Clinical trial results:
An open, multicentre, post-marketing surveillance (PMS) study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals' DTPa-IPV/Hib vaccine administered at 3 and 4 months of age and DTPa-HBV-IPV/Hib vaccine (INFANRIX HEXA) administered at 5 months of age, as primary vaccination course, followed by administration of GSK Biologicals' DTPa-IPV/Hib vaccine at 18 months of age in healthy infants who received hepatitis B vaccine at birth and at one month of age.

Summary

EudraCT number	2012-002439-26
Trial protocol	Outside EU/EEA
Global end of trial date	01 February 2007

Results information

Result version number	v2 (current)
This version publication date	18 May 2018
First version publication date	31 May 2015
Version creation reason	• Correction of full data set Minor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	217744/100

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00325143
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, 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	10 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2007
Global end of trial reached?	Yes
Global end of trial date	01 February 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of the DTPa-HBV-IPV/Hib vaccine and the DTPa-IPV/Hib vaccine.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2003
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Singapore: 702
Worldwide total number of subjects	702
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)	702
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	Not applicable
Blinding used	Not blinded

Arms

Arm title	Infanrix hexa Group

Arm description:

Healthy male or female subjects between and including 11 to 17 weeks of age, who were previously vaccinated with Rotarix in study 444563/028, additionally received 2 doses of Infanrix-IPV/Hib vaccine (at 3 and 4 months of age), 2 doses of Rotarix vaccine (at 2 and 4 months of age) and one dose of Infanrix Hexa vaccine (at 5 months of age) as a primary vaccination course, followed by administration of a booster dose of Infanrix-IPV/Hib vaccine (at 18 months of age). The Infanrix-IPV/Hib and Infanrix Hexa vaccines were administered intramuscularly into the right antero-lateral thigh, while the Rotarix vaccine was given orally.

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:

Single dose intramuscular injection in the right anterolateral thigh at 5 months of age.

Investigational medicinal product name	Infanrix IPV/Hib
Investigational medicinal product code	
Other name	DTPa-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection in the right anterolateral thigh at 3, 4 and 18 months of age.

Number of subjects in period 1	Infanrix hexa Group
Started	702
Completed	676
Not completed	26
Consent withdrawn by subject	8
Lost to follow-up (incomplete vaccination course)	4

Lost to follow-up (complete vaccination course)	13
Migrated/moved from study area	1

Baseline characteristics

Reporting groups

Reporting group title	Infanrix hexa Group

Reporting group description:

Healthy male or female subjects between and including 11 to 17 weeks of age, who were previously vaccinated with Rotarix in study 444563/028, additionally received 2 doses of Infanrix-IPV/Hib vaccine (at 3 and 4 months of age), 2 doses of Rotarix vaccine (at 2 and 4 months of age) and one dose of Infanrix Hexa vaccine (at 5 months of age) as a primary vaccination course, followed by administration of a booster dose of Infanrix-IPV/Hib vaccine (at 18 months of age). The Infanrix-IPV/Hib and Infanrix Hexa vaccines were administered intramuscularly into the right antero-lateral thigh, while the Rotarix vaccine was given orally.

Reporting group values	Infanrix hexa Group	Total	
Number of subjects	702	702	
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	13.5		
standard deviation	± 0.99	-	
Gender categorical Units: Subjects			
Female	349	349	
Male	353	353	
Race/Ethnicity Units: Subjects			
White/Caucasian	1	1	
Japanese	1	1	
Not specified	27	27	
Chinese	366	366	
Malay	269	269	
Indian	38	38	

End points

End points reporting groups

Reporting group title	Infanrix hexa Group

Reporting group description:

Healthy male or female subjects between and including 11 to 17 weeks of age, who were previously vaccinated with Rotarix in study 444563/028, additionally received 2 doses of Infanrix-IPV/Hib vaccine (at 3 and 4 months of age), 2 doses of Rotarix vaccine (at 2 and 4 months of age) and one dose of Infanrix Hexa vaccine (at 5 months of age) as a primary vaccination course, followed by administration of a booster dose of Infanrix-IPV/Hib vaccine (at 18 months of age). The Infanrix-IPV/Hib and Infanrix Hexa vaccines were administered intramuscularly into the right antero-lateral thigh, while the Rotarix vaccine was given orally.

Primary: Number of subjects reporting any solicited local symptoms

End point title	Number of subjects reporting any solicited local symptoms[1]

End point description:

Assessed solicited local and general symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.

End point type	Primary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Infanrix hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	697			
Units: Subjects				
Any Pain, Dose 1 [N=697]	130			
Any Redness, Dose 1 [N=697]	120			
Any Swelling, Dose 1 [N=697]	89			
Any Pain, Dose 2 [N=695]	134			
Any Redness, Dose 2 [N=695]	137			
Any Swelling, Dose 2 [N=695]	100			
Any Pain, Dose 3 [N=661]	97			
Any Redness, Dose 3 [N=661]	126			
Any Swelling, Dose 3 [N=661]	100			
Any Pain, Booster dose [N=565]	166			
Any Redness, Booster dose [N=565]	148			
Any Swelling, Booster dose [N=565]	115			
Any Pain, Across doses [N=697]	301			
Any Redness, Across doses [N=697]	273			
Any Swelling, Across doses [N=697]	215			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting any solicited general symptoms

End point title	Number of subjects reporting any solicited general symptoms[2]

End point description:

Assessed solicited general symptoms were drowsiness, fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)], irritability and loss of appetite. Any = occurrence of the symptom regardless of intensity grade.

End point type	Primary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Infanrix hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	697			
Units: Subjects				
Any Drowsiness, Dose 1 [N=697]	165			
Any Temperature (Axillary) (°C), Dose 1 [N=697]	139			
Any Irritability, Dose 1 [N=697]	229			
Any Loss of appetite, Dose 1 [N=697]	173			
Any Drowsiness, Dose 2 [N=695]	140			
Any Temperature (Axillary) (°C), Dose 2 [N=695]	124			
Any Irritability, Dose 2 [N=695]	192			
Any Loss of appetite, Dose 2 [N=695]	155			
Any Drowsiness, Dose 3 [N=661]	106			
Any Temperature (Axillary) (°C), Dose 3 [N=661]	100			
Any Irritability, Dose 3 [N=661]	161			
Any Loss of appetite, Dose 3 [N=661]	106			
Any Drowsiness, Booster [N=565]	89			
Any Temperature (Axillary) (°C), Booster [N=565]	152			
Any Irritability, Booster [N=565]	163			
Any Loss of appetite, Booster [N=565]	118			
Any Drowsiness, Across doses [N=697]	290			
Any Temperature (Axillary) (°C),Across doses [697]	330			
Any Irritability, Across doses [N=697]	381			
Any Loss of appetite, Across doses [N=697]	324			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs)

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

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 31-day (Day 0-30) period after vaccination.

End point values	Infanrix hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	702			
Units: Subjects				
Any AE(s)	321			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any large swelling reactions

End point title	Number of subjects reporting any large swelling reactions

End point description:

A large swelling reaction was defined as swelling with a diameter greater than (>) 50 millimeters (mm), noticeable diffuse swelling or noticeable increase of limb circumference.

End point type	Secondary

End point timeframe:

At Month 15, post-booster dose

End point values	Infanrix hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	702			
Units: Subjects				
Any large swelling reactions	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

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

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

During the entire study period (from Month 0 up to Month 21)

End point values	Infanrix hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	702			
Units: Subjects				
Any SAE(s)	108			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local/general symptoms: during the 4-day (Days 0-3) post-vaccination period; Unsolicited AE(s): during the 30-day (Days 0-29) post-vaccination period; SAE(s): during the entire study period (Month 0 to Month 21).

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Infanrix hexa Group

Reporting group description:

Healthy male or female subjects between and including 11 to 17 weeks of age, who were previously vaccinated with Rotarix in study 444563/028, additionally received 2 doses of Infanrix-IPV/Hib vaccine (at 3 and 4 months of age), 2 doses of Rotarix vaccine (at 2 and 4 months of age) and one dose of Infanrix Hexa vaccine (at 5 months of age) as a primary vaccination course, followed by administration of a booster dose of Infanrix-IPV/Hib vaccine (at 18 months of age). The Infanrix-IPV/Hib and Infanrix Hexa vaccines were administered intramuscularly into the right antero-lateral thigh, while the Rotarix vaccine was given orally.

Serious adverse events	Infanrix hexa Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 702 (15.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Head injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 702 (0.71%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Foreign body trauma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 702 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			

alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Febrile convulsion				
alternative assessment type: Non-systematic				
subjects affected / exposed	13 / 702 (1.85%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
Convulsion				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia, obstructive				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
alternative assessment type: Non-systematic				
subjects affected / exposed	5 / 702 (0.71%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Asthmatic crisis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis atopic				

alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urticaria papular				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Stag horn calculus				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchiolitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	30 / 702 (4.27%)			
occurrences causally related to treatment / all	0 / 30			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	11 / 702 (1.57%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	11 / 702 (1.57%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Gastritis viral				
alternative assessment type: Non-systematic				

subjects affected / exposed	7 / 702 (1.00%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	5 / 702 (0.71%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	4 / 702 (0.57%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
alternative assessment type: Non-systematic				
subjects affected / exposed	4 / 702 (0.57%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	4 / 702 (0.57%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	3 / 702 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hand-foot-and-mouth disease				
alternative assessment type: Non-systematic				

subjects affected / exposed	3 / 702 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
alternative assessment type: Non-systematic				
subjects affected / exposed	3 / 702 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Abscess				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Kawasaki’s disease				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Pharyngitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Viral infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 702 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Exanthema subitum				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpangina				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral pharyngitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral skin infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 702 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 702 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Infanrix hexa Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	594 / 702 (84.62%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	301 / 697 (43.19%)		
occurrences (all)	301		
Redness			
subjects affected / exposed[2]	273 / 697 (39.17%)		
occurrences (all)	273		
Swelling			
subjects affected / exposed[3]	215 / 697 (30.85%)		
occurrences (all)	215		
Drowsiness			
subjects affected / exposed[4]	290 / 697 (41.61%)		
occurrences (all)	290		
Fever (Axillary) (°C)			
subjects affected / exposed[5]	330 / 697 (47.35%)		
occurrences (all)	330		
Irritability			
subjects affected / exposed[6]	381 / 697 (54.66%)		
occurrences (all)	381		
Loss of appetite			
subjects affected / exposed[7]	324 / 697 (46.48%)		
occurrences (all)	324		
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	46 / 702 (6.55%)		
occurrences (all)	46		

Gastrointestinal disorders Diarrhoea alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 40 / 702 (5.70%) 40		
Skin and subcutaneous tissue disorders Rash alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 40 / 702 (5.70%) 40		
Infections and infestations Upper respiratory tract infection alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 125 / 702 (17.81%) 125		

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: Solicited local symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited local symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited local symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited general symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited general symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited general symptoms were only tabulated for subjects with a symptom sheet completed.

[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: Solicited general symptoms were only tabulated for subjects with a symptom sheet completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 September 2003	Protocol Amenment 1 The following changes were done following input given by the ethics review committee and the study team. • The title was changed to include the study of the safety and reactogenicity of DTPa-IPV/Hib vaccine to keep it in line with the protocol objectives. • The study was changed from a multi-centre study to a single centre study. Hence only one principal investigator was retained at one study centre. • The target enrolment was changed to 500 subjects to be recruited at a single centre. • Treatment allocation was modified to reflect that subjects would retain the subject numbers allocated to them in the Rota-028 study. • Addition of an inclusion criteria that states that only subjects enrolled in the Rota-028 study will be included in this study. • Additional statement to reflect that the causality of SAEs which is not known to occur in routine vaccinations with the DTPa-IPV/Hib vaccines should be assigned to the investigational rotavirus vaccine to ensure that the safety data of the rotavirus vaccine is adequately captured. · Change of the estimated sample size section to reflect the change in the target enrolment of subjects. • Additional statement to reflect that Safety data (SAEs) from the DTPa-HBV-IPV-100 study and the Rota-028 study will be reconciled into two databases. • Additional statement to reflect that the safety data will be collected and analysed regardless of administration of the rotavirus vaccine to ensure that the blinding of the Rota-028 study will not be compromised. • Modification of the text in the analysis of safety section to make the description more clear. • Specification of the two different Hib vaccines required for reconstitution with the DTPa-HBV-IPV and the DTPa-IPV vaccines. · Change in the number of doses of the vaccines to be supplied by GSK Biologicals to reflect the change in the sample size.
08 July 2004	Protocol Amendment 2 The study was changed from a single center study to a multicenter study. - Faith Fung was replaced by Amy Tay as a study monitor in the study. - The target enrolment was changed to 700 subjects to be recruited at three study centers. - The interval between study visits was made indicative and subjects outside this interval would not be excluded from analysis. - The interval between Visit 4 and Visit 5 was defined. - Diary cards distributed at Visit 4 were to be returned by mail. - The number of doses of the vaccines to be supplied by GSK Biologicals was changed to reflect the change in the sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported