1

Gender categorical			
Units: Subjects			
Female	109	118	110
Male	141	112	117

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## End points

### End points reporting groups

Reporting group title	Group A
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 3, and 4 months of age.	
Reporting group title	Group B
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 3, 4, and 5 months of age.	
Reporting group title	Group C
Reporting group description: Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) at 3, 4, and 5 months of age.	
Reporting group title	Group A
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) booster dose at 18 to 20 months of age.	
Reporting group title	Group B
Reporting group description: Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) booster dose at 18 to 20 months of age.	
Reporting group title	Group C
Reporting group description: Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) booster dose at 18 to 20 months of age.	
Subject analysis set title	Group A; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects received a booster dose of DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 20 months of age.	
Subject analysis set title	Group B; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects received a booster dose of DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 18 to 20 months of age.	
Subject analysis set title	Group C; Post-Booster Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects received a booster dose of Wuhan's DTacP, Sanofi Pasteur's Hib tetanus conjugate (Act-HIB™) and IPV (IMOVAX Polio™) monovalent vaccines at 18 to 20 months of age.	

### **Primary: Percentage of Subjects with Seroconversion/Seroconversion to Vaccine Antigens One Month after a Primary Series with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines**

End point title	Percentage of Subjects with Seroconversion/Seroconversion to Vaccine Antigens One Month after a Primary Series with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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#### End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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.

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, and  $\geq 0.15$   $\mu$ g/mL for Anti-PRP. Seroconversion for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers  $\geq 4$ -fold increase EU/mL.

End point type	Primary
End point timeframe:	
1 month post-primary vaccination series	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	254	229	232	
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria	100	100	100	
Anti-Tetanus	100	100	100	
Anti-Polio 1	100	100	100	
Anti-Polio 2	100	100	99.57	
Anti-Polio 3	100	99.56	99.57	
Anti-PRP	97.64	99.12	100	
Anti-Pertussis toxoid	100	100	97.38	
Anti-FHA	98.02	99.56	89.08	

## Statistical analyses

<b>Statistical analysis title</b>	Anti-Diphtheria; Group A-Group C
Statistical analysis description:	
This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Diphtheria.	
Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	1.63

Notes:

[1] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Tetanus; Group A-Group C
Statistical analysis description:	
This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Tetanus.	
Comparison groups	Group A v Group C

Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	1.63

Notes:

[2] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Polio 1; Group A-Group C
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Statistical analysis description:

This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Polio 1.

Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	1.63

Notes:

[3] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Polio 2; Group A-Group C
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Statistical analysis description:

This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Polio 2.

Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.4

Notes:

[4] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Polio 3; Group A-Group C
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**Statistical analysis description:**

This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Polio 3.

Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[5]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.4

**Notes:**

[5] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-PRP; Group A-Group C
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**Statistical analysis description:**

This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-PRP.

Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[6]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	-2.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	-0.29

**Notes:**

[6] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Pertussis toxoid; Group A-Group C
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**Statistical analysis description:**

This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-Pertussis toxoid.

Comparison groups	Group A v Group C
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[7]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	5.6

Notes:

[7] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-FHA; Group A-Group C
Statistical analysis description: This non-inferiority analysis assessed the difference between Group A minus Group C for Anti-FHA.	
Comparison groups	Group C v Group A
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[8]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	8.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.66
upper limit	13.77

Notes:

[8] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group A was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Diphtheria; Group B-Group C
Statistical analysis description: This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Diphtheria.	
Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[9]</sup>
Parameter estimate	Difference; Group A-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	1.63

Notes:

[9] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Tetanus; Group B-Group C
Statistical analysis description: This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Tetanus.	
Comparison groups	Group B v Group C

Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[10]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	1.63

Notes:

[10] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Polio 1; Group B-Group C
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Statistical analysis description:

This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Polio 1.

Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[11]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	1.63

Notes:

[11] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Polio 2; Group B-Group C
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Statistical analysis description:

This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Diphtheria.

Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[12]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	2.4

Notes:

[12] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group B was non-inferior to Group C.



<b>Statistical analysis title</b>	Anti-Polio 3; Group B-Group C
Statistical analysis description:	
This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Polio 3.	
Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[13]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	1.99

Notes:

[13] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-PRP; Group B-Group C
Statistical analysis description:	
This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-PRP.	
Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[14]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.14
upper limit	0.87

Notes:

[14] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority (> -10%). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-Pertussis toxoid; Group B-Group C
Statistical analysis description:	
This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-Pertussis toxoid.	
Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[15]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	5.6

Notes:

[15] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group B was non-inferior to Group C.

<b>Statistical analysis title</b>	Anti-FHA; Group B-Group C
Statistical analysis description: This non-inferiority analysis assessed the difference between Group B minus Group C for Anti-FHA.	
Comparison groups	Group B v Group C
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[16]</sup>
Parameter estimate	Difference; Group B-Group C
Point estimate	10.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.52
upper limit	15.19

Notes:

[16] - Non-inferiority was demonstrated if the 95% confidence interval of the difference (study vaccine minus control vaccine) lay entirely above the clinically acceptable limit for non-inferiority ( $> -10\%$ ). Group B was non-inferior to Group C.

**Secondary: Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and Following A Three Dose Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines**

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and Following A Three Dose Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
End point description: Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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.	
End point type	Secondary
End point timeframe: Pre- and post-primary vaccination	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	254	229	232	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Pre-primary	0.01 (0.01 to 0.012)	0.01 (0.009 to 0.011)	0.011 (0.01 to 0.012)	
Anti-Diphtheria; Post-primary	0.431 (0.405 to 0.459)	0.516 (0.489 to 0.544)	0.41 (0.39 to 0.43)	
Anti-Tetanus; Pre-primary	0.02 (0.02 to 0.02)	0.02 (0.02 to 0.02)	0.02 (0.02 to 0.02)	

Anti-Tetanus; Post-primary	2.88 (2.79 to 2.98)	3.02 (2.92 to 3.12)	3.05 (2.94 to 3.16)	
Anti-PRP; Pre-primary	0.06 (0.05 to 0.07)	0.05 (0.05 to 0.06)	0.06 (0.05 to 0.07)	
Anti-PRP; Post-primary	4.31 (3.71 to 5.02)	6.32 (5.52 to 7.23)	12.61 (11.21 to 14.18)	
Anti-Polio 1; Pre-primary	7.7 (6.7 to 8.8)	8.1 (7 to 9.5)	6.9 (6.1 to 7.8)	
Anti-Polio 1; Post-primary	322.5 (281.1 to 369.9)	299.2 (258.9 to 345.9)	130.1 (116.9 to 144.8)	
Anti-Polio 2; Pre-primary	6.1 (5.5 to 6.7)	6.6 (5.8 to 7.6)	5.7 (5.3 to 6.2)	
Anti-Polio 2; Post-primary	166.3 (144.7 to 191)	160.1 (138.2 to 185.5)	78.8 (69.8 to 88.9)	
Anti-Polio 3; Pre-primary	4.9 (4.5 to 5.3)	5.1 (4.7 to 5.5)	4.5 (4.2 to 4.7)	
Anti-Polio 3; Post-primary	587.5 (506.8 to 681)	525.5 (451.8 to 611.2)	222.6 (195.7 to 253.1)	
Anti-Pertussis toxoid; Pre-primary	1.9 (1.7 to 2)	1.9 (1.7 to 2)	1.8 (1.6 to 1.9)	
Anti-Pertussis toxoid; Post-primary	98.4 (93.7 to 103.4)	101.5 (96.3 to 107)	37.4 (34.9 to 40.1)	
Anti-FHA; Pre-primary	3.7 (3.4 to 4.1)	4 (3.6 to 4.3)	3.8 (3.5 to 4.1)	
Anti-FHA; Post-primary	92.9 (87.8 to 98.3)	103.6 (97.9 to 109.5)	47.1 (44 to 50.4)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Following A Three Dose Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Following A Three Dose Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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.

Geometric mean titer ratios of post-primary/pre-primary are reported.

End point type	Secondary
End point timeframe:	
Pre- and post-primary vaccination	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	228	231	
Units: Titer ratio (1/dil)				
geometric mean (confidence interval 95%)				

Anti-Diphtheria; Post-primary	41.225 (36.021 to 47.181)	50.467 (44.933 to 56.684)	38.033 (33.961 to 42.593)	
Anti-Tetanus; Post-primary	147.7 (131.91 to 165.37)	176.46 (155.05 to 200.83)	157.76 (137.8 to 180.6)	
Anti-PRP; Post-primary	76.54 (62.45 to 93.81)	114.67 (93.73 to 140.29)	206.18 (168.14 to 252.82)	
Anti-Polio 1; Post-primary	42 (34.3 to 51.3)	36.4 (29.3 to 45.3)	18.8 (16 to 22.1)	
Anti-Polio 2; Post-primary	27.7 (23 to 33.4)	24.1 (19.5 to 29.9)	13.7 (11.7 to 16.2)	
Anti-Polio 3; Post-primary	122.3 (102.7 to 145.6)	102.5 (86.5 to 121.5)	49.6 (42.6 to 57.6)	
Anti-Pertussis toxoid	52.8 (47.8 to 58.2)	54.7 (49.1 to 61)	21 (19 to 23.3)	
Anti-FHA	24.8 (22.2 to 27.7)	26.1 (23.5 to 29)	12.5 (11.1 to 14.1)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Seroprotection/Seroconversion to Antigens Before and One Month after A Primary Series with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or A DTacP, Hib conjugate (Act-HIB) and IPV (IMOVAX Polio) Monovalent Vaccine

End point title	Percentage of Subjects with Seroprotection/Seroconversion to Antigens Before and One Month after A Primary Series with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM) or A DTacP, Hib conjugate (Act-HIB) and IPV (IMOVAX Polio) Monovalent Vaccine
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#### End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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. Seroprotection for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers  $\geq 0.01$  IU/mL,  $\geq 8$  (dil) for Anti-Polio types 1, 2, and 3, and  $\geq 0.15$   $\mu$ g/mL for Anti-PRP. Seroconversion (post-primary only) for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers  $\geq 4$ -fold increase EU/mL.

End point type	Secondary
End point timeframe:	
Pre- and post-primary vaccination	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	254	229	232	
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria; Pre-primary	58.9	61.8	63.2	
Anti-Diphtheria; Post-primary	100	100	100	

Anti-Tetanus; Pre-primary	85	78.5	79.7	
Anti-Tetanus; Post-primary	100	100	100	
Anti-PRP; Pre-primary	15.1	13.3	16.5	
Anti-PRP; Post-primary	97.6	99.1	100	
Anti-Polio 1; Pre-primary	34.5	37.2	34.1	
Anti-Polio 1; Post-primary	100	100	100	
Anti-Polio 2; Pre-primary	26.5	30.1	27.9	
Anti-Polio 2; Post-primary	100	100	99.6	
Anti-Polio 3; Pre-primary	11.6	15	7.9	
Anti-Polio 3; Post-primary	100	99.6	99.6	
Anti-Pertussis toxoid; Pre-primary	0	0	0	
Anti-Pertussis toxoid; Post-primary	100	100	97.4	
Anti-FHA; Pre-primary	0	0	0	
Anti-FHA; Post-primary	98	99.6	89.1	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and Following A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or A DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and Following A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or A DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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End point description:

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

End point type	Secondary
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End point timeframe:

Pre- and post-booster vaccination

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	230	227	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Pre-booster	0.122 (0.115 to 0.129)	0.137 (0.128 to 0.147)	0.106 (0.1 to 0.112)	
Anti-Diphtheria; Post-booster	1.399 (1.291 to 1.516)	1.583 (1.459 to 1.719)	1.047 (0.97 to 1.13)	
Anti-Tetanus; Pre-booster	0.49 (0.46 to 0.53)	0.54 (0.5 to 0.58)	0.64 (0.6 to 0.68)	
Anti-Tetanus; Post-booster	6.19 (5.82 to 6.57)	6.13 (5.79 to 6.49)	5.63 (5.35 to 5.92)	

Anti-PRP; Pre-booster	2.18 (1.86 to 2.55)	2.65 (2.26 to 3.11)	3.76 (3.18 to 4.44)
Anti-PRP; Post-booster	61.81 (54.35 to 70.29)	81.86 (71.82 to 93.3)	109.33 (94.71 to 126.22)
Anti-Polio 1; Pre-booster	53.2 (45.2 to 62.7)	59 (49.7 to 70.2)	55.6 (47.5 to 65.1)
Anti-Polio 1; Post-booster	2405.7 (2142.8 to 2701)	2365.3 (2114.5 to 2645.8)	2241.3 (1993.5 to 2519.9)
Anti-Polio 2; Pre-booster	52.2 (42.5 to 64.1)	62.2 (49.2 to 78.5)	73.4 (59.6 to 90.4)
Anti-Polio 2; Post-booster	1688.3 (1498.6 to 1902.1)	1566 (1395.5 to 1757.3)	1286 (1151.7 to 1435.9)
Anti-Polio 3; Pre-booster	68.3 (55.2 to 84.4)	68 (54 to 85.7)	62.2 (50.1 to 77.2)
Anti-Polio 3; Post-booster	4223.4 (3713.9 to 4802.8)	4048.9 (3539.1 to 4632)	3970.8 (3512.7 to 4488.7)
Anti-Pertussis toxoid; Pre-booster	13.6 (12.6 to 14.6)	14.9 (13.8 to 16.1)	7.5 (7 to 8.1)
Anti-Pertussis toxoid; Post-booster	194.4 (182.8 to 206.8)	198.1 (185.4 to 211.6)	51.9 (47.8 to 56.2)
Anti-FHA; Pre-booster	12 (10.7 to 13.3)	14.2 (12.7 to 15.9)	5.2 (4.6 to 5.8)
Anti-FHA; Post-booster	131.5 (124 to 139.5)	137.9 (130 to 146.3)	68.7 (64.1 to 73.6)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Following A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Following A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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.

Geometric mean titer ratios of post-booster/pre-booster are reported.

End point type	Secondary
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End point timeframe:

Pre- and post-booster vaccination

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	230	227	
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Post-booster	11.509 (10.58 to 12.52)	11.552 (10.536 to 12.666)	9.916 (9.19 to 10.701)	
Anti-Tetanus; Post-booster	12.55 (11.59 to 13.6)	11.36 (10.44 to 12.37)	8.83 (8.21 to 9.51)	
Anti-PRP; Post-booster	28.37 (23.69 to 33.98)	30.87 (25.95 to 36.72)	29.1 (24.28 to 34.89)	
Anti-Polio 1; Post-booster	45.2 (38.2 to 53.4)	40.2 (33.1 to 48.7)	40.3 (33.3 to 48.8)	
Anti-Polio 2; Post-booster	32.4 (25.9 to 40.5)	25.3 (19.7 to 32.5)	17.4 (13.9 to 21.9)	
Anti-Polio 3; Post-booster	61.9 (49.9 to 76.7)	59.8 (47.7 to 75)	64.2 (51 to 80.9)	
Anti-Pertussis toxoid; Post-booster	14.3 (13.2 to 15.6)	13.3 (12.1 to 14.6)	6.9 (6.3 to 7.5)	
Anti-FHA; Post-booster	11 (9.9 to 12.1)	9.7 (8.7 to 10.8)	13.3 (11.9 to 14.8)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with Seroprotection/Seroconversion to Antigens Before and One Month After A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Percentage of Subjects with Seroprotection/Seroconversion to Antigens Before and One Month After A Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP), 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. Seroprotection for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers  $\geq 0.01$  IU/mL,  $\geq 8$  (dil) for Anti-Polio types 1, 2, and 3, and  $\geq 0.15$   $\mu$ g/mL for Anti-PRP. Seroconversion (post-primary only) for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers  $\geq 4$ -fold increase EU/mL.

End point type	Secondary
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End point timeframe:

Pre- and post-booster vaccination

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	230	227	
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria; Pre-booster	100	100	100	
Anti-Diphtheria; Post-booster	100	100	100	
Anti-Tetanus; Pre-booster	100	100	100	
Anti-Tetanus; Post-booster	100	100	100	
Anti-PRP; Pre-booster	99.6	100	100	
Anti-PRP; Post-booster	100	100	100	
Anti-Polio 1; Pre-booster	94	93.9	94.2	
Anti-Polio 1; Post-booster	100	100	100	
Anti-Polio 2; Pre-booster	88.4	89.5	96.5	
Anti-Polio 2; Post-booster	100	100	100	
Anti-Polio 3; Pre-booster	87.6	89.1	89.8	
Anti-Polio 3; Post-booster	100	100	100	
Anti-Pertussis toxoid; Post-booster	97.6	95.2	80.4	
Anti-FHA; Post-booster	89.9	85.5	92.4	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions After Any Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions After Any Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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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 (China SFDA): Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, > 3 cm. Grade 3 systemic reactions (China SFDA): 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	Secondary
End point timeframe:	
Day 0 up to Day 7 post-any primary vaccination	



End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	243	244	
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; Post-Any inj.; DTacP	43	41.3	40.1	
Grade 3 Inj. site Tenderness; Post-Any inj.; DTacP	0.4	0	0.8	
Any Inj. site Tenderness; Post-Any inj.; PRP~T	0	0	40.1	
Grade 3 Inj. site Tenderness; Post-Any inj.; PRP~T	0	0	0.8	
Any Inj. site Tenderness; Post-Any inj.; IPV	0	0	44.2	
Grade 3 Inj. site Tenderness; Post-Any inj.; IPV	0	0	0.8	
Any Inj. site Erythema; Post-Any inj.; DTacP	35	36	18.2	
Grade 3 Inj. site Erythema; Post-Any inj.; DTacP	1.1	2.5	0	
Any Inj. site Erythema; Post-Any inj.; PRP~T	0	0	17.8	
Grade 3 Inj. site Erythema; Post-Any inj.; PRP~T	0	0	0.8	
Any Inj. site Erythema; Post-Any inj.; IPV	0	0	15.7	
Grade 3 Inj. site Erythema; Post-Any inj.; IPV	0	0	0	
Any Inj. site Swelling; Post-Any injection; DTacP	25.9	21.5	9.1	
Grade 3 Inj. site Swelling; Post-Any inj.; DTacP	2.3	0.4	0	
Any Inj. site Swelling; Post-Any inj.; PRP~T	0	0	7	
Grade 3 Inj. site Swelling; Post-Any inj.; PRP~T	0	0	0.4	
Any Inj. site Swelling; Post-Any inj.; IPV	0	0	6.2	
Grade 3 Inj. site Swelling; Post-Any inj.; IPV	0	0	0	
Any Fever; Post-Any injection	57.4	62	61.6	
Grade 3 Fever; Post-Any injection	0.8	1.7	2.5	
Any Vomiting; Post-Any injection	46	33.1	31.4	
Grade 3 Vomiting; Post-Any injection	0	0	0	
Any Crying abnormal; Post-Any injection	39.5	38	51.7	
Grade 3 Crying abnormal; Post-Any injection	1.1	0	1.2	
Any Drowsiness; Post-Any injection	30.4	26.4	29.3	
Grade 3 Drowsiness; Post-Any injection	0.8	0.4	0.4	
Any Appetite lost; Post-Any injection	31.2	32.6	31.8	
Grade 3 Appetite lost; Post-Any injection	1.1	0	0.4	
Any Irritability; Post-Any injection	30.4	29.3	37.6	
Grade 3 Irritability; Post-Any injection	1.5	0.4	2.9	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each Primary Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccines
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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 (China SFDA): Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, > 3 cm. Grade 3 systemic reactions (China SFDA): 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	Secondary
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End point timeframe:

Day 0 up to Day 7 post-each primary vaccination

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	243	244	
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; Post-dose 1; DTacP	31.6	24.8	30.6	
Grade 3 Inj. site Tenderness; Post-dose 1; DTacP	0.4	0	0.8	
Any Inj. site Tenderness; Post-dose 1; PRP~T	0	0	32.6	
Grade 3 Inj. site Tenderness; Post-dose 1; PRP~T	0	0	0.8	
Any Inj. site Tenderness; Post-dose 1; IPV	0	0	33.9	
Grade 3 Inj. site Tenderness; Post-dose 1; IPV	0	0	0.8	
Any Inj. site Tenderness; Post-dose 2; DTacP	25.3	27.9	24.3	
Grade 3 Inj. site Tenderness; Post-dose 2; DTacP	0	0	0	
Any Inj. site Tenderness; Post-dose 2; PRP~T	0	0	23	
Grade 3 Inj. site Tenderness; Post-dose 2; PRP~T	0	0	0	
Any Inj. site Tenderness; Post-dose 2; IPV	0	0	25.1	
Grade 3 Inj. site Tenderness; Post-dose 2; IPV	0	0	0	
Any Inj. site Tenderness; Post-dose 3; DTacP	22.2	22.2	22.4	

Grade 3 Inj. site Tenderness; Post-dose 3; DTacP	0	0	0	
Any Inj. site Tenderness; Post-dose 3; PRP~T	0	0	22.8	
Grade 3 Inj. site Tenderness; Post-dose 3; PRP~T	0	0	0	
Any Inj. site Tenderness; Post-dose 3; IPV	0	0	24.1	
Grade 3 Inj. site Tenderness; Post-dose 3; IPV	0	0	0	
Any Inj. site Erythema; Post-dose 1; DTacP	17.1	15.7	8.3	
Grade 3 Inj. site Erythema; Post-dose 1; DTacP	0	0	0	
Any Inj. site Erythema; Post-dose 1; PRP~T	0	0	9.5	
Grade 3 Inj. site Erythema; Post-dose 1; PRP~T	0	0	0.8	
Any Inj. site Erythema; Post-dose 1; IPV	0	0	7.4	
Grade 3 Inj. site Erythema; Post-dose 1; IPV	0	0	0	
Any Inj. site Erythema; Post-dose 2; DTacP	21.4	23.8	9.2	
Grade 3 Inj. site Erythema; Post-dose 2; DTacP	0	1.7	0	
Any Inj. site Erythema; Post-dose 2; PRP~T	0	0	7.9	
Grade 3 Inj. site Erythema; Post-dose 2; PRP~T	0	0	0	
Any Inj. site Erythema; Post-dose 2; IPV	0	0	8.4	
Grade 3 Inj. site Erythema; Post-dose 2; IPV	0	0	0	
Any Inj. site Erythema; Post-dose 3; DTacP	24.1	20.1	9.3	
Grade 3 Inj. site Erythema; Post-dose 3; DTacP	1.2	1.3	0	
Any Inj. site Erythema; Post-dose 3; PRP~T	0	0	8.4	
Grade 3 Inj. site Erythema; Post-dose 3; PRP~T	0	0	0	
Any Inj. site Erythema; Post-dose 3; IPV	0	0	8.9	
Grade 3 Inj. site Erythema; Post-dose 3; IPV	0	0	0	
Any Inj. site Swelling; Post-dose 1; DTacP	12.9	8.3	3.3	
Grade 3 Inj. site Swelling; Post-dose 1; DTacP	0.4	0	0	
Any Inj. site Swelling; Post-dose 1; PRP~T	0	0	2.9	
Grade 3 Inj. site Swelling; Post-dose 1; PRP~T	0	0	0.4	
Any Inj. site Swelling; Post-dose 1; IPV	0	0	2.9	
Grade 3 Inj. site Swelling; Post-dose 1; IPV	0	0	0	
Any Inj. site Swelling; Post-dose 2; DTacP	10.9	13.8	3.8	
Grade 3 Inj. site Swelling; Post-dose 2; DTacP	1.2	0	0	

Any Inj. site Swelling; Post-dose 2; PRP~T	0	0	2.5	
Grade 3 Inj. site Swelling; Post-dose 2; PRP~T	0	0	0	
Any Inj. site Swelling; Post-dose 2; IPV	0	0	3.3	
Grade 3 Inj. site Swelling; Post-dose 2; IPV	0	0	0	
Any Inj. site Swelling; Post-dose 3; DTacP	17.1	13.8	5.9	
Grade 3 Inj. site Swelling; Post-dose 3; DTacP	1.2	0.4	0	
Any Inj. site Swelling; Post-dose 3; PRP~T	0	0	5.5	
Grade 3 Inj. site Swelling; Post-dose 3; PRP~T	0	0	0	
Any Inj. site Swelling; Post-dose 3; IPV	0	0	4.2	
Grade 3 Inj. site Swelling; Post-dose 3; IPV	0	0	0	
Any Fever; Post-dose 1	29.3	37.6	38.8	
Grade 3 Fever; Post-dose 1	0	0.4	0.8	
Any Fever; Post-dose 2	33.5	35.4	29.7	
Grade 3 Fever; Post-dose 2	0	0	1.3	
Any Fever; Post-dose 3	23.3	23.8	24.1	
Grade 3 Fever; Post-dose 3	0.8	1.3	0.4	
Any Vomiting; Post-dose 1	35	21.9	21.9	
Grade 3 Vomiting; Post-dose 1	0	0	0	
Any Vomiting; Post-dose 2	21.8	16.3	15.9	
Grade 3 Vomiting; Post-dose 2	0	0	0	
Any Vomiting; Post-dose 3	14.4	12.1	11	
Grade 3 Vomiting; Post-dose 3	0	0	0	
Any Crying abnormal; Post-dose 1	30	26.9	41.3	
Grade 3 Crying abnormal; Post-dose 1	1.1	0	1.2	
Any Crying abnormal; Post-dose 2	17.9	20	26.4	
Grade 3 Crying abnormal; Post-dose 2	0	0	0	
Any Crying abnormal; Post-dose 3	14.8	16.7	15.2	
Grade 3 Crying abnormal; Post-dose 3	0	0	0	
Any Drowsiness; Post-dose 1	25.1	22.3	19.8	
Grade 3 Drowsiness; Post-dose 1	0.8	0.4	0.4	
Any Drowsiness; Post-dose 2	12.5	9.6	13.4	
Grade 3 Drowsiness; Post-dose 2	0	0	0	
Any Drowsiness; Post-dose 3	6.6	8.8	8	
Grade 3 Drowsiness; Post-dose 3	0	0	0	
Any Appetite lost; Post-dose 1	20.2	21.9	21.9	
Grade 3 Appetite lost; Post-dose 1	1.1	0	0.4	
Any Appetite lost; Post-dose 2	14	17.1	13	
Grade 3 Appetite lost; Post-dose 2	0.4	0	0	
Any Appetite lost; Post-dose 3	10.9	12.6	12.7	
Grade 3 Appetite lost; Post-dose 3	0	0	0	
Any Irritability; Post-dose 1	23.6	21.1	28.5	
Grade 3 Irritability; Post-dose 1	0.8	0.4	1.7	
Any Irritability; Post-dose 2	13.6	17.5	18	
Grade 3 Irritability; Post-dose 2	0.4	0	1.3	
Any Irritability; Post-dose 3	11.7	10.5	11.8	
Grade 3 Irritability; Post-dose 3	0.4	0	0.4	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following a Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or A DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccine

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following a Booster Vaccination with Either DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) or A DTacP, Hib conjugate (Act-HIB™) and IPV (IMOVAX Polio™) Monovalent Vaccine
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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 (China SFDA): Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, > 3 cm. Grade 3 systemic reactions (China SFDA): 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	Secondary
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End point timeframe:

Day 0 up to Day 7 post-booster vaccination

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	252	234	228	
Units: Percentage of subjects				
number (not applicable)				
Any Inj. site Tenderness; DTacP	33.9	39.5	25	
Grade 3 Inj. site Tenderness; DTacP	0	0	0	
Any Inj. site Tenderness; PRP~T	0	0	24.6	
Grade 3 Inj. site Tenderness; PRP~T	0	0	0.9	
Any Inj. site Tenderness; IPV	0	0	27.2	
Grade 3 Inj. site Tenderness; IPV	0	0	0.9	
Any Inj. site Erythema; DTacP	37.1	36.9	13.6	
Grade 3 Inj. site Erythema; DTacP	8.8	6.9	0.4	
Any Inj. site Erythema; PRP~T	0	0	10.5	
Grade 3 Inj. site Erythema; PRP~T	0	0	0.4	
Any Inj. site Erythema; IPV	0	0	11.8	
Grade 3 Inj. site Erythema; IPV	0	0	0	
Any Inj. site Swelling; DTacP	27.5	26.6	7.5	
Grade 3 Inj. site Swelling; DTacP	6.8	6	0	
Any Inj. site Swelling; PRP~T	0	0	5.7	

Grade 3 Inj. site Swelling; PRP~T	0	0	0	
Any Inj. site Swelling; IPV	0	0	5.3	
Grade 3 Inj. site Swelling; IPV	0	0	0	
Any Fever	32.7	37.8	21.5	
Grade 3 Fever	0.8	1.3	1.3	
Any Vomiting	6.4	9.4	3.9	
Grade 3 Vomiting	0	0	0	
Any Crying abnormal	15.1	18.5	15.8	
Grade 3 Crying abnormal	0	0.4	0.4	
Any Drowsiness	6.8	11.2	4.8	
Grade 3 Drowsiness	0	0	0	
Any Appetite lost	19.5	24.5	14.9	
Grade 3 Appetite lost	0	0	0	
Any Irritability	16.3	18.9	15.8	
Grade 3 Irritability	0.4	0	0.9	

### 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	7.1
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### Reporting groups

Reporting group title	Group A
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Reporting group description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 2, 3, and 4 months of age and a booster dose at 18 to 20 months of age.

Reporting group title	Group B
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Reporting group description:

Subjects received Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) at 3, 4, and 5 months of age and a booster dose at 18 to 20 months of age.

Reporting group title	Group C
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Reporting group description:

Subjects received the control vaccine (Wuhan's DTacP, Act-HIB™ and IMOVAX Polio™) at 3, 4, and 5 months of age and a booster dose at 18 to 20 months of age.

Serious adverse events	Group A	Group B	Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 264 (2.27%)	7 / 243 (2.88%)	5 / 244 (2.05%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 264 (1.14%)	3 / 243 (1.23%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 264 (0.38%)	1 / 243 (0.41%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 264 (0.38%)	3 / 243 (1.23%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enteritis			
subjects affected / exposed	1 / 264 (0.38%)	0 / 243 (0.00%)	0 / 244 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infantile bronchitis			
subjects affected / exposed	0 / 264 (0.00%)	1 / 243 (0.41%)	0 / 244 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute enteritis			
subjects affected / exposed	0 / 264 (0.00%)	0 / 243 (0.00%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infant pneumonia			
subjects affected / exposed	0 / 264 (0.00%)	0 / 243 (0.00%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthmatic bronchitis			
subjects affected / exposed	0 / 264 (0.00%)	0 / 243 (0.00%)	1 / 244 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Group A	Group B	Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	151 / 264 (57.20%)	150 / 243 (61.73%)	149 / 244 (61.07%)
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	80 / 264 (30.30%)	64 / 243 (26.34%)	71 / 244 (29.10%)
occurrences (all)	80	64	71
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			



subjects affected / exposed occurrences (all)	113 / 264 (42.80%) 113	100 / 243 (41.15%) 100	107 / 244 (43.85%) 107
Injection site Erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	92 / 264 (34.85%) 92	87 / 243 (35.80%) 87	44 / 244 (18.03%) 44
Injection site Swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all)	68 / 264 (25.76%) 68	52 / 243 (21.40%) 52	22 / 244 (9.02%) 22
Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)	151 / 264 (57.20%) 151	150 / 243 (61.73%) 150	149 / 244 (61.07%) 149
Gastrointestinal disorders Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	121 / 264 (45.83%) 121	80 / 243 (32.92%) 80	76 / 244 (31.15%) 76
Psychiatric disorders Crying abnormal alternative assessment type: Systematic subjects affected / exposed occurrences (all)	104 / 264 (39.39%) 104	92 / 243 (37.86%) 92	125 / 244 (51.23%) 125
Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	80 / 264 (30.30%) 80	71 / 243 (29.22%) 71	91 / 244 (37.30%) 91
Metabolism and nutrition disorders Appetite lost alternative assessment type: Systematic subjects affected / exposed occurrences (all)	82 / 264 (31.06%) 82	79 / 243 (32.51%) 79	77 / 244 (31.56%) 77

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2007	The number of planned subjects was modified and the sample labeling and storage procedures were updated.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported