Clinical trial results:
A phase III, open-label, randomised, multicentre study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' combined DTPa-HBV-IPV/Hib vaccine (Infanrix™ hexa) administered to Indian infants according to a 6-10-14 weeks schedule and a 2-4-6 months schedule.

Summary

EudraCT number	2013-003427-10
Trial protocol	Outside EU/EEA
Global end of trial date	25 February 2013

Results information

Result version number	v2
This version publication date	02 June 2016
First version publication date	30 May 2015
Version creation reason	• New data added to full data set Data for primary and secondary endpoints have been added.

Trial information

Trial identification

Sponsor protocol code	111157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01353703
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.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?	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	16 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2013
Global end of trial reached?	Yes
Global end of trial date	25 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunological response to the study vaccine in terms of seroprotection status for diphtheria, tetanus, polio, hepatitis B and Hib antigens, and in terms of vaccine response for the pertussis, one month after the third dose of the primary vaccination.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2012
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	India: 224
Worldwide total number of subjects	224
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)	224
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Infanrix Hexa 6-10-14 Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of Infanrix hexa™ were administered by injection intramuscularly into the right side of the thigh, at 6, 10 and 14 weeks of age.

Arm title	Infanrix Hexa 2-4-6 Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of Infanrix hexa™ were administered by injection intramuscularly into the right side of the thigh, at 2, 4 and 6 months of age.

Number of subjects in period 1	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group
Started	112	112
Completed	111	112
Not completed	1	0
Migrated/moved from study area	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix Hexa 6-10-14 Group
Reporting group description: -	
Reporting group title	Infanrix Hexa 2-4-6 Group
Reporting group description: -	

Reporting group values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group	Total
Number of subjects	112	112	224
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)			0
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: weeks			
arithmetic mean	6.7	6.8	
standard deviation	± 1.04	± 1.13	-
Gender categorical			
Units: Subjects			
Female	52	52	104
Male	60	60	120

End points

End points reporting groups

Reporting group title	Infanrix Hexa 6-10-14 Group
Reporting group description: -	
Reporting group title	Infanrix Hexa 2-4-6 Group
Reporting group description: -	

Primary: Number of seroprotected subjects against anti-diphteria (anti-D) and anti-tetanus (anti-T) antigens

End point title	Number of seroprotected subjects against anti-diphteria (anti-D) and anti-tetanus (anti-T) antigens[1]

End point description:

A seroprotected subject is defined as a vaccinated subject with anti-D and anti-T antibody concentration greater than or equal to (≥) 0.1 international units per millilitre (IU/mL)

End point type	Primary

End point timeframe:

One month post Dose 3

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: Subjects				
Anti-D, [N=105;106]	105	106		
Anti-T, [N=105;106]	105	106		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-hepatitis B (anti-HBs) antigens

End point title	Number of seroprotected subjects against anti-hepatitis B (anti-HBs) antigens[2]

End point description:

A seroprotected subject is defined as a vaccinated subject with anti-HBS antibody concentration ≥ 10 miliinternational units per millilitre (mIU/mL)

End point type	Primary

End point timeframe:

One month post Dose 3

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	105		
Units: Subjects				
Anti-HBs, [N=101;105]	101	104		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-poliovirus (anti-Polio) types 1,2,3 antigens

End point title	Number of seroprotected subjects against anti-poliovirus (anti-Polio) types 1,2,3 antigens[3]

End point description:

Seroprotection is defined as anti-Poliovirus 1,2 and 3 antibody titres ≥ 8 effective dose, for 50% of people receiving the vaccine (ED50)

End point type	Primary

End point timeframe:

One month post Dose 3

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	99		
Units: Subjects				
Anti-Polio 1, [N=99;99]	99	99		
Anti-Polio 2, [N=77;88]	77	88		
Anti-Polio 3, [N=74;79]	73	79		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-polyribosyl-ribitol phosphate (anti-PRP) antigens

End point title	Number of seroprotected subjects against anti-polyribosyl-ribitol phosphate (anti-PRP) antigens[4]

End point description:

Seroprotection is defined as antibody concentration ≥ 0.15 micrograms per millilitre (µg/mL)

End point type	Primary

End point timeframe:

One month post Dose 3

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: Subjects				
Anti-PRP, [N=105;106]	104	105		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with vaccine response for pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN)

End point title	Number of subjects with vaccine response for pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN)[5]

End point description:

Vaccine response defined as :
For initially seronegative subjects, antibody concentration ≥ 5 ELU/mL at 1 month after third dose
For initially seropositive subjects: antibody concentration at 1 month after third dose ≥ 1 fold increase the pre-vaccination antibody concentration

End point type	Primary

End point timeframe:

One month post Dose 3

Notes:

[5] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: Subjects				
Anti-PT, S- [N=61;67]	61	67		
Anti-PT, S+ [N=44;37]	44	36		
Anti-FHA, S- [N=12;12]	12	12		
Anti-FHA, S+ [N=89;90]	86	88		
Anti-PRN, S- [N=86;89]	86	89		
Anti-PRN, S+ [N=19;15]	18	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post vaccination, after each dose

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	112		
Units: Subjects				
Any Pain, D1 [N=111,112]	23	11		
Any Redness, D1 [N=111,112]	3	1		
Any Swelling, D1 [N=111,112]	7	4		
Any Pain, D2 [N=111,112]	13	3		
Any Redness, D2 [N=111,112]	0	1		
Any Swelling, D2 [N=111,112]	2	2		
Any Pain, D3 [N=111,112]	10	6		
Any Redness, D3 [N=111,112]	3	0		
Any Swelling, D3 [N=111,112]	2	3		
Any Pain, Across [N=111,112]	28	15		
Any Redness, Across [N=111,112]	6	2		
Any Swelling, Across [N=111,112]	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post vaccination, after each dose

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	112		
Units: Subjects				
Any Drowsiness, D1 [N=111,112]	0	2		
Any Irritability/fussiness, D1 [N=111,112]	8	5		
Any Loss of appetite, D1 [N=111,112]	1	3		
Any Temperature/(Axillary), D1 [N=111,112]	10	7		
Any Drowsiness, D2 [N=111,112]	0	0		
Any Irritability/fussiness, D2 [N=111,112]	2	5		
Any Loss of appetite, D2 [N=111,112]	0	1		
Any Temperature/(Axillary), D2 [N=111,112]	5	7		
Any Drowsiness, D3 [N=111,112]	0	0		
Any Irritability/fussiness, D3 [N=111,112]	3	3		
Any Loss of appetite, D3 [N=111,112]	1	1		
Any Temperature/(Axillary), D3 [N=111,112]	3	6		
Any Drowsiness, Across [N=111,112]	0	2		
Any Irritability/fussiness, Across [N=111,112]	13	10		
Any Loss of appetite, Across [N=111,112]	2	5		
Any Temperature/(Axillary), Across [N=111,112]	17	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

During the 31-day (Days 0-30) post vaccination

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any AEs [N=112,112]	40	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

During the entire study period

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any SAEs [N=112,112]	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and Anti-T antibody concentrations

End point title	Anti-D and Anti-T antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, [N=105;106]	2.334 (2.049 to 2.659)	3.726 (3.26 to 4.258)		
Anti-T, [N=105;106]	3.307 (2.925 to 3.739)	4.904 (4.378 to 5.493)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	105		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, [N=101;105]	1695.7 (1395.2 to 2060.9)	3314.5 (2645.2 to 4153.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Polio types 1, 2, 3 antibody titers

End point title	Anti-Polio types 1, 2, 3 antibody titers

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	99		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-Polio1, [N=99;99]	884.3 (666.6 to 1173.1)	1799.2 (1429 to 2265.5)		
Anti-Polio2, [N= 77;88]	840.2 (616.9 to 1144.2)	2138.7 (1658.1 to 2758.7)		
Anti-Polio3, [N= 74;79]	923.7 (691.9 to 1233.2)	2245.5 (1866.1 to 2702.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, [N=105;106]	2.697 (2.176 to 3.343)	5.404 (4.168 to 7.006)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT, [N=105;106]	107.3 (96.6 to 119.1)	108.2 (97.4 to 120.2)		
Anti-FHA, [N=105;106]	293.7 (259.4 to 332.6)	369.3 (335.5 to 406.5)		
Anti-PRN, [N=105;106]	224.4 (194.2 to 259.3)	243.6 (213.2 to 278.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies with cut-off ≥ 5 EU/mL

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies with cut-off ≥ 5 EU/mL

End point description:

End point type	Secondary

End point timeframe:

One month post Dose 3

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	106		
Units: Subjects				
Anti-PT, [N=105;106]	105	106		
Anti-FHA, [N=105;106]	105	106		
Anti-PRN, [N=105;106]	105	106		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against anti-Polio 1, 2, 3 antibodies

End point title	Number of seroprotected subjects against anti-Polio 1, 2, 3 antibodies

End point description:

End point type	Secondary

End point timeframe:

Prior to Dose 1

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	102		
Units: Subjects				
Anti-Polio 1, [N=97;102]	71	70		
Anti-Polio 2, [N=56;55]	38	42		
Anti-Polio 3, [N=88;91]	23	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies with cut-off ≥ 5 EU/mL

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies with cut-off ≥ 5 EU/mL

End point description:

End point type	Secondary

End point timeframe:

Prior to Dose 1

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	104		
Units: Subjects				
Anti-PT, [N=105;104]	44	37		
Anti-FHA, [N=101;102]	89	90		
Anti-PRN, [N=105;104]	19	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against anti-HBs antigens

End point title	Number of seroprotected subjects against anti-HBs antigens

End point description:

End point type	Secondary

End point timeframe:

Prior to Dose 1

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	81		
Units: Subjects				
Anti-HBs, [N=80;81]	14	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Polio types 1, 2, 3 antibody titers

End point title	Anti-Polio types 1, 2, 3 antibody titers

End point description:

End point type	Secondary

End point timeframe:

Prior to Dose 1

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	102		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-Polio 1, [N=97;102]	53.5 (33.5 to 85.3)	31.9 (21.5 to 47.2)		
Anti-Polio 2, [N=56;55]	32.5 (19.2 to 55)	36.2 (22.2 to 59)		
Anti-Polio 3, [N=88;91]	8 (5.9 to 10.8)	11.9 (8.3 to 17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

Prior to Dose 1

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	104		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT, [N=105;104]	5 (4.2 to 6)	4.6 (3.8 to 5.6)		
Anti-FHA, [N=101;102]	18.7 (15 to 23.3)	20.1 (16.1 to 25.2)		
Anti-PRN, [N=105;104]	3.4 (2.9 to 3.9)	3.2 (2.8 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

End point type	Secondary
End point timeframe:	
Prior to Dose 1	

End point values	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	81		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, [N=80;81]	5.9 (4.2 to 8.3)	5.6 (4.1 to 7.7)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period, Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire study period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Infanrix Hexa 6-10-14 Group
Reporting group description: -	
Reporting group title	Infanrix Hexa 2-4-6 Group

Reporting group description: -

Serious adverse events	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 112 (1.79%)	3 / 112 (2.68%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 112 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 112 (0.89%)	1 / 112 (0.89%)	
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	Infanrix Hexa 6-10-14 Group	Infanrix Hexa 2-4-6 Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 112 (35.71%)	25 / 112 (22.32%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	28 / 111 (25.23%)	15 / 112 (13.39%)	
occurrences (all)	28	15	
Redness			
subjects affected / exposed[2]	6 / 111 (5.41%)	2 / 112 (1.79%)	
occurrences (all)	6	2	
Swelling			
subjects affected / exposed[3]	8 / 111 (7.21%)	9 / 112 (8.04%)	
occurrences (all)	8	9	
Drowsiness			
subjects affected / exposed[4]	0 / 111 (0.00%)	2 / 112 (1.79%)	
occurrences (all)	0	2	
Irritability/fussiness			
subjects affected / exposed[5]	13 / 111 (11.71%)	10 / 112 (8.93%)	
occurrences (all)	13	10	
Loss of appetite			
subjects affected / exposed[6]	2 / 111 (1.80%)	5 / 112 (4.46%)	
occurrences (all)	2	5	
Temperature/Axillary			
subjects affected / exposed[7]	17 / 111 (15.32%)	17 / 112 (15.18%)	
occurrences (all)	17	17	
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 112 (16.07%)	11 / 112 (9.82%)	
occurrences (all)	18	11	
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 112 (3.57%)	6 / 112 (5.36%)	
occurrences (all)	4	6	

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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

[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: Assessment for this event was performed solely on subjects with available results.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2012	As per the request of the regulatory authorities in India, sub-group analyses will be performed based on the hepatitis B status of the mother and number of OPV doses given to the subject since birth. Also, an analysis based on the prevaccination status of anti-HBs antibodies will be performed. As these exploratory analyses are not powered to draw conclusions, the analyses will be performed for information only. • The secondary objectives and endpoints have been updated to include analysis of anti-HBs antibody concentrations before the first dose of primary vaccination. • The outline of study procedures table has been updated to include the information about the hepatitis B status of the mother based on medical history. • The names of the contributing authors have been updated in the title page. The name of the sponsor signatory has also been updated in the protocol amendment 1 sponsor signatory approval page.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported