Clinical trial results:
Large Scale Safety Study of a DTaP IPV Hep B PRP T Combined Vaccine, in Comparison to Tritanrix Hep B/Hib™ and OPV Administered at 2, 4, and 6 Months of Age in Latin American Infants

Summary

EudraCT number	2011-004431-31
Trial protocol	Outside EU/EEA
Global end of trial date	02 January 2008

Results information

Result version number	v1 (current)
This version publication date	03 February 2016
First version publication date	31 July 2014

Trial information

Trial identification

Sponsor protocol code	A3L04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00313911
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex, France, F 69367
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com

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?	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	10 July 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that DTaP-IPV-Hep B-PRP-T combined vaccine + OPV placebo does not induce a higher incidence rate of high fever than Tritanrix-Hep B/Hib™ + OPV after any of the three vaccinations at 2, 4, and 6 months of age for each subject.

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2006
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	Mexico: 1067
Country: Number of subjects enrolled	Peru: 1066
Worldwide total number of subjects	2133
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)	2133
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:

Eligible subjects that met all the inclusion and none of the exclusion criteria were enrolled and vaccinated in the study.

Pre-assignment

Screening details:

A total of 2133 participants who met the inclusion and non of the exclusion criteria were enrolled and vaccinated.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

The investigator (blind observer or assessor) and subject's parents or guardians did not know the vaccine administered. The assessor was in charge of the assessment of safety held in a separate room and away from where the vaccines were prepared. A nurse/vaccinator was in charge of the preparation and administration of the vaccine(s) in another room away from the assessor. When necessary the scratch off emergency decoding procedure described in the study protocol were to be followed.

Arms

Are arms mutually exclusive?	Yes
Arm title	DTaP-IPV-Hep B-PRP~T Group

Arm description:

Participants received Diphtheria (D), tetanus (T), pertussis (acellular, component) (aP), hepatitis B (hep B [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) plus a Placebo, oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.

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, administered at 2, 4, and 6 months of age.

Investigational medicinal product name	OPV Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

0.1 mL, oral administration

Arm title	Tritanrix-Hep B/Hib™ + OPV Group

Arm description:

Participants received Tritanrix-Hep B/Hib™ + oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.

Arm type	Active comparator

Investigational medicinal product name	Tritanrix HepB/Hib™
Investigational medicinal product code	Tritanrix HepB/Hib™
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular

Investigational medicinal product name	OPVERO (Oral Poliomyelitis Vaccine)
Investigational medicinal product code	OPV
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Each dose is 0.1 mL administered by Oral route.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The investigator of the study served as observer or assessor that was masked for the actual vaccine administered to each subject.

Number of subjects in period 1	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group
Started	1422	711
Completed	1328	670
Not completed	94	41
Consent withdrawn by subject	39	12
Adverse event, non-fatal	2	3
Lost to follow-up	27	14
Serious Adverse Events	6	1
' Did not meet age criteria'	1	1
Protocol deviation	19	10

Baseline characteristics

Reporting groups	
Reporting group title	DTaP-IPV-Hep B-PRP~T Group
Reporting group description:	
Participants received Diphtheria (D), tetanus (T), pertussis (acellular, component) (aP), hepatitis B (hep B [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) plus a Placebo, oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.	
Reporting group title	Tritanrix-Hep B/Hib™ + OPV Group
Reporting group description:	
Participants received Tritanrix-Hep B/Hib™ + oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.	

Reporting group values	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group	Total
Number of subjects	1422	711	2133
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)	1422	711	2133
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	1.89	1.88	
standard deviation	± 0.195	± 0.197	-
Gender categorical Units: Subjects			
Female	706	344	1050
Male	716	367	1083

End points

End points reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP~T Group
Reporting group description:	
Participants received Diphtheria (D), tetanus (T), pertussis (acellular, component) (aP), hepatitis B (hep B [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) plus a Placebo, oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.	
Reporting group title	Tritanrix-Hep B/Hib™ + OPV Group
Reporting group description:	
Participants received Tritanrix-Hep B/Hib™ + oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.	

Primary: Number of Participants With High Fever Observed After Either DTaP-IPV-Hep B-PRP~T or Tritanrix Hep B/Hib™ + Placebo or Tritanrix-Hep B/Hib™ + Placebo Injection

End point title	Number of Participants With High Fever Observed After Either DTaP-IPV-Hep B-PRP~T or Tritanrix Hep B/Hib™ + Placebo or Tritanrix-Hep B/Hib™ + Placebo Injection
End point description:	
High fever was defined as rectal temperature equivalent to ≥ 39.6ºC.	
End point type	Primary
End point timeframe:	
Day 0 up to Day 7 post-injection	

End point values	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1422[1]	711[2]		
Units: Participants				
Post Any Dose	56	39		
Post Dose 1	5	4		
Post Dose 2	25	15		
Post Dose 3	26	23		

Notes:

[1] - N for outcomes adjusted to include participant in Group 2 that got vaccine assigned to this group.

[2] - A subject in this group mistakenly got Group 1 vaccine. N in outcomes adjusted accordingly

Statistical analyses

Statistical analysis title	High Fever Post-vaccination
Statistical analysis description:	
The occurrence of at least one high fever episode (≥39.6°C rectal temperature equivalent) observed within 7 days after any of the three injections and the resulting risk ratio	
Comparison groups	DTaP-IPV-Hep B-PRP~T Group v Tritanrix-Hep B/Hib™ + OPV Group

Number of subjects included in analysis	2133
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Risk ratio (RR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.07

Notes:

[3] - Confidence interval was calculated using the normal approximation for the log transformation of Risk Ratio (RR) as described by Blackwelder

Secondary: Geometric Mean Titers of Anti Hepatitis B Antibodies Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine + Placebo or Tritanrix-Hep B/Hib™ + Placebo

End point title	Geometric Mean Titers of Anti Hepatitis B Antibodies Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine + Placebo or Tritanrix-Hep B/Hib™ + Placebo

End point description:

Anti-hepatitis B (Hep B) antibodies were measured by automated enhanced chemiluminescence assay.

End point type	Secondary

End point timeframe:

Day 30 post-dose 3

End point values	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	95		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti Hepatitis B Antibodies	1075 (891 to 1298)	3376 (2672 to 4338)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reaching Seroprotection Threshold Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine + Placebo or Tritanrix-Hep B/Hib™ + Placebo

End point title	Percentage of Participants Reaching Seroprotection Threshold Following Vaccination With Either DTaP-IPV-Hep B-PRP~T Vaccine + Placebo or Tritanrix-Hep B/Hib™ + Placebo

End point description:

Anti hepatitis B (Hep B) antibodies were measured by automated enhanced chemiluminescence assay. Two Seroprotection thresholds were defined: a titer ≥ 10 mIU/mL and ≥ 100 mIU/mL, respectively.

End point type	Secondary

End point timeframe:

Day 30 post-dose 3

End point values	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	95		
Units: mIU/mL				
number (not applicable)				
≥ 10 mIU/mL	100	100		
≥ 100 mIU/mL	96	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting at Least One Solicited Injection Site or Systemic Reaction Following Each Vaccination

End point title	Number of Participants Reporting at Least One Solicited Injection Site or Systemic Reaction Following Each Vaccination

End point description:

Solicited Injection Site Reactions: Pain, Erythema, Swelling. Solicited Systemic Reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia, Irritability.
Severe solicited reactions were defined as follows: Pain, cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm; Fever ≥39.6 ºC; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying, >3 hours; Somnolence, sleeping most of the time or difficulty to wake up; Anorexia, refuses ≥3 feeds or refuses most feeds; Irritability, inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 Post-injection

End point values	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1422	711		
Units: Participants				
Any Pain Post Dose 1	831	574		
Severe Pain Post Dose 1	175	193		
Any Pain Post Dose 2	744	506		
Severe Pain Post Dose 2	105	95		
Any Pain Post Dose 3	519	448		
Severe Pain Post Dose 3	29	65		

Any Erythema Post Dose 1	245	234		
Severe Erythema Post Dose 1	11	15		
Any Erythema Post Dose 2	427	308		
Severe Erythema Post Dose 2	6	16		
Any Erythema Post Dose 3	587	340		
Severe Erythema Post Dose 3	23	12		
Any Swelling Post Dose 1	151	188		
Severe Swelling Post Dose 1	8	24		
Any Swelling Post Dose 2	259	270		
Severe Swelling Post Dose 2	3	11		
Any Swelling Post Dose 3	400	323		
Severe Swelling Post Dose 3	3	7		
Any Pyrexia Post Dose 1	538	473		
Severe Pyrexia Post Dose 1	5	4		
Any Pyrexia Post Dose 2	675	457		
Severe Pyrexia Post Dose 2	27	16		
Any Pyrexia Post Dose 3	552	445		
Severe Pyrexia Post Dose 3	30	23		
Any Vomiting Post Dose 1	230	120		
Severe Vomiting Post Dose 1	10	4		
Any Vomiting Post Dose 2	152	75		
Severe Vomiting Post Dose 2	2	4		
Any Vomiting Post Dose 3	167	95		
Severe Vomiting Post Dose 3	17	10		
Any Crying Post Dose 1	800	564		
Severe Crying Post Dose 1	21	26		
Any Crying Post Dose 2	721	481		
Severe Crying Post Dose 2	9	8		
Any Crying Post Dose 3	466	391		
Severe Crying Post Dose 3	9	8		
Any Somnolence Post Dose 1	635	375		
Severe Somnolence Post Dose 1	46	26		
Any Somnolence Post Dose 2	405	247		
Severe Somnolence Post Dose 2	16	12		
Any Somnolence Post Dose 3	272	204		
Severe Somnolence Post Dose 3	12	11		
Any Anorexia Post Dose 1	388	278		
Severe Anorexia Post Dose 1	11	14		
Any Anorexia Post Dose 2	327	195		
Severe Anorexia Post Dose 2	12	11		
Any Anorexia Post Dose 3	294	189		
Severe Anorexia Post Dose 3	18	17		
Any Irritability Post Dose 1	945	576		
Severe Irritability Post Dose 1	42	47		
Any Irritability Post Dose 2	799	492		
Severe Irritability Post Dose 2	41	25		
Any Irritability Post Dose 3	546	416		
Severe Irritability Post Dose 3	11	17		

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 the day of the first injection (Day 0) through 6 months after the last injection.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP~T Group

Reporting group description:

Participants received Diphtheria (D), tetanus (T), pertussis (acellular, component) (aP), hepatitis B (hep B [recombinant DNA]) and poliomyelitis (Inactivated [IPV]), and Haemophilus influenzae type b (Hib) conjugated vaccine adsorbed (DTaP-IPV-Hep B-PRP~T) plus a Placebo, oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.

Reporting group title	Tritanrix-Hep B/Hib™ + OPV Group

Reporting group description:

Participants received Tritanrix-Hep B/Hib™ + oral poliovirus vaccine (OPV) in a 3-dose series with single doses at 2, 4, and 6 months of age.

Serious adverse events	DTaP-IPV-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 1423 (6.39%)	46 / 710 (6.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	2 / 1423 (0.14%)	3 / 710 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hip Dysplasia			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio Respiratory Distress			

subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Encephalitis			
subjects affected / exposed	1 / 1423 (0.07%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 1423 (0.07%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Convulsion			
subjects affected / exposed	4 / 1423 (0.28%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonic Hyporesponsive Episode			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 1423 (0.14%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric Haemorrhage			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia, Obstructive			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Choledochal Cyst			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial Hyperactivity			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial Obstruction			
subjects affected / exposed	9 / 1423 (0.63%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Foreign Body Aspiration			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive Airways Disorder			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Purpura			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess Neck			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	12 / 1423 (0.84%)	6 / 710 (0.85%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	13 / 1423 (0.91%)	3 / 710 (0.42%)	
occurrences causally related to treatment / all	0 / 13	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	21 / 1423 (1.48%)	18 / 710 (2.54%)	
occurrences causally related to treatment / all	0 / 21	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis rotavirus			
subjects affected / exposed	1 / 1423 (0.07%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kawasaki's disease			
subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngotracheitis			
subjects affected / exposed	2 / 1423 (0.14%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital Cellulitis			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (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	2 / 1423 (0.14%)	0 / 710 (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	5 / 1423 (0.35%)	3 / 710 (0.42%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	6 / 1423 (0.42%)	2 / 710 (0.28%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			

subjects affected / exposed	0 / 1423 (0.00%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma Streptococcal			
subjects affected / exposed	1 / 1423 (0.07%)	0 / 710 (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	1 / 1423 (0.07%)	1 / 710 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
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-Hep B-PRP~T Group	Tritanrix-Hep B/Hib™ + OPV Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	945 / 1423 (66.41%)	576 / 710 (81.13%)	
Nervous system disorders			
Solicited Somnolence Post-dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[1]	635 / 1410 (45.04%)	375 / 703 (53.34%)	
occurrences (all)	635	375	
General disorders and administration site conditions			
Solicited Vomiting Post-dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[2]	230 / 1410 (16.31%)	120 / 703 (17.07%)	
occurrences (all)	230	120	
Injection Site Haemorrhage			

subjects affected / exposed[3]	39 / 1411 (2.76%)	63 / 703 (8.96%)	
occurrences (all)	39	63	
Solicited Injection Site Pain Post-dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[4]	831 / 1410 (58.94%)	574 / 703 (81.65%)	
occurrences (all)	831	574	
Solicited Injection Site Swelling Post-dose 3			
alternative assessment type: Systematic			
subjects affected / exposed	400 / 1423 (28.11%)	323 / 710 (45.49%)	
occurrences (all)	400	323	
Solicited Irritability post-dose 1			
subjects affected / exposed[5]	945 / 1410 (67.02%)	576 / 703 (81.93%)	
occurrences (all)	945	576	
Solicited Pyrexia Post-dose 2			
alternative assessment type: Systematic			
subjects affected / exposed[6]	675 / 1411 (47.84%)	457 / 703 (65.01%)	
occurrences (all)	675	457	
Solicited Injection Site Erythema Post-dose 3			
alternative assessment type: Systematic			
subjects affected / exposed[7]	587 / 1410 (41.63%)	340 / 703 (48.36%)	
occurrences (all)	587	340	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed[8]	131 / 1411 (9.28%)	70 / 703 (9.96%)	
occurrences (all)	131	70	
Diarrhoea			
subjects affected / exposed[9]	264 / 1411 (18.71%)	123 / 703 (17.50%)	
occurrences (all)	264	123	
Injection Site Nodule			
subjects affected / exposed[10]	81 / 1411 (5.74%)	79 / 703 (11.24%)	
occurrences (all)	81	79	
Respiratory, thoracic and mediastinal disorders			

Bronchospasm			
subjects affected / exposed[11]	163 / 1411 (11.55%)	74 / 703 (10.53%)	
occurrences (all)	163	74	
Rhinitis allergic			
subjects affected / exposed[12]	75 / 1411 (5.32%)	36 / 703 (5.12%)	
occurrences (all)	75	36	
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed[13]	160 / 1411 (11.34%)	54 / 703 (7.68%)	
occurrences (all)	160	54	
Psychiatric disorders			
Solicited Crying Post-dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[14]	800 / 1411 (56.70%)	564 / 703 (80.23%)	
occurrences (all)	800	564	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed[15]	101 / 1411 (7.16%)	40 / 703 (5.69%)	
occurrences (all)	101	40	
Nasopharyngitis			
subjects affected / exposed[16]	742 / 1411 (52.59%)	353 / 703 (50.21%)	
occurrences (all)	742	353	
Pharyngitis			
subjects affected / exposed[17]	395 / 1411 (27.99%)	161 / 703 (22.90%)	
occurrences (all)	395	161	
Rhinitis			
subjects affected / exposed[18]	136 / 1411 (9.64%)	56 / 703 (7.97%)	
occurrences (all)	136	56	
Metabolism and nutrition disorders			
Solicited Anorexia Post-dose 1			
alternative assessment type: Systematic			
subjects affected / exposed[19]	388 / 1410 (27.52%)	278 / 703 (39.54%)	
occurrences (all)	388	278	

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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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 reported for this adverse event reflects those for which data were available for the event
[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 reported for this adverse event reflects those for which data were available for the event.
[10] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[11] - 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 reported for this adverse event reflects those for which data were available for the event.
[12] - 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 reported for this adverse event reflects those for which data were available for the event.
[13] - 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 reported for this adverse event reflects those for which data were available for the event.
[14] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[15] - 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 reported for this solicited adverse event reflects those for which data were available for the event.

[16] - 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 reported for this adverse event reflects those for which data were available for the event.
[17] - 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 reported for this adverse event reflects those for which data were available for the event.
[18] - 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 reported for this adverse event reflects those for which data were available for the event.
[19] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) 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
22 November 2005	This amendment was implemented prior to the inclusion of the first subject. Changes revision of immunogenicity endpoints; study design from open label to blind observer with notes on procedures for blinding, randomization and vaccine allocation, and code breaking. An IDMC was also adopted to review safety data at predefined intervals.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not Applicable

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22531237