Clinical trial results:
A phase II, observer-blind, randomized study to evaluate the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' combined DSSITGDPa-HBV-IPV/Hib vaccine containing diphtheria toxoid from the Statens Serum Institute (SSI) of Denmark and tetanus toxoid from GSK Biologicals' Kft [GD], compared to the currently licensed GSK Biologicals' DTPa-HBV-IPV/Hib vaccine (Infanrix hexa) when administered to healthy infants at 2, 3 and 4 months of age.

Summary

EudraCT number	2006-000554-46
Trial protocol	FI
Global end of trial date	31 May 2007

Results information

Result version number	v1
This version publication date	02 May 2016
First version publication date	03 June 2015

Trial information

Trial identification

Sponsor protocol code	106786

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00376779
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 Advisor Call Center, GlaxoSmithKline Biologicals, 004 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Advisor Call Center, GlaxoSmithKline Biologicals, 004 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	07 August 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2007
Global end of trial reached?	Yes
Global end of trial date	31 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of the DSSITGDPa-HBV-IPV/Hib vaccine (preservative-free formulation) in terms of antibody response to all vaccine antigens is non-inferior to that of the DTPa-HBV-IPV/Hib vaccine, one month after a three-dose primary vaccination course.

Protection of trial subjects:

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	12 October 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 455
Worldwide total number of subjects	455
EEA total number of subjects	455

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)	455
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 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Preservative-Free Fromulation Group

Arm description:

Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib.

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

Dosage and administration details:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

Arm title	Preservative-Containing Formulation Group

Arm description:

Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib.

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

Dosage and administration details:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

Arm title	Infanrix-hexa Group

Arm description:

Subjects received the licensed formulation of DTPa-HBV-IPV/Hib.

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:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

Number of subjects in period 1	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group
Started	153	150	152
Completed	151	148	152
Not completed	2	2	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	1	-
Migrated/moved from study area	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Preservative-Free Fromulation Group
Reporting group description:	
Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib.	
Reporting group title	Preservative-Containing Formulation Group
Reporting group description:	
Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib.	
Reporting group title	Infanrix-hexa Group
Reporting group description:	
Subjects received the licensed formulation of DTPa-HBV-IPV/Hib.	

Reporting group values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group
Number of subjects	153	150	152
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: weeks			
arithmetic mean	9.9	10	10.1
standard deviation	± 1.51	± 1.45	± 1.35
Gender categorical Units: Subjects			
Female	68	75	64
Male	85	75	88

Reporting group values	Total		
Number of subjects	455		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	207		
Male	248		

End points

End points reporting groups

Reporting group title	Preservative-Free Fromulation Group
Reporting group description:	
Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib.	
Reporting group title	Preservative-Containing Formulation Group
Reporting group description:	
Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib.	
Reporting group title	Infanrix-hexa Group
Reporting group description:	
Subjects received the licensed formulation of DTPa-HBV-IPV/Hib.	

Primary: Number of subjects with anti-diphtheria (Anti-D) [by Vero-cell neutralization assay] antibody concentrations equal to or above (≥) 0.016 international units per milliliter (IU/mL)

End point title	Number of subjects with anti-diphtheria (Anti-D) [by Vero-cell neutralization assay] antibody concentrations equal to or above (≥) 0.016 international units per milliliter (IU/mL)[1]
End point description:	
End point type	Primary
End point timeframe:	
One month after the third dose of vaccine (POST)	

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	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	145	
Units: Subjects				
Anti-diphtheria, POST	135	133	145	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-tetanus toxoids (Anti-TT) antibody concentrations ≥ 0.1 IU/mL

End point title	Number of subjects with anti-tetanus toxoids (Anti-TT) antibody concentrations ≥ 0.1 IU/mL[2]
End point description:	

End point type	Primary

End point timeframe:

One month after the third dose of vaccine (POST)

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	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	146	
Units: Subjects				
Anti-tetanus, POST	138	134	146	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations ≥ 10.0 mili-international units per illilitre (mIU/mL)

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations ≥ 10.0 mili-international units per illilitre (mIU/mL)[3]

End point description:

End point type	Primary

End point timeframe:

One month after the third dose of vaccine (POST)

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

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135	131	143	
Units: Subjects				
Anti-HBs, POST	125	125	141	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polio type 1, 2 and 3 antibody titers ≥ 8

End point title	Number of subjects with anti-polio type 1, 2 and 3 antibody titers ≥ 8[4]

End point description:

End point type	Primary

End point timeframe:

One month after the third dose of vaccine (POST)

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

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131	123	130	
Units: Subjects				
Anti-Polio 1, POST [N=128;123;121]	119	114	117	
Anti-Polio 2, POST [N=121;119;130]	90	95	99	
Anti-Polio 3, POST [N=131;122;128]	126	116	125	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL

End point title	Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL[5]

End point description:

End point type	Primary

End point timeframe:

One month after the third dose of vaccine (POST)

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

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	145	
Units: Subjects				
Anti-PRP, POST	132	129	138	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations[6]

End point description:

End point type	Primary

End point timeframe:

One month after the third dose of vaccine (POST)

Notes:

[6] - 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	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	146	
Units: EL.U/ml				
geometric mean (confidence interval 95%)				
Anti-PT, POST [N=138;134;146]	59.2 (54.2 to 64.5)	49.6 (44.9 to 54.8)	67.4 (61.9 to 73.3)	
Anti-FHA, POST [N=138;134;146]	135 (120.7 to 151.1)	137.5 (122.8 to 154)	200.3 (181.1 to 221.5)	
Anti-PRN, POST [N=138;134;146]	68.6 (59.8 to 78.6)	75.3 (64.6 to 87.7)	119.9 (105.5 to 136.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations[7]

End point description:

End point type	Primary

End point timeframe:

Before the first dose of the vaccine (PRE)

Notes:

[7] - 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	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	139	145	
Units: EL.U/ml				
geometric mean (confidence interval 95%)				
Anti-PT, PRE [N=140;139;145]	3.4 (3 to 3.8)	3.7 (3.3 to 4.2)	3.4 (3.1 to 3.8)	
Anti-FHA, PRE [N=138;139;143]	11.2 (9.3 to 13.4)	8.8 (7.3 to 10.6)	10 (8.5 to 11.8)	
Anti-PRN, PRE [N=140;139;145]	5.8 (4.9 to 7)	5.8 (4.9 to 7)	4.9 (4.2 to 5.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point description:

Vaccine response defined as appearance of antibodies in subjects who were initially seronegative (i.e. with concentrations < cut-off value) or at least maintenance of pre-vaccination antibody concentrations in subjects who were initially seropositive (i.e. with concentrations ≥ cut-off value), taking into consideration the decreasing maternal antibodies.

End point type	Secondary

End point timeframe:

One month after the third dose of vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	131	142	
Units: Subjects				
Anti-PT, POST [N=134;131;142]	132	127	141	
Anti-FHA, POST [N=133;131;140]	126	124	139	
Anti-PRN, POST [N=134;131;142]	120	121	137	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (Anti-DT) antibody concentrations ≥ 0.1 IU/mL

End point title	Number of subjects with anti-diphtheria (Anti-DT) antibody concentrations ≥ 0.1 IU/mL

End point description:

End point type	Secondary

End point timeframe:

One month after the third dose of vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	146	
Units: Subjects				
Anti-diphtheria, POST	136	134	146	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point title	Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

Before the first dose (PRE) and one month after the third dose of the vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	139	146	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria, PRE [N=140;139;145]	0.174 (0.144 to 0.21)	0.227 (0.184 to 0.282)	0.183 (0.148 to 0.226)	
Anti-diphtheria, POST [N=138;134;146]	0.51 (0.441 to 0.59)	0.513 (0.445 to 0.592)	0.75 (0.658 to 0.854)	
Anti-tetanus, PRE [N=140;139;145]	0.654 (0.562 to 0.76)	0.71 (0.606 to 0.833)	0.708 (0.627 to 0.8)	
Anti-tetanus, POST [N=138;134;146]	1.423 (1.28 to 1.582)	1.438 (1.296 to 1.596)	1.758 (1.591 to 1.941)	

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 after the third dose of vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135	131	143	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, POST	166.1 (131.6 to 209.5)	173.4 (140.3 to 214.3)	299 (254.1 to 351.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 antibody titers

End point title	Anti-polio type 1, 2 and 3 antibody titers

End point description:

End point type	Secondary

End point timeframe:

One month after the third dose of vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131	123	130	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, POST [N=128;123;121]	36.8 (29.8 to 45.4)	41.8 (33.5 to 52.1)	74.6 (57.5 to 96.7)	
Anti-Polio 2, POST [N=121;119;130]	21.5 (16.4 to 28.1)	16.9 (13.5 to 21.1)	22.4 (17.6 to 28.5)	
Anti-Polio 3, POST [N=131;122;128]	51.4 (41.4 to 63.9)	67 (52.1 to 86.1)	113.9 (85.6 to 151.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP concentrations

End point title	Anti-PRP concentrations

End point description:

End point type	Secondary

End point timeframe:

One month after the third dose of vaccine (POST)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	134	145	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, POST [N=138;134;145]	1.174 (0.961 to 1.435)	1.098 (0.894 to 1.349)	1.661 (1.326 to 2.081)	

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:

Within 8 days (Day 0-Day 7) after each vaccine dose

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	150	152	
Units: Subjects				
Any Pain Dose 1 [N=153;150;152]	55	38	48	
Any Redness Dose 1 [N=153;150;152]	41	33	37	
Any Swelling Dose 1 [N=153;150;152]	36	28	32	
Any Pain Dose 2 [N=152;149;152]	34	27	35	
Any Redness Dose 2 [N=152;149;152]	46	66	73	
Any Swelling Dose 2 [N=152;149;152]	33	36	46	
Any Pain Dose 3 [N=151;148;152]	17	16	24	
Any Redness Dose 3 [N=151;148;152]	49	53	67	
Any Swelling Dose 3 [N=151;148;152]	32	31	44	
Any Pain Across doses [N=153;150;152]	73	52	65	
Any Redness Across doses [N=153;150;152]	81	89	97	
Any Swelling Across doses [N=153;150;152]	62	65	75	

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:

Within 8 days (Day 0-Day 7) after each vaccine dose

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	150	152	
Units: Subjects				
Any Drowsiness Dose 1 [N=153;150;152]	88	82	85	
Any Fever Dose 1 [N=153;150;152]	29	30	24	
Any Irritability Dose 1 [N=153;150;152]	114	102	112	
Any Loss of appetite Dose 1 [N=153;150;152]	45	32	32	
Any Drowsiness Dose 2 [N=152;149;152]	55	55	63	
Any Fever Dose 2 [N=152;149;152]	29	17	34	
Any Irritability Dose 2 [N=152;149;152]	87	85	99	
Any Loss of appetite Dose 2 [N=152;149;152]	28	32	19	
Any Drowsiness Dose 3 [N=151;148;152]	47	44	47	
Any Fever Dose 3 [N=151;148;152]	24	17	36	
Any Irritability Dose 3 [N=151;148;152]	74	68	82	
Any Loss of appetite Dose 3 [N=151;148;152]	28	25	20	
Any Drowsiness Across doses [N=153;150;152]	111	105	103	
Any Fever Across doses [N=153;150;152]	58	51	67	
Any Irritability Across doses [N=153;150;152]	140	128	135	
Any Loss of appetite Across doses [N=153;150;152]	66	58	51	

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:
Within 31 days (Day 0-Day 30)

End point values	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	150	152	
Units: Subjects				
AEs	111	110	117	

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	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	150	152	
Units: Subjects				
SAEs	2	5	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Preservative-Free Fromulation Group
Reporting group description: -	
Reporting group title	Preservative-Containing Formulation Group
Reporting group description: -	
Reporting group title	Infanrix-hexa Group
Reporting group description: -	

Serious adverse events	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 153 (1.31%)	5 / 150 (3.33%)	5 / 152 (3.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 153 (0.00%)	0 / 150 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Listless			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Laryngitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 150 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 153 (0.00%)	0 / 150 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 150 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 150 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 150 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 153 (0.00%)	1 / 150 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Preservative-Free Fromulation Group	Preservative-Containing Formulation Group	Infanrix-hexa Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 153 (72.55%)	110 / 150 (73.33%)	117 / 152 (76.97%)
General disorders and administration site conditions			
Injection site induration			
subjects affected / exposed	10 / 153 (6.54%)	18 / 150 (12.00%)	19 / 152 (12.50%)
occurrences (all)	10	18	19
Pyrexia			
subjects affected / exposed	15 / 153 (9.80%)	18 / 150 (12.00%)	11 / 152 (7.24%)
occurrences (all)	15	18	11
Eye disorders			
Conjunctivitis			
subjects affected / exposed	15 / 153 (9.80%)	16 / 150 (10.67%)	9 / 152 (5.92%)
occurrences (all)	15	16	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 153 (7.84%)	6 / 150 (4.00%)	21 / 152 (13.82%)
occurrences (all)	12	6	21
Constipation			

subjects affected / exposed	5 / 153 (3.27%)	11 / 150 (7.33%)	4 / 152 (2.63%)
occurrences (all)	5	11	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 153 (5.23%)	13 / 150 (8.67%)	9 / 152 (5.92%)
occurrences (all)	8	13	9
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 153 (3.27%)	9 / 150 (6.00%)	10 / 152 (6.58%)
occurrences (all)	5	9	10
Infections and infestations			
Rhinitis			
subjects affected / exposed	28 / 153 (18.30%)	23 / 150 (15.33%)	22 / 152 (14.47%)
occurrences (all)	28	23	22
Upper respiratory tract infection			
subjects affected / exposed	35 / 153 (22.88%)	16 / 150 (10.67%)	22 / 152 (14.47%)
occurrences (all)	35	16	22
Otitis media			
subjects affected / exposed	6 / 153 (3.92%)	12 / 150 (8.00%)	13 / 152 (8.55%)
occurrences (all)	6	12	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2006	Amendment 2 GSK Biologicals is currently validating new providers of the diphtheria toxoid (Statens Serum Institute [SSI], Denmark) and of the tetanus toxoid (GSK Biologicals Korlatolt Felelossegu Tarsasag [Kft] in Gödöllö [GD], Hungary) for inclusion in DTPa based vaccines. The purpose of this study is to demonstrate that the immunogenicity of the hexavalent DSSITGDPa-HBV-IPV/Hib vaccine containing diphtheria toxoid provided by the Statens Serum Institute of Denmark (DSSI) and tetanus toxoid provided by GSK Biologicals Kft in Gödöllö (TGD) is non-inferior to the immunogenicity of the currently licensed formulation of the vaccine. The vaccine will be administered as a primary vaccination course to healthy infants at 2, 3 and 4 months of age and its safety and reactogenicity will also be assessed. Two formulations of the DSSITGDPa-HBV-IPV/Hib vaccine will be evaluated: one in which the vaccine will be manufactured according to the new preservative-free process and the other in which the vaccine will be manufactured with preservative as the currently licensed formulation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported