Clinical trial results:
An open, phase IIIb, randomized, multicentric clinical trial to compare the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' DTPa-IPV vaccine versus co-administration of GSK Biologicals' DTPa vaccine and Sanofi-Pasteurs' IPV vaccine at different injection sites, to healthy children at 2, 4 and 6 months of age.

Summary

EudraCT number	2015-001508-71
Trial protocol	Outside EU/EEA
Global end of trial date	23 January 2007

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	10 July 2015

Trial information

Trial identification

Sponsor protocol code	104871

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00290342
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, 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?	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	16 November 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 January 2007
Global end of trial reached?	Yes
Global end of trial date	23 January 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the DTPa-IPV vaccine to DTPa and IPV vaccines administered separately, in terms of antibody response against all vaccine antigens, one month after the three-dose primary vaccination course.

Protection of trial subjects:

The vaccines were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 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	Korea, Republic of: 458
Worldwide total number of subjects	458
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)	458
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:

Of the 458 subjects enrolled in the study, 6 subjects (5 from Infanrix-IPV Group and 1 from Infanrix + IMOVAX Polio Group) were not administered the study vaccine due to consent withdrawal from parents/guardians and received an elimination code.

Pre-assignment period milestones

Number of subjects started	458
Number of subjects completed	452

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 6

Period 1

Period 1 title	Overall period (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-IPV Group

Arm description: -

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

Dosage and administration details:

Subjects received 3 doses of Infanrix™-IPV at 2, 4 and 6 months of age as an intramuscular injection into the anterolateral thigh.

Arm title	Infanrix + IMOVAX Polio Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Infanrix™ co-administered with IMOVAX Polio® at 2, 4 and 6 months of age as an intramuscular injection into the anterolateral sides of opposite thighs.

Investigational medicinal product name	IMOVAX Polio®
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Infanrix™ co-administered with IMOVAX Polio® at 2, 4 and 6 months of age as an intramuscular injection into the anterolateral sides of opposite thighs.

Number of subjects in period 1[1]	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group
Started	224	228
Completed	217	223
Not completed	7	5
Consent withdrawn by subject	6	4
Unspecified	-	1
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 458 subjects enrolled in the study, 6 subjects (5 from Infanrix-IPV Group and 1 from Infanrix + IMOVAX Polio Group) were not administered the study vaccine due to consent withdrawal from parents/guardians and received an elimination code.

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix-IPV Group
Reporting group description: -	
Reporting group title	Infanrix + IMOVAX Polio Group
Reporting group description: -	

Reporting group values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group	Total
Number of subjects	224	228	452
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	8.8	8.8	
standard deviation	± 0.9	± 0.91	-
Gender categorical Units: Subjects			
Female	112	110	222
Male	112	118	230

End points

End points reporting groups

Reporting group title	Infanrix-IPV Group
Reporting group description: -	
Reporting group title	Infanrix + IMOVAX Polio Group
Reporting group description: -	

Primary: Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies above the cut-off.

End point title	Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies above the cut-off.
End point description:	
End point type	Primary
End point timeframe:	
One month after the three-dose primary vaccination course.	

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	211		
Units: Subjects				
Anti-D ≥ 0.1 IU/mL (N=204; 211)	204	211		
Anti-T≥ 0.1 IU/mL (N=204; 211)	204	211		

Statistical analyses

Statistical analysis title	Non-inferiority in terms of vaccine response to D
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	1.79

Notes:

[1] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to diphtheria, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.

Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Statistical analysis title	Non-inferiority in terms of vaccine response to T
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	1.79

Notes:

[2] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to tetanus, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Primary: Number of subjects with anti-poliovirus (anti-polio) types 1, 2 and 3 above the cut-off.

End point title	Number of subjects with anti-poliovirus (anti-polio) types 1, 2 and 3 above the cut-off.

End point description:

End point type	Primary

End point timeframe:

One month after the three-dose primary vaccination course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	207		
Units: Subjects				
Anti-polio 1 ≥ 8 (N=204; 207)	204	207		
Anti-polio 2 ≥ 8 (N=204; 205)	204	204		
Anti-polio 3 ≥ 8 (N=204; 207)	203	206		

Statistical analyses

Statistical analysis title	Immune response non-inferiority - Anti-Polio 1
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group

Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	1.82

Notes:

[3] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to poliovirus type 1, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Statistical analysis title	Immune response non-inferiority - Anti-Polio 2
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in seroprotection rate
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	2.71

Notes:

[4] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to poliovirus type 2, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Statistical analysis title	Immune response non-inferiority - Anti-Polio 3
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroprotection rate
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.28
upper limit	2.24

Notes:

[5] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to poliovirus type 3, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Primary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-pertactin

(anti-PRN) and anti-filamentous haemagglutinin (anti-FHA) antibodies above the cut-off.

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous haemagglutinin (anti-FHA) antibodies above the cut-off.

End point description:

End point type	Primary

End point timeframe:

One month after the three-dose primary vaccination course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	211		
Units: Subjects				
Anti-PT ≥ 5 EL.U/mL	204	211		
Anti-FHA ≥ 5 EL.U/mL	204	211		
Anti-PRN ≥ 5 EL.U/mL	204	210		

Statistical analyses

Statistical analysis title	Immune response non-inferiority - Anti-PT
Comparison groups	Infanrix + IMOVAX Polio Group v Infanrix-IPV Group
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in seroprotection rate
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	4.13

Notes:

[6] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to pertussis toxoid, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Statistical analysis title	Immune response non-inferiority - Anti-FHA
Comparison groups	Infanrix-IPV Group v Infanrix + IMOVAX Polio Group

Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in seroprotection rate
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	2.95

Notes:

[7] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to filamentous haemagglutinin, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Statistical analysis title	Immune response non-inferiority - Anti-PRN
Comparison groups	Infanrix + IMOVAX Polio Group v Infanrix-IPV Group
Number of subjects included in analysis	415
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in seroprotection rate
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	2.64

Notes:

[8] - To assess the Non-inferiority of the Infanrix-IPV Group compared to the Infanrix + IMOVAX Polio Group in terms of vaccine response to pertactin, standardized asymptotic 95% CI for the groups' difference (Infanrix-IPV Group minus Infanrix + IMOVAX Polio Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was above -10%.

Primary: Number of subjects with vaccine response to PT, PRN and FHA.

End point title	Number of subjects with vaccine response to PT, PRN and

End point description:

The subjects were initially (i.e. before vaccination) seronegative (i.e. with concentrations < 5 EL.U/mL), or at least maintenance of pre-vaccination antibody concentrations in subjects who are initially seropositive (i.e. with concentrations ≥ 5 EL.U/mL value).

End point type	Primary

End point timeframe:

One month after the three-dose primary vaccination course.

Notes:

[9] - 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-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	211		
Units: Subjects				
Anti-PT (N=200; 209)	200	206		
Anti-FHA (N=202; 211)	201	209		
Anti-PRN (N=202; 211)	202	210		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T antibodies above the cut-offs.

End point title	Number of subjects with anti-D and anti-T antibodies above the cut-offs.

End point description:

End point type	Secondary

End point timeframe:

Before the first dose at the first study visit and one month after the three-dose primary vaccination course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	212		
Units: Subjects				
Anti-D, PRE, ≥ 1 IU/mL (N=202; 212)	0	0		
Anti-D, POST, ≥ 1 IU/mL (N=204; 211)	194	187		
Anti-T, PRE, ≥ 1 IU/mL (N=202; 212)	1	1		
Anti-T, POST, ≥ 1 IU/mL (N=204; 211)	204	208		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-D and anti-T.

End point title	Concentrations for anti-D and anti-T.

End point description:

End point type	Secondary

End point timeframe:

Before the first dose at the first study visit and one month after the three-dose primary vaccination

course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	212		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, PRE (N=202; 212)	0.052 (0.051 to 0.054)	0.053 (0.05 to 0.055)		
Anti-D, POST (N=204; 211)	4.333 (3.902 to 4.813)	2.63 (2.36 to 2.932)		
Anti-T, PRE (N=202; 212)	0.059 (0.055 to 0.064)	0.06 (0.056 to 0.065)		
Anti-T, POST (N=204; 211)	10.306 (9.5 to 11.18)	7.139 (6.512 to 7.826)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for anti-polio 1, 2 and 3.

End point title	Titers for anti-polio 1, 2 and 3.

End point description:

End point type	Secondary

End point timeframe:

Before the first dose at the first study visit and one month after the three-dose primary vaccination course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	212		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1, PRE (N=199; 212)	6.3 (5.5 to 7.1)	6.1 (5.4 to 6.9)		
Anti-polio 1, POST (N=204; 207)	755.5 (643.5 to 887.4)	263 (232.1 to 298)		
Anti-polio 2, PRE (N=202; 211)	5.8 (5.2 to 6.5)	6.5 (5.8 to 7.3)		
Anti-polio 2, POST (N=204; 205)	704.7 (599.5 to 828.4)	267.6 (233.4 to 306.8)		
Anti-polio 3, PRE (N=202; 212)	5 (4.5 to 5.4)	4.9 (4.5 to 5.3)		

Anti-polio 3, POST (N=204; 207)	1209.5 (1040.1 to 1406.5)	438.3 (383.1 to 501.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PT, anti-FHA and anti-PRN.

End point title	Concentrations for anti-PT, anti-FHA and anti-PRN.

End point description:

End point type	Secondary

End point timeframe:

Before the first dose at the first study visit and one month after the three-dose primary vaccination course.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	212		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, PRE (N=200; 210)	3 (2.8 to 3.2)	3.2 (3 to 3.5)		
Anti-PT, POST (N=204; 211)	63.3 (58.7 to 68.2)	55.6 (50.9 to 60.7)		
Anti-FHA, PRE (N=202; 212)	7.4 (6.5 to 8.4)	8.5 (7.4 to 9.7)		
Anti-FHA, POST (N=204; 211)	294.3 (269.5 to 321.4)	259.6 (235.1 to 286.6)		
Anti-PRN, PRE (N=202; 212)	2.7 (2.5 to 2.8)	2.7 (2.6 to 2.9)		
Anti-PRN, POST (N=204; 211)	205 (187.7 to 223.9)	155.6 (140.7 to 172.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms.

End point title	Number of subjects reporting solicited local symptoms.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0-3) follow up period after vaccination.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	226		
Units: Subjects				
Any Pain	92	96		
Any Redness	115	116		
Any Swelling	74	79		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms.

End point title	Number of subjects reporting solicited general symptoms.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0-3) follow up period after vaccination.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	226		
Units: Subjects				
Any Drowsiness	95	99		
Any Fever (axillary)	63	38		
Any Irritability	140	139		
Any Loss of appetite	84	78		

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:

End point type	Secondary

End point timeframe:

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

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	228		
Units: Subjects				
Any AE(s)	135	138		

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:

End point type	Secondary

End point timeframe:

During the entire study period.

End point values	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	228		
Units: Subjects				
Any SAE(s)	15	17		

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 and SAEs during the entire period

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Infanrix-IPV Group
Reporting group description: -	
Reporting group title	Infanrix + IMOVAX Polio Group
Reporting group description: -	

Serious adverse events	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 224 (6.70%)	17 / 228 (7.46%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	0 / 224 (0.00%)	1 / 228 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 224 (0.45%)	0 / 228 (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	2 / 224 (0.89%)	1 / 228 (0.44%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Inguinal hernia			
subjects affected / exposed	0 / 224 (0.00%)	2 / 228 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 224 (0.45%)	0 / 228 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	7 / 224 (3.13%)	3 / 228 (1.32%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 224 (1.79%)	5 / 228 (2.19%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 224 (1.34%)	5 / 228 (2.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 224 (0.89%)	2 / 228 (0.88%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kawasaki’s disease			
subjects affected / exposed	0 / 224 (0.00%)	1 / 228 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 224 (0.45%)	0 / 228 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis acute			
subjects affected / exposed	1 / 224 (0.45%)	0 / 228 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 228 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Infanrix-IPV Group	Infanrix + IMOVAX Polio Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	140 / 224 (62.50%)	139 / 228 (60.96%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	92 / 224 (41.07%)	96 / 228 (42.11%)	
occurrences (all)	92	96	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	115 / 224 (51.34%)	116 / 228 (50.88%)	
occurrences (all)	115	116	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	74 / 224 (33.04%)	79 / 228 (34.65%)	
occurrences (all)	74	79	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	95 / 224 (42.41%)	99 / 228 (43.42%)	
occurrences (all)	95	99	
Fever (Axillary)			
alternative assessment type: Systematic			

subjects affected / exposed	63 / 224 (28.13%)	38 / 228 (16.67%)	
occurrences (all)	63	38	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	140 / 224 (62.50%)	139 / 228 (60.96%)	
occurrences (all)	140	139	
Loss of appetite			
subjects affected / exposed	84 / 224 (37.50%)	78 / 228 (34.21%)	
occurrences (all)	84	78	
Diarrhea			
subjects affected / exposed	12 / 224 (5.36%)	8 / 228 (3.51%)	
occurrences (all)	12	8	
Pyrexia			
subjects affected / exposed	17 / 224 (7.59%)	0 / 228 (0.00%)	
occurrences (all)	17	0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	16 / 224 (7.14%)	17 / 228 (7.46%)	
occurrences (all)	16	17	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	72 / 224 (32.14%)	61 / 228 (26.75%)	
occurrences (all)	72	61	
Gastroenteritis			
subjects affected / exposed	12 / 224 (5.36%)	14 / 228 (6.14%)	
occurrences (all)	12	14	
Bronchiolitis			
subjects affected / exposed	16 / 224 (7.14%)	9 / 228 (3.95%)	
occurrences (all)	16	9	
Bronchitis			
subjects affected / exposed	7 / 224 (3.13%)	12 / 228 (5.26%)	
occurrences (all)	7	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2005	This amendment was written to reflect the changes in study design following discussions with KFDA, ad to clarify some study aspects. Major changes in study design being: - Usage of IMOVAX Polio™ instead of IPOL® in the study. Both vaccines are manufactured by Sanofi-Pasteur and both have the same content. IMOVAX Polio™ will be used instead of IPOL® in order to source the vaccine supply directly from Belgium instead of the United States. - Perform Hib vaccine administration out of the study context. - Inclusion of vaccine response to pertussis antigens as a primary endpoint and recalculation of sample size accordingly.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported