Clinical trial results:
Immunogenicity and safety of Sanofi Pasteur's DTaP-IPV combined vaccine (TETRAXIM™) given as a three-dose primary vaccination in South Korean healthy infants, as compared to commercially available DTaP and IPV monovalent vaccines

Summary

EudraCT number	2015-005348-33
Trial protocol	Outside EU/EEA
Global end of trial date	23 June 2007

Results information

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

Trial information

Trial identification

Sponsor protocol code	E2I28

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00319852
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Ltd
Sponsor organisation address	8th floor, Handok Building, 735, Yoksam 1-dong, Kangnam-ku, Seoul, Korea, Republic of,
Public contact	Medical Director, Sanofi Pasteur Ltd, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com
Scientific contact	Medical Director, Sanofi Pasteur Ltd, 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	06 May 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 June 2007
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) and seroconversion/vaccine response rates to Pertussis antigens (PT, FHA) of Sanofi Pasteur's DTaP-IPV combined vaccine versus commercially available Biken's DTaP (CJ purified PDT vaccine ™) and Aventis Pasteur's IPV (IMOVAX POLIO™) monovalent vaccines, one month after the three-dose primary vaccination.

Protection of trial subjects:

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

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	18 April 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Republic of: 442
Worldwide total number of subjects	442
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)	442
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 April 2006 to 23 January 2007 at 9 clinic sites in South Korea.

Pre-assignment

Screening details:

A total of 442 infants who met all inclusion and none of the exclusion criteria were randomized and vaccinated in this study.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	DTaP-IPV combined vaccine

Arm description:

Healthy infants received Sanofi Pasteur's DTaP-IPV combined vaccine (TETRAXIM™) at 2, 4, and 6 months of age.

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

Dosage and administration details:

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

Arm title	DTaP and IPV monovalent vaccines

Arm description:

Healthy infants received Biken's DTaP (Cheil Jedang [CJ] purified PDT vaccine™) and Sanofi Pasteur's IPV (IMOVAX POLIO™) monovalent vaccines at separate injection sites at 2, 4, and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	DTaP vaccine (CJ purified PDT vaccine™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

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

Investigational medicinal product name	Inactivated polio virus (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 injection into the left anterolateral thigh, 1 injection each at 2, 4, and 6 months of age.

Number of subjects in period 1	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines
Started	219	223
Completed	216	218
Not completed	3	5
Consent withdrawn by subject	3	4
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	DTaP-IPV combined vaccine
Reporting group description:	
Healthy infants received Sanofi Pasteur's DTaP-IPV combined vaccine (TETRAXIM™) at 2, 4, and 6 months of age.	
Reporting group title	DTaP and IPV monovalent vaccines
Reporting group description:	
Healthy infants received Biken's DTaP (Cheil Jedang [CJ] purified PDT vaccine™) and Sanofi Pasteur's IPV (IMOVAX POLIO™) monovalent vaccines at separate injection sites at 2, 4, and 6 months of age.	

Reporting group values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines	Total
Number of subjects	219	223	442
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)	219	223	442
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	
standard deviation	± 0.1	± 0.1	-
Gender categorical			
Units: Subjects			
Female	103	102	205
Male	116	121	237

End points

End points reporting groups

Reporting group title	DTaP-IPV combined vaccine
Reporting group description:	
Healthy infants received Sanofi Pasteur's DTaP-IPV combined vaccine (TETRAXIM™) at 2, 4, and 6 months of age.	
Reporting group title	DTaP and IPV monovalent vaccines
Reporting group description:	
Healthy infants received Biken's DTaP (Cheil Jedang [CJ] purified PDT vaccine™) and Sanofi Pasteur's IPV (IMOVAX POLIO™) monovalent vaccines at separate injection sites at 2, 4, and 6 months of age.	

Primary: Percentage of Subjects with Seroprotection Against Vaccine Antigens Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point title	Percentage of Subjects with Seroprotection Against Vaccine Antigens Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines
End point description:	
Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization. Seroprotection for Anti-Tetanus and Anti-Diptheria was defined as antibody titers ≥ 0.1 IU/mL and for Anti-Poliovirus types 1, 2, and 3 antibody titers ≥ 8 (1/dil). Seroconversion or vaccine response for Anti-PT and Anti-FHA was defined as ≥ 4-fold increase.	
End point type	Primary
End point timeframe:	
1 month post-dose 3 of primary vaccination	

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	205		
Units: Percentage of subjects				
number (not applicable)				
Anti-Tetanus	99	99		
Anti-Diphtheria	100	100		
Anti-Polio 1	100	99.5		
Anti-Polio 2	100	99		
Anti-Polio 3	100	99		
Anti-PT	97	94.6		
Anti-FHA	92.4	78.4		

Statistical analyses

Statistical analysis title	Non-inferiority; Anti-Tetanus

Statistical analysis description:

Non-inferiority analysis of Anti-Tetanus in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.75
upper limit	2.61

Notes:

[1] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-Diphtheria

Statistical analysis description:

Non-inferiority analysis of Anti-Diphtheria in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	1.88

Notes:

[2] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-Polio 1

Statistical analysis description:

Non-inferiority analysis of Anti-Polio 1 in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	2.75

Notes:

[3] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-Polio 2

Statistical analysis description:

Non-inferiority analysis of Anti-Polio 2 in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	3.52

Notes:

[4] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-Polio 3

Statistical analysis description:

Non-inferiority analysis of Anti-Polio 3 in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	3.52

Notes:

[5] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-PT

Statistical analysis description:

Non-inferiority analysis of Anti-PT in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	6.67

Notes:

[6] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Statistical analysis title	Non-inferiority; Anti-FHA

Statistical analysis description:

Non-inferiority analysis of Anti-FHA in DTaP-IPV vaccine (TETRAXIM™) minus DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines group.

Comparison groups	DTaP-IPV combined vaccine v DTaP and IPV monovalent vaccines
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Percentage observed (TETRAXIM-Control)
Point estimate	13.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.12
upper limit	20.77

Notes:

[7] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. If the lower bound of the 95% CI was greater than -10% than the null hypothesis H0 was rejected and it could be concluded for the non-inferiority of valence i. DTaP-IPV vaccine (TETRAXIM™) was non-inferior to DTaP (CJ purified PDT vaccine) and IPV (IMOVAX POLIO™) monovalent vaccines.

Secondary: Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens

	Before and Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point description:

Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization.

End point type	Secondary

End point timeframe:

Day 0 (pre-primary vaccination) and Day 30 post-dose 3 primary vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	205		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Pre-vaccination	0.005 (0.004 to 0.006)	0.004 (0.004 to 0.005)		
Anti-Diphtheria; Post-vaccination	0.718 (0.623 to 0.826)	0.705 (0.616 to 0.807)		
Anti-Tetanus; Pre-vaccination	0.022 (0.018 to 0.026)	0.019 (0.016 to 0.023)		
Anti-Tetanus; Post-vaccination	3.98 (3.53 to 4.5)	3.68 (3.28 to 4.13)		
Anti-Polio 1; Pre-vaccination	4.18 (3.59 to 4.85)	4.65 (3.99 to 5.43)		
Anti-Polio 1; Post-vaccination	1385 (1158 to 1657)	497 (425 to 581)		
Anti-Polio 2; Pre-vaccination	6.69 (5.74 to 7.8)	9.52 (8 to 11.3)		
Anti-Polio 2; Post-vaccination	1554 (1284 to 1880)	605 (518 to 708)		
Anti-Polio 3; Pre-vaccination	3.93 (3.43 to 4.5)	4.35 (3.82 to 4.95)		
Anti-Polio 3; Post-vaccination	1718 (1410 to 2093)	632 (531 to 752)		
Anti-PT; Pre-vaccination	2.24 (1.96 to 2.57)	2.78 (2.38 to 3.24)		
Anti-PT; Post-vaccination	206 (180 to 236)	199 (172 to 230)		
Anti-FHA; Pre-vaccination	4.09 (3.6 to 4.65)	4.15 (3.61 to 4.78)		
Anti-FHA; Post-vaccination	134 (121 to 148)	44.5 (40.7 to 48.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens

Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Following A Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point description:

Anti-Tetanus, Anti-Pertussis toxoid (PT), and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA), Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization. The post-primary/pre-primary vaccination geometric mean ratio is reported.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-primary vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	204		
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	141 (110 to 180)	175 (145 to 212)		
Anti-Tetanus	186 (145 to 239)	199 (159 to 250)		
Anti-Polio 1	341 (270 to 430)	108 (85.2 to 138)		
Anti-Polio 2	234 (179 to 307)	65.3 (49.8 to 85.7)		
Anti-Polio 3	439 (347 to 554)	148 (120 to 182)		
Anti-PT	91.3 (74.5 to 112)	71.3 (56.8 to 89.5)		
Anti-FHA	32.5 (27.3 to 38.7)	10.9 (9.11 to 13.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection Against Diphtheria, Tetanus, and Polio Types 1, 2 and 3 Antigens Before and After A Three-Dose Primary Series Vaccination with DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercial DTaP and IPV Monovalent Vaccines

End point title	Percentage of Subjects with Seroprotection Against Diphtheria, Tetanus, and Polio Types 1, 2 and 3 Antigens Before and After A Three-Dose Primary Series Vaccination with DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercial DTaP and IPV Monovalent Vaccines

End point description:

Anti-Tetanus antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA) and Anti-Diphtheria and Anti-Poliovirus types 1, 2, 3 antibody titers were measured using seroneutralization. Seroprotection for Anti-Tetanus and Anti-Diptheria was defined as antibody titers ≥ 0.01 IU/mL and ≥ 0.1 IU/mL and for Anti-Poliovirus types 1, 2, and 3 antibody titers ≥ 8 (1/dil).

End point type	Secondary

End point timeframe:

Day 0 (pre-primary vaccination) and Day 30 post-primary vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	205		
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria; ≥ 0.01 IU/mL; Pre-vaccination	27.4	21		
Anti-Diphtheria; ≥ 0.01 IU/mL; Post-vaccination	100	100		
Anti-Diphtheria; ≥ 0.1 IU/mL; Pre-vaccination	3	0		
Anti-Diphtheria; ≥ 0.1 IU/mL; Post-vaccination	93.8	95.5		
Anti-Tetanus; ≥ 0.01 IU/mL; Pre-vaccination	65.3	65		
Anti-Tetanus; ≥ 0.01 IU/mL; Post-vaccination	100	100		
Anti-Tetanus; ≥ 0.1 IU/mL; Pre-vaccination	15.8	13.3		
Anti-Tetanus; ≥ 0.1 IU/mL; Post-vaccination	99	99		
Anti-Polio 1; Pre-vaccination	24.5	30.2		
Anti-Polio 1; Post-vaccination	100	99.5		
Anti-Polio 2; Pre-vaccination	45.2	56.9		
Anti-Polio 2; Post-vaccination	100	99		
Anti-Polio 3; Pre-vaccination	20.8	27.3		
Anti-Polio 3; Post-vaccination	100	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ≥ 2-Fold and ≥ 4-Fold Increases Against Anti-Pertussis Toxoid and Anti-Filamentous Haemagglutinin Antigens After A Three-Dose Primary Series with DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercial DTaP and IPV Vaccines

End point title	Percentage of Subjects with ≥ 2-Fold and ≥ 4-Fold Increases Against Anti-Pertussis Toxoid and Anti-Filamentous Haemagglutinin Antigens After A Three-Dose Primary Series with DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercial DTaP and IPV Vaccines

End point description:

Anti-Pertussis toxoid (PT) and Anti-Filamentous hemagglutinin (FHA) antibody titers were measured using an enzyme-linked immunosorbent assay (ELISA). The percentage of subjects with ≥ 2-fold and ≥ 4-fold increases (post-primary/pre-primary vaccination) against Anti-PT and Anti-FHA antigens is reported.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-primary vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	204		
Units: Percentage of subjects				
number (not applicable)				
Anti-PT; ≥ 2-fold increase	97.5	95.1		
Anti-PT; ≥ 4-fold increase	97	94.6		
Anti-FHA; ≥ 2-fold increase	97	89.7		
Anti-FHA; ≥ 4-fold increase	92.4	78.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any of Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any of Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point description:

Solicited injection site reactions: Tenderness, Erythema, 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 Solicited systemic reactions: Fever, ≥ 39°C, Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficulty to wake up; Appetite lost, Refuses ≥ 3 feeds/meals or refuses most meals; Irritability, Inconsolable.

The DTaP-IPV (TETRAXIM™) group reported solicited injection site and systemic reactions following vaccination with DTaP-IPV combined vaccine whereas solicited injection site reactions in the DTaP and IPV monovalent vaccine group are reported by vaccine (DTaP and IPV).

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-any vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	222		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness; Post-Any injection	50.2	40.5		
Grade 3 Injection site Tenderness; Post-Any inj.	0.9	1.4		
Any Inj. site Tenderness; Post-Any inj. (DTaP)	0	38.7		
Grade 3 Inj. site Tenderness; Post-Any inj. (DTaP)	0	0.9		
Any Inj. site Tenderness; Post-Any inj. (IPV)	0	34.7		
Grade 3 Inj. site Tenderness; Post-Any inj. (IPV)	0	0.9		
Any Inj. site Erythema; Post-Any injection	60.4	42.3		
Grade 3 Inj. site Erythema; Post-Any injection	0.5	1.4		
Any Inj. site Erythema; Post-Any inj. (DTaP)	0	41		
Grade 3 Inj. site Erythema; Post-Any inj. (DTaP)	0	1.4		
Any Inj. site Erythema; Post-Any inj. (IPV)	0	17.1		
Grade 3 Inj. site Erythema; Post-Any inj. (IPV)	0	0.5		
Any Injection site Swelling; Post-Any injection	45.6	29.3		
Grade 3 Injection site Swelling; Post-Any inj.	0.5	0.5		
Any Injection site Swelling; Post-Any inj. (DTaP)	0	26.6		
Grade 3 Inj. site Swelling; Post-Any inj. (DTaP)	0	0.5		
Any Injection site Swelling; Post-Any inj. (IPV)	0	11.7		
Grade 3 Inj. site Swelling; Post-Any inj. (IPV)	0	0.5		
Any Fever; Post-Any injection	23.5	17.1		
Grade 3 Fever; Post-Any injection	0.9	0.5		
Any Vomiting; Post-Any injection	41	39.6		
Grade 3 Vomiting; Post-Any injection	0.5	0		
Any Crying abnormal; Post-Any injection	46.1	41.4		
Grade 3 Crying abnormal; Post-Any injection	0.9	0.5		
Any Drowsiness; Post-Any injection	42.9	38.7		
Grade 3 Drowsiness; Post-Any injection	0.5	0		
Any Appetite lost; Post-Any injection	51.2	47.7		
Grade 3 Appetite lost; Post-Any injection	1.4	0.5		

Any Irritability; Post-Any injection	45.6	46.4		
Grade 3 Irritability; Post-Any injection	1.8	0.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each of Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each of Three-Dose Primary Series Vaccination with Either DTaP-IPV Combined Vaccine (TETRAXIM™) or Commercially Available DTaP and IPV Monovalent Vaccines

End point description:

Solicited injection site reactions: Tenderness, Erythema, 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 Solicited systemic reactions: Fever, ≥ 39°C, Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficulty to wake up; Appetite lost, Refuses ≥ 3 feeds/meals or refuses most meals; Irritability, Inconsolable.

The DTaP-IPV (TETRAXIM™) group reported solicited injection site and systemic reactions following vaccination with DTaP-IPV combined vaccine whereas solicited injection site reactions in the DTaP and IPV monovalent vaccine group are reported by vaccine (DTaP and IPV).

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-each vaccination

End point values	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	222		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness; Post-injection 1	37.8	28.8		
Grade 3 Injection site Tenderness; Post-inj. 1	0	0.5		
Any Injection site Tenderness; Post-inj. 1 (DTaP)	0	26.1		
Grade 3 Inj. site Tenderness; Post-inj. 1 (DTaP)	0	0.5		
Any Injection site Tenderness; Post-inj. 1 (IPV)	0	26.6		
Grade 3 Inj. site Tenderness; Post-inj. 1 (IPV)	0	0.5		

Any Injection site Tenderness; Post-injection 2	31.3	26.1		
Grade 3 Injection site Tenderness; Post-inj. 2	0.9	0		
Any Injection site Tenderness; Post-inj. 2 (DTaP)	0	23.4		
Grade 3 Inj. site Tenderness; Post-inj. 2 (DTaP)	0	0		
Any Injection site Tenderness; Post-inj. 2 (IPV)	0	17.1		
Grade 3 Inj. site Tenderness; Post-inj. 2 (IPV)	0	0		
Any Injection site Tenderness; Post-injection 3	30	24.5		
Grade 3 Injection site Tenderness; Post-inj. 3	0	0.9		
Any Injection site Tenderness; Post-inj. 3 (DTaP)	0	22.3		
Grade 3 Inj. site Tenderness; Post-inj. 3 (DTaP)	0	0.5		
Any Injection site Tenderness; Post-inj. 3 (IPV)	0	16.8		
Grade 3 Inj. site Tenderness; Post-inj. 3 (IPV)	0	0.5		
Any Injection site Erythema; Post-injection 1	0	23.9		
Grade 3 Injection site Erythema; Post-injection 1	0	0.3		
Any Injection site Erythema; Post-inj. 1 (DTaP)	0	20.2		
Grade 3 Inj. site Erythema; Post-inj. 1 (DTaP)	0	0.3		
Any Injection site Erythema; Post-inj. 1 (IPV)	31.3	10.4		
Grade 3 Injection site Erythema; Post-inj. 1 (IPV)	0.5	0		
Any Injection site Erythema; Post-injection 2	0	7.2		
Grade 3 Injection site Erythema; Post-injection 2	0	0		
Any Injection site Erythema; Post-inj. 2 (DTaP)	0	9.5		
Grade 3 Inj. site Erythema; Post-inj. 2 (DTaP)	0	0		
Any Injection site Erythema; Post-inj. 2 (IPV)	41.9	33.8		
Grade 3 Injection site Erythema; Post-inj. 2 (IPV)	0	1.4		
Any Injection site Erythema; Post-injection 3	0	32.9		
Grade 3 Injection site Erythema; Post-injection 3	0	1.4		
Any Injection site Erythema; Post-inj. 3 (DTaP)	0	9.9		
Grade 3 Inj. site Erythema; Post-inj. 3 (DTaP)	0	0.5		
Any Injection site Erythema; Post-inj. 3 (IPV)	37.3	23.2		
Grade 3 Injection site Erythema; Post-inj. 3 (IPV)	0	0.5		
Any Injection site Swelling; Post-injection 1	0	20.8		

Grade 3 Injection site Swelling; Post-injection 1	0	0.6		
Any Injection site Swelling; Post-inj. 1 (DTaP)	0	10.4		
Grade 3 Inj. site Swelling; Post-inj. 1 (DTaP)	0	0.2		
Any Injection site Swelling; Post-inj. 1 (IPV)	22.1	5.9		
Grade 3 Injection site Swelling; Post-inj. 1 (IPV)	0.5	0		
Any Injection site Swelling; Post-injection 2	0	4.1		
Grade 3 Injection site Swelling; Post-injection 2	0	0		
Any Injection site Swelling; Post-inj. 2 (DTaP)	0	5.4		
Grade 3 Inj. site Swelling; Post-inj. 2 (DTaP)	0	0		
Any Injection site Swelling; Post-inj. 2 (IPV)	30	19.4		
Grade 3 Injection site Swelling; Post-inj. 2 (IPV)	0	0.5		
Any Injection site Swelling; Post-injection 3	0	18.5		
Grade 3 Injection site Swelling; Post-injection 3	0	0.5		
Any Injection site Swelling; Post-inj. 3 (DTaP)	0	5.9		
Grade 3 Inj. site Swelling; Post-inj. 3 (DTaP)	0	0.5		
Any Injection site Swelling; Post-inj. 3 (IPV)	29	14.5		
Grade 3 Injection site Swelling; Post-inj. 3 (IPV)	0	0		
Any Fever; Post-injection 1	0	11.6		
Grade 3 Fever; Post-injection 1	0	0.2		
Any Fever; Post-injection 2	0	6		
Grade 3 Fever; Post-injection 2	0	0.2		
Any Fever; Post-injection 3	9.7	6.3		
Grade 3 Fever; Post-injection 3	0	0		
Any Vomiting; Post-injection 1	9.7	8.6		
Grade 3 Vomiting; Post-injection 1	0.5	0.5		
Any Vomiting; Post-injection 2	9.5	7.1		
Grade 3 Vomiting; Post-injection 2	0.3	0.2		
Any Vomiting; Post-injection 3	30.9	27.5		
Grade 3 Vomiting; Post-injection 3	0.5	0		
Any Crying abnormal; Post-injection 1	13.4	12.7		
Grade 3 Crying abnormal; Post-injection 1	0	0		
Any Crying abnormal; Post-injection 2	20.6	19.1		
Grade 3 Crying abnormal; Post-injection 2	0.2	0		
Any Crying abnormal; Post-injection 3	33.6	28.4		
Grade 3 Crying abnormal; Post-injection 3	0.9	0.5		
Any Drowsiness; Post-injection 1	18.9	18.6		
Grade 3 Drowsiness; Post-injection 1	0	0		
Any Drowsiness; Post-injection 2	25.7	23.6		

Grade 3 Drowsiness; Post-injection 2	0.3	0.2		
Any Drowsiness; Post-injection 3	32.7	29.3		
Grade 3 Drowsiness; Post-injection 3	0.5	0		
Any Appetite lost; Post-injection 1	15.2	15.5		
Grade 3 Appetite lost; Post-injection 1	0	0		
Any Appetite lost; Post-injection 2	22.4	21.1		
Grade 3 Appetite lost; Post-injection 2	0.2	0		
Any Appetite lost; Post-injection 3	32.7	32.4		
Grade 3 Appetite lost; Post-injection 3	0.9	0		
Any Irritability; Post-injection 1	22.6	18.6		
Grade 3 Irritability; Post-injection 1	0	0		
Any Irritability; Post-injection 2	27	24.5		
Grade 3 Irritability; Post-injection 2	0.5	0.2		
Any Irritability; Post-injection 3	34.1	32.4		
Grade 3 Irritability; Post-injection 3	0.5	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 30 post-dose 3 of the primary vaccination series.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	DTaP-IPV combined vaccine

Reporting group description:

Healthy infants received Sanofi Pasteur's DTaP-IPV combined vaccine (TETRAXIM™) at 2, 4, and 6 months of age.

Reporting group title	DTaP and IPV monovalent vaccines

Reporting group description:

Healthy infants received Biken's DTaP (Cheil Jedang [CJ] purified PDT vaccine™) and Sanofi Pasteur's IPV (IMOVAX POLIO™) monovalent vaccines at separate injection sites at 2, 4, and 6 months of age.

Serious adverse events	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 217 (6.45%)	12 / 222 (5.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	6 / 217 (2.76%)	4 / 222 (1.80%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiopneumonia			
subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pyelonephritis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abcess axilla left after BCG vaccination			

subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 217 (0.92%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suspected gastroenteritis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suspected sepsis			
subjects affected / exposed	1 / 217 (0.46%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute bronchiolitis			
subjects affected / exposed	1 / 217 (0.46%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 217 (0.46%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 217 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DTaP-IPV combined vaccine	DTaP and IPV monovalent vaccines	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	131 / 217 (60.37%)	106 / 222 (47.75%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	93 / 217 (42.86%)	86 / 222 (38.74%)	
occurrences (all)	93	86	
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	109 / 217 (50.23%)	86 / 222 (38.74%)	
occurrences (all)	109	86	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	131 / 217 (60.37%)	91 / 222 (40.99%)	
occurrences (all)	131	91	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	99 / 217 (45.62%)	59 / 222 (26.58%)	
occurrences (all)	99	59	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 217 (23.50%)	38 / 222 (17.12%)	
occurrences (all)	51	38	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	89 / 217 (41.01%)	88 / 222 (39.64%)	
occurrences (all)	89	88	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			

subjects affected / exposed	100 / 217 (46.08%)	92 / 222 (41.44%)	
occurrences (all)	100	92	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	99 / 217 (45.62%)	103 / 222 (46.40%)	
occurrences (all)	99	103	
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed	111 / 217 (51.15%)	106 / 222 (47.75%)	
occurrences (all)	111	106	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2006	Added clarification of the stipends for participation, the approval of the administration of other vaccines during the trial period, and clarified that only the Hib vaccine would be free of charge to subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported