Clinical trial results:
Evaluation of Antibody Persistence Following a Primary Series at 2, 4, and 6 Months on Trial A3L24 and Booster Effect of the DTaP-IPV-Hep B-PRP-T Combined Vaccine or Infanrix hexa® Concomitantly Administered with Prevenar® at 12 to 24 Months of Age in Healthy Latin American Infants

Summary

EudraCT number	2011-004428-36
Trial protocol	Outside EU/EEA
Global end of trial date	10 December 2012

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	27 September 2014

Trial information

Trial identification

Sponsor protocol code	A3L27

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01444781
WHO universal trial number (UTN)	U1111-1112-8473

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur S.A
Sponsor organisation address	1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280
Public contact	Director, Clinical Development, Sanofi Pasteur S.A, 33 (0)4 37 37 58 43, emmanuel.feroldi@sanofipasteur.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001201-PIP01-11
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 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity
• To describe the antibody (Ab) persistence for all valences (except Prevenar [PCV7] and Rotarix), following a three-dose primary series vaccination, of either DTaP-IPV-Hep B-PRP-T or Infanrix hexa at 2, 4 and 6 months of age
• To describe the immunogenicity of a booster dose of DTaP-IPV-Hep B-PRP-T or Infanrix hexa given at 12 to 24 months concomitantly with a booster dose of Prevenar (PCV7)
• To describe the immunogenicity of a booster dose of Prevenar (PCV7) given at 12 to 24 months in the same subset of subjects that participated in the Prevenar (PCV7) immunogenicity analysis in A3L24 Study (maximum of 544 subjects)

Safety
To describe the safety profile after a booster dose of DTaP-IPV-Hep B-PRP-T or Infanrix hexa given at 12 to 24 months of age concomitantly with a booster dose of Prevenar (PCV7)

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 were also available on site in case of any immediate allergic reactions.

Background therapy:

Subjects randomized to the DTaP-IPV-Hep B-PRP-T vaccine included in Group 1 were to receive one of the 3 batches of this vaccine already used for the primary series trial A3L24 (same batch number as the one used in study A3L24). The subjects included in Group 2 (primed with DTaPIPV-Hep B-PRP-T vaccine) were to receive a booster dose of Infanrix hexa. The subjects included in the Group 3 (primed with Infanrix hexa) were to receive a DTaP-IPV-Hep B-PRP-T booster dose of one of the 3 batches used in study A3L24.

Evidence for comparator:

Infanrix hexa was chosen as the comparator vaccine as it is currently the licensed hexavalent vaccine in Colombia and Costa Rica. Prevenar (PCV7) was to be co-administered with both the DTaP-IPV-Hep B-PRP-T and Infanrix hexa vaccines in order to document the effect of this co-administration. Prevenar vaccine is also licensed in Colombia and Costa Rica.

Actual start date of recruitment	26 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 704
Country: Number of subjects enrolled	Costa Rica: 402

Worldwide total number of subjects	1106
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)	1106
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:

The study participants were enrolled from 26 September 2011 through 19 July 2012 at 2 clinic centers in Colombia and Costa Rica.

Pre-assignment

Screening details:

A total of 1106 participants who met all of the 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	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

A blind-observer procedure was followed for the DTaP-IPV-Hep B-PRP-T/Infanrix hexa comparison so that neither the Investigator (who was in charge of the safety assessment), nor the subject (or his/her parent[s]/guardian[s]), nor the Sponsor knew which vaccine was administered. The product preparation and administration were performed by an unblinded individual and the assessment of safety was performed by a blinded individual in 2 different rooms.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster

Arm description:

Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of DTaP-IPV-Hep B-PRP~T vaccine and one dose of Prevenar (PCV7)

Arm type	Experimental
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one primary dose series at 2, 4, and 6 months of age and a booster dose at 12 to 24 months of age.

Arm title	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster

Arm description:

Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of Infanrix Hexa vaccine and one dose of PCV7

Arm type	Active comparator
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one primary dose series at 2, 4, and 6 months of age.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one booster dose at 12 to 24 months of age.

Investigational medicinal product name	Prevenar (PCV7)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one booster dose coadministered with Infanrix hexa® at 12 to 24 months of age.

Arm title	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster

Arm description:

Subjects who were previously primed with Infanrix Hexa vaccine received one dose of DTaP-IPV-Hep B-PRP~T and one dose of PCV7

Arm type	Active comparator
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one booster dose at 12 to 24 months of age.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one primary dose series at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevenar (PCV7)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, one booster dose coadministered with DTaP-IPV-Hep BPRP-T combined vaccine at 12 to 24 months of age.

Number of subjects in period 1	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Started	416	415	275
Completed	413	411	272
Not completed	3	4	3
Consent withdrawn by subject	3	1	2
Lost to follow-up	-	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster
Reporting group description:	
Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of DTaP-IPV-Hep B-PRP~T vaccine and one dose of Prevenar (PCV7)	
Reporting group title	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster
Reporting group description:	
Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of Infanrix Hexa vaccine and one dose of PCV7	
Reporting group title	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Reporting group description:	
Subjects who were previously primed with Infanrix Hexa vaccine received one dose of DTaP-IPV-Hep B-PRP~T and one dose of PCV7	

Reporting group values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Number of subjects	416	415	275
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)	416	415	275
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	17.6	17.6	17.8
standard deviation	± 3.25	± 3.34	± 3.26
Gender categorical Units: Subjects			
Female	203	186	128
Male	213	229	147

Reporting group values	Total		
Number of subjects	1106		
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)	1106		
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	517		
Male	589		

End points

End points reporting groups

Reporting group title	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster
Reporting group description:	
Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of DTaP-IPV-Hep B-PRP~T vaccine and one dose of Prevenar (PCV7)	
Reporting group title	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster
Reporting group description:	
Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of Infanrix Hexa vaccine and one dose of PCV7	
Reporting group title	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Reporting group description:	
Subjects who were previously primed with Infanrix Hexa vaccine received one dose of DTaP-IPV-Hep B-PRP~T and one dose of PCV7	

Primary: Summary of Diphtheria and Tetanus Post Primary Series Antibodies, Persistence and Booster Response Following Vaccination With Either DTaP-IPV Hep B-PRP T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Diphtheria and Tetanus Post Primary Series Antibodies, Persistence and Booster Response Following Vaccination With Either DTaP-IPV Hep B-PRP T Vaccine or Infanrix Hexa Vaccine[1]

End point description:

Anti-Diphtheria (D) antibodies were measured by a toxin neutralization test. Anti-Tetanus (T) antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Antibody persistence for anti-Diphtheria and anti-Tetanus antibodies was defined as titers ≥0.01 IU/mL and ≥0.1 IU/mL before the booster dose at Day 0. Booster response to Diphtheria and Tetanus was defined as antibody titers ≥0.01 IU/mL and ≥0.1 IU/mL at Day 30 post-booster vaccination.

Day 140 = Primary series; Day 0 = Pre-booster; and Day 30 = Post-booster titers

End point type	Primary

End point timeframe:

Day 140 (Primary series) and Day 0 (Pre-booster)

Notes:

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

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-Diphtheria Day140 ≥0.01 IU/mL	392	391	259	
Anti-Diphtheria Day 140 ≥0.1 IU/mL	308	290	197	

Anti-Diphtheria Day 0 ≥0.01 IU/mL	382	378	246	
Anti-Diphtheria Day 0 ≥0.1 IU/mL	156	153	70	
Anti-Diphtheria Day 30 ≥0.01 IU/mL	393	387	254	
Anti-Diphtheria Day 30 ≥0.1 IU/mL	393	386	254	
Anti-Tetanus Day 140 ≥0.01 IU/mL	392	391	258	
Anti-Tetanus Day 140 ≥0.1 IU/mL	392	390	258	
Anti-Tetanus Day 0 ≥0.01 IU/mL	389	386	255	
Anti-Tetanus Day 0 ≥0.1 IU/mL	289	286	196	
Anti-Tetanus Day 30 ≥0.01 IU/mL	392	385	254	
Anti-Tetanus Day 30 ≥0.1 IU/mL	391	385	254	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Pertussis and Filamentous Haemagglutinin Post Primary Series Antibodies, Persistence and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Pertussis and Filamentous Haemagglutinin Post Primary Series Antibodies, Persistence and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine[2]

End point description:

Anti-Pertussis toxin (PT) and anti-Filamentous haemagglutinin (FHA) antibodies were measured by ELISA. Antibody persistence for anti-PT and anti-FHA was defined as titers ≥ lower limit of quantitation (LLOQ) before the booster dose at Day 0. Booster responses for PT and FHA at Day 30 were defined as: pre-vaccination antibody concentrations < LLOQ and post-vaccination levels ≥ 4 x LLOQ, pre-vaccination antibody concentrations ≥ LLOQ but < 4 x LLOQ and post/pre vaccination ≥ 4, and pre-vaccination antibody concentrations ≥ 4 x LLOQ and post/pre-vaccination ≥ 2.

Day 140 = Primary series; Day 0 = Pre-booster; and Day 30 = Post-booster titers.

End point type	Primary

End point timeframe:

Day 140 after primary vaccination, Day 0 (pre-vaccination), and Day 30 after final booster vaccination

Notes:

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

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-PT Day 140 ≥2 EU/mL	393	391	259	
Anti-PT Day 0 ≥2 EU/mL	344	349	225	
A-PT Day 30 ≥ 2 EU/mL	391	383	254	
Anti-PT 4-fold increase	353	351	234	

Anti-PT booster response	375	365	245	
Anti-FHA Day 140 ≥2 EU/mL	391	390	259	
Anti-FHA Day 0 ≥2 EU/mL	389	384	253	
Anti-FHA Day 30 ≥2 EU/mL	390	385	254	
Anti-FHA 4-fold increase	336	334	235	
Anti-FHA booster response	370	367	249	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Polio Antibodies Post Primary Series, Persistence and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Polio Antibodies Post Primary Series, Persistence and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine[3]

End point description:

Anti-Poliovirus types 1, 2, and 3 antibodies were measured by neutralization assay. Antibody persistence for anti-Poliovirus 1, 2, and 3 was defined as antibody titers ≥8 (1/dil) before the booster dose at Day 0. Booster response to Poliovirus 1, 2, and 3 was defined as antibody titers ≥8 (1/dil) at Day 30.

Day 140 = Primary series; Day 0 = Pre-booster; and Day 30 = Post-booster titers.

End point type	Primary

End point timeframe:

Day 140 after primary vaccination, Day 0 (pre-vaccination), and Day 30 after final booster vaccination

Notes:

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

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-Polio 1 Day 140	338	329	214	
Anti-Polio 1 Day 0	334	320	210	
Anti-Polio 1 Day 30	339	327	212	
Anti-Polio 2 Day 140	338	327	214	
Anti-Polio 2 Day 0	335	328	213	
Anti-Polio 2 Day 30	340	327	212	
Anti-Polio 3 Day 140	338	328	214	
Anti-Polio 3 Day 0	324	309	211	
Anti-Polio 3 Day 30	340	326	212	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Hepatitis B and Haemophilus Influenzae Type B Post Primary Series Antibodies; Antibody Persistence, and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Hepatitis B and Haemophilus Influenzae Type B Post Primary Series Antibodies; Antibody Persistence, and Booster Response Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine[4]

End point description:

Anti-Hepatitis B antibodies were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System. Anti-Haemophilus influenza type b capsular polyribosyl ribitol phosphate (PRP) antibodies were measured using a Farr type radioimmunoassay that used radiolabeled PRP (3H PRP) in the presence of 36Cl (volume marker). Anti-Hepatitis antibody titers ≥ 10 mIU/mL and ≥ 100 mIU/mL at Day 0 confirmed antibody persistence and booster response at Day 30. Anti-PRP antibody titers ≥ 0.15 µg/ml and ≥ 1.0 µg/ml at Day 0 confirmed antibody persistence and booster response at Day 30.

Day 140 = Primary series; Day 0 = Pre-booster; and Day 30 = Post-booster titers.

End point type	Primary

End point timeframe:

Day 140 after primary vaccination, Day 0 (pre-vaccination), and Day 30 after final booster vaccination

Notes:

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

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-Hep B Day 140 ≥10 mIU/mL	391	391	260	
Anti-Hep B Day 140 ≥100 mIU/mL	389	387	259	
Anti-Hep B Day 0 ≥10 mIU/mL	386	382	257	
Anti-Hep B Day 0 ≥100 mIU/mL	327	333	213	
Anti-Hep B Day 30 ≥10 mIU/mL	394	391	259	
Anti-Hep B Day 30 ≥100 mIU/mL	386	384	257	
Anti-PRP Day 140 ≥0.15 µg/mL	370	375	246	
Anti-PRP Day 140 ≥1.0 µg/mL	297	305	188	
Anti-PRP Day 0 ≥0.15 µg/mL	290	304	197	
Anti-PRP Day 0 ≥1.0 µg/mL	110	129	73	

Anti-PRP Day 30 ≥0.15 µg/mL	395	391	258	
Anti-PRP Day 30 ≥1.0 µg/mL	391	387	258	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers to Vaccine Antibodies Post Primary Vaccination Series; Before and After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Geometric Mean Titers to Vaccine Antibodies Post Primary Vaccination Series; Before and After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point description:

Anti-Diphtheria antibodies were measured by a toxin neutralization test. Anti-Tetanus, anti-PT, and anti-FHA antibodies were measured by ELISA. Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay. Anti-Hepatitis B antibodies were measured by the commercially available VITROS ECi/ECiQ Immunodiagnostic System. Anti-PRP antibodies were measured using a Farr type radioimmunoassay that used radiolabeled PRP (3H PRP) in the presence of 36Cl (volume marker).

Day 140 = Primary series; Day 0 = Pre-booster; and Day 30 = Post-booster titers.

End point type	Secondary

End point timeframe:

Day 140 after primary vaccination, Day 0 (pre-vaccination), and Day 30 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria Day 140	0.265 (0.237 to 0.295)	0.254 (0.227 to 0.285)	0.251 (0.22 to 0.286)	
Anti-Diphtheria Day 0	0.077 (0.069 to 0.086)	0.074 (0.066 to 0.083)	0.059 (0.051 to 0.068)	
Anti-Diphtheria Day 30	5.55 (5.07 to 6.08)	4.4 (3.99 to 4.86)	6.05 (5.41 to 6.76)	
Anti-Tetanus Day 140	1.5 (1.39 to 1.61)	1.54 (1.44 to 1.65)	1.8 (1.68 to 1.93)	
Anti-Tetanus Day 0	0.208 (0.188 to 0.231)	0.224 (0.2 to 0.251)	0.201 (0.18 to 0.225)	
Anti-Tetanus Day 30	5.72 (5.21 to 6.27)	5.21 (4.78 to 5.68)	7.52 (6.63 to 8.52)	
Anti-PT Day 140	99.6 (94 to 106)	102 (96.6 to 108)	97 (90.1 to 105)	

Anti-PT Day 0	7.43 (6.63 to 8.32)	8.47 (7.52 to 9.56)	7.41 (6.38 to 8.61)	
Anti PT Day 30	154 (143 to 166)	191 (178 to 206)	140 (127 to 153)	
Anti-FHA Day 140	179 (169 to 190)	187 (176 to 199)	120 (112 to 129)	
Anti-FHA Day 0	21.2 (18.9 to 23.8)	23.4 (20.8 to 26.3)	14.4 (12.5 to 16.8)	
Anti-FHA Day 30	316 (293 to 342)	418 (386 to 454)	260 (231 to 293)	
Anti-Polio 1 Day 140	656 (587 to 734)	705 (625 to 796)	1276 (1098 to 1484)	
Anti-Polio 1 Day 0	132 (116 to 150)	134 (116 to 154)	224 (188 to 267)	
Anti-Polio 1 Day 30	2140 (1937 to 2364)	2633 (2363 to 2933)	2978 (2592 to 3421)	
Anti-Polio 2 Day 140	1152 (1035 to 1282)	1241 (1101 to 1398)	1945 (1676 to 2256)	
Anti-Polio 2 Day 0	251 (214 to 294)	289 (245 to 341)	380 (313 to 461)	
Anti-Polio 2 Day 30	4232 (3821 to 4688)	4887 (4372 to 5463)	6369 (5569 to 7283)	
Anti-Polio 3 Day 140	1169 (1025 to 1332)	1108 (979 to 1255)	1948 (1647 to 2304)	
Anti-Polio 3 Day 0	128 (109 to 149)	126 (106 to 150)	207 (173 to 248)	
Anti-Polio 3 Day 30	3569 (3164 to 4027)	3322 (2939 to 3755)	6015 (5244 to 6898)	
Anti-Hepatitis B Day 140	3050 (2715 to 3427)	3180 (2834 to 3568)	2910 (2556 to 3313)	
Anti-Hepatitis B Day 0	386 (332 to 449)	406 (349 to 472)	336 (284 to 397)	
Anti-Hepatitis B Day 30	8462 (7154 to 10010)	11218 (9482 to 13272)	9688 (7940 to 11821)	
Anti-PRP Day 140	3.19 (2.69 to 3.78)	3.6 (3.05 to 4.25)	2.13 (1.78 to 2.54)	
Ant-PRP Day 0	0.482 (0.406 to 0.573)	0.556 (0.472 to 0.656)	0.455 (0.375 to 0.553)	
Anti-PRP Day 30	42.4 (37 to 48.6)	41.5 (36.6 to 47)	56.5 (48.4 to 65.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Immune Response Against Serotypes in the Prevenar Vaccine After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Immune Response Against Serotypes in the Prevenar Vaccine After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point description:

Anti-Streptococcus pneumococcal type specific antibody (anti-Pn PS) was measured by ELISA. Booster response to pneumococcal serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F was defined as antibody titers ≥0.35 µg/mL at Day 30.

End point type	Secondary

End point timeframe:

Day 30 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-Pneumococcal 4	160	146	94	
Anti-Pneumococcal 6B	155	145	93	
Anti-Pneumococcal 9V	161	147	94	
Anti-Pneumococcal 14	161	147	94	
Anti-Pneumococcal 18C	160	147	94	
Anti-Pneumococcal 19F	161	144	94	
Anti-Pneumococcal 23F	158	144	93	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers to Prevenar Vaccine Antibodies After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Summary of Geometric Mean Titers to Prevenar Vaccine Antibodies After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point description:

Anti-Streptococcus pneumococcal type specific antibody (anti-Pn PS) was measured by ELISA.

End point type	Secondary

End point timeframe:

Day 30 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-Pneumococcal 4	2.79 (2.47 to 3.15)	3.03 (2.64 to 3.47)	3.58 (3.07 to 4.17)	
Anti-Pneumococcal 6B	6.87 (5.68 to 8.31)	8.98 (7.86 to 10.3)	9.34 (7.76 to 11.2)	
Anti-Pneumococcal 9V	2.51 (2.22 to 2.85)	2.86 (2.57 to 3.19)	2.92 (2.5 to 3.42)	
Anti-Pneumococcal 14	11.6 (10.2 to 13.2)	13.2 (11.5 to 15.2)	12.3 (10.2 to 14.7)	
Anti-Pneumococcal 18C	2.37 (2.1 to 2.67)	2.63 (2.35 to 2.95)	3.4 (2.92 to 3.94)	
Anti-Pneumococcal 19F	3.01 (2.62 to 3.47)	3.74 (3.19 to 4.38)	3.72 (3.19 to 4.32)	
Anti-Pneumococcal 23F	6.98 (6.14 to 7.94)	7.2 (6.23 to 8.33)	9.3 (7.79 to 11.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Booster Response to Vaccine Antigens Before and After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine By Age Strata

End point title	Summary of Booster Response to Vaccine Antigens Before and After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine By Age Strata

End point description:

Anti-PT and anti-FHA antibodies were measured by ELISA.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Subjects				
number (not applicable)				
Anti-PT ≥12 to <15 month Day 0	100	104	61	
Anti-PT ≥12 to <15 moth Day 30 4-fold	87	92	53	
Anti-PT ≥12 to <15 months Booster	100	99	56	
Anti-PT ≥15 to <19 month Day 0	133	118	86	
Anti-PT ≥15 to <19 moth Day 30 4-fold	132	121	89	
Anti-PT ≥15 to <19 month Booster	138	125	94	
Anti-PT ≥19 to ≤24 months Day 0	111	127	78	
AntiPT ≥19 to ≤24 month Day 30 4 fold	134	138	92	
Anti-PT ≥19 to ≤24 months Booster	136	141	95	
Anti-FHA ≥12 to <15 months Day 0	103	105	59	

Anti-FHA ≥12 to <15 mos Day 30 4-fold	76	78	53	
Anti-FHA ≥12 to <15 months Booster	96	99	58	
Anti-FHA ≥15 to <19 month Day 0	143	130	95	
Anti-FHA ≥15 to <19 mos Day 30 4-fold	127	118	88	
Anti-FHA ≥15 to <19 months Booster	136	124	94	
Anti-FHA ≥19 to ≤24 month Day 0	143	149	99	
Anti-FHA ≥19 to ≤24 mos Day 30 4-fold	133	138	94	
Anti-FHA ≥19 to ≤ 24 months Booster	138	144	97	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Geometric Mean Titers to Vaccine Antigens After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine by Age Strata

End point title	Summary of Geometric Mean Titers to Vaccine Antigens After Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine by Age Strata

End point description:

Anti-Diphtheria antibodies were measured by a toxin neutralization test. Anti-FHA antibodies were measured by ELISA. Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay.

End point type	Secondary

End point timeframe:

Day 30 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	393	260	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria ≥12 to <15 months	3.2 (2.72 to 3.76)	2.73 (2.3 to 3.24)	3.82 (3.01 to 4.84)	
Anti-Diphtheria ≥15 to <19 months	6.39 (5.56 to 7.34)	4.77 (3.98 to 5.72)	6.56 (5.43 to 7.92)	
Anti-Diphtheria ≥19 to ≤24 months	7.14 (6.17 to 8.26)	5.77 (5 to 6.66)	7.34 (6.3 to 8.56)	
Anti-FHA ≥12 to <15 months	235 (209 to 263)	268 (233 to 308)	197 (156 to 248)	
Anti-FHA ≥15 to <19 months	339 (294 to 392)	453 (392 to 524)	280 (236 to 331)	
Anti-FHA ≥19 to ≤24 months	365 (322 to 414)	533 (473 to 599)	287 (232 to 356)	
Anti-Polio 3 ≥12 to <15 months	2509 (1944 to 3240)	2616 (2098 to 3263)	5617 (4006 to 7876)	

Anti-Polio 3 ≥15 to <19 months	3944 (3265 to 4764)	3261 (2585 to 4113)	5409 (4359 to 6713)	
Anti-Polio 3 ≥19 to ≤24 months	4119 (3398 to 4993)	4061 (3387 to 4869)	6889 (5583 to 8499)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point title	Number of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Booster Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine or Infanrix Hexa Vaccine

End point description:

Solicited injection site: Pain, Erythema, Swelling, and Extensive swelling of vaccinated limb; Solicited systemic reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia, and Irritability. Grade 3 Injection site: Pain, Cries if limb is moved or reduced movement; Erythema and Swelling, ≥5 cm; Extensive swelling of limb, Severe. Grade 3 Systemic reactions: Pyrexia (Temperature) >39.5°C; Vomiting, ≥ 6 times per 24 hours or needing parenteral nutrition; Crying, >3 hours; Somnolence, Sleeping often or difficulty waking; Anorexia, refuses ≥3 meals; and Irritability, Inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	416	415	275	
Units: Subjects				
number (not applicable)				
Injection site Pain	232	205	160	
Grade 3 inj. site Pain	10	6	6	
Injection site Erythema	112	100	86	
Grade 3 inj. site Erythema	4	3	7	
Injection site Swelling	60	56	49	
Grade 3 inj. site Swelling	3	3	1	
Extensive swelling of limb	0	0	0	
Grade 3 Extensive swelling of limb	0	0	0	
Pyrexia	114	99	91	
Grade 3 Pyrexia	2	6	1	
Vomiting	34	39	19	
Grade 3 Vomiting	1	1	0	
Crying	148	139	102	
Grade 3 Crying	1	1	2	
Somnolence	124	113	85	

Grade 3 Somnolence	2	1	2	
Anorexia	118	121	90	
Grade 3 Anorexia	3	3	4	
Irritability	201	176	146	
Grade 3 Irritability	1	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting a Solicited Injection Site Following Booster Vaccination With Prevenar Vaccine

End point title	Number of Subjects Reporting a Solicited Injection Site Following Booster Vaccination With Prevenar Vaccine

End point description:

Solicited injection site: Pain, Erythema, Swelling, and Extensive swelling of vaccinated limb. Grade 3 Injection site: Pain, cries if limb is moved or reduced movement; Erythema and Swelling, ≥5 cm; and Extensive swelling of limb, Severe.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 after final booster vaccination

End point values	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	416	415	275	
Units: Subjects				
number (not applicable)				
Injection site Pain	224	184	140	
Grade 3 Injection site Pain	9	9	5	
Injection site Erythema	84	77	52	
Grade 3 Injection site Erythema	0	0	0	
Injection site Swelling	51	42	33	
Grade 3 Injection site Swelling	1	1	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 30 after final booster vaccination.

Adverse event reporting additional description:

The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster

Reporting group description:

Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of DTaP-IPV-Hep B-PRP~T vaccine and one dose of Prevenar (PCV7)

Reporting group title	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster

Reporting group description:

Subjects who were previously primed with DTaP-IPV-Hep B-PRP~T received one dose of Infanrix Hexa vaccine and one dose of PCV7

Reporting group title	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster

Reporting group description:

Subjects who were previously primed with Infanrix Hexa vaccine received one dose of DTaP-IPV-Hep B-PRP~T and one dose of PCV7

Serious adverse events	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 416 (3.13%)	15 / 415 (3.61%)	9 / 275 (3.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	2 / 416 (0.48%)	2 / 415 (0.48%)	1 / 275 (0.36%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Idiopathic thrombocytopenic purpura			

subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 416 (0.24%)	0 / 415 (0.00%)	0 / 275 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 416 (0.48%)	1 / 415 (0.24%)	0 / 275 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
Cellulitis			
subjects affected / exposed	1 / 416 (0.24%)	0 / 415 (0.00%)	1 / 275 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	1 / 416 (0.24%)	0 / 415 (0.00%)	1 / 275 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kawasaki's disease			
subjects affected / exposed	1 / 416 (0.24%)	0 / 415 (0.00%)	0 / 275 (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
Osteomyelitis acute			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
Pneumonia			
subjects affected / exposed	5 / 416 (1.20%)	4 / 415 (0.96%)	5 / 275 (1.82%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 416 (0.00%)	0 / 415 (0.00%)	1 / 275 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 416 (0.00%)	2 / 415 (0.48%)	0 / 275 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 416 (0.00%)	1 / 415 (0.24%)	0 / 275 (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

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

Non-serious adverse events	Group 1: DTaP-IPV-Hep B-PRP~T + Prevenar™ Primary and Booster	Group2: DTaPIPV-Hep B-PRP~T Primary/Infanrix Hexa+PCV7 Booster	Group3: Infanrix Hexa Primary/DTaPIPV-Hep B PRP~T+PCV7 Booster
Total subjects affected by non-serious adverse events			
subjects affected / exposed	253 / 416 (60.82%)	221 / 415 (53.25%)	168 / 275 (61.09%)
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	124 / 413 (30.02%)	113 / 412 (27.43%)	85 / 272 (31.25%)
occurrences (all)	124	113	85
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	232 / 416 (55.77%)	205 / 412 (49.76%)	160 / 272 (58.82%)
occurrences (all)	232	205	160
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	112 / 413 (27.12%)	100 / 412 (24.27%)	86 / 272 (31.62%)
occurrences (all)	112	100	86
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	60 / 412 (14.56%)	56 / 412 (13.59%)	49 / 272 (18.01%)
occurrences (all)	60	56	49
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed[5]	114 / 413 (27.60%)	99 / 412 (24.03%)	91 / 272 (33.46%)
occurrences (all)	114	99	91
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[6]	34 / 413 (8.23%)	39 / 412 (9.47%)	19 / 272 (6.99%)
occurrences (all)	34	39	19
Psychiatric disorders			

Crying			
alternative assessment type: Systematic			
subjects affected / exposed[7]	148 / 413 (35.84%)	139 / 412 (33.74%)	102 / 272 (37.50%)
occurrences (all)	148	139	102
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[8]	201 / 413 (48.67%)	176 / 412 (42.72%)	146 / 272 (53.68%)
occurrences (all)	201	176	146
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	27 / 416 (6.49%)	23 / 415 (5.54%)	12 / 275 (4.36%)
occurrences (all)	27	23	12
Metabolism and nutrition disorders			
Anorexia			
alternative assessment type: Systematic			
subjects affected / exposed[9]	118 / 413 (28.57%)	121 / 412 (29.37%)	90 / 272 (33.09%)
occurrences (all)	118	121	90

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The total number (N) for solicited adverse events in the table reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2011	Protocol was amended to add measles, mumps, rubella and varicella, and yellow fever vaccinations and to take into account the National Campaign of Intensification against polio in Costa Rica.
06 October 2011	A 5th dose of a pneumococcal conjugate vaccine (administered after completing V02 and at least one month after the PCV7 booster dose) was added by using the 13-valent PCV as result of a change of the National Vaccination calendar in Costa Rica.
17 September 2012	The principal Investigator was changed in Costa Rica.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported