Clinical trial results:
An open-label study to assess the immune persistence in healthy Chinese toddlers primed in infancy with three doses of GSK Biologicals' DTPa-IPV/Hib vaccine, and to assess the safety and immunogenicity of a booster dose of IPV and DTPa/Hib administered at 18 to 24 months of age.

Summary

EudraCT number	2012-003324-20
Trial protocol	Outside EU/EEA
Global end of trial date	16 January 2012
Results information	
Result version number	v3 (current)
This version publication date	18 May 2018
First version publication date	10 July 2015
Version creation reason	• Correction of full data set Minor corrections of the full study results.

Trial information

Trial identification	
Sponsor protocol code	114386
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01449812
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 2989904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2989904466, 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	01 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2012
Global end of trial reached?	Yes
Global end of trial date	16 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To assess the persistence of antibodies to all vaccine antigens before the booster dose.
•To assess the immune response to the study vaccines in terms of seroprotection to diphtheria, tetanus, Haemophilus influenzae type b and poliovirus types 1, 2 and 3, and in terms of vaccine response to the pertussis antigens, one month after booster vaccination.
•To assess the immune response to the study vaccines in terms of antibody concentrations or titres for all antigens, one month after the booster dose.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 October 2011
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	China: 825
Worldwide total number of subjects	825
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)	825
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:

6 subjects did not receive vaccination.

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Infanrix+Hib/Poliorix 1 Group

Arm description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Arm type	Experimental
Investigational medicinal product name	Infanrix+Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3, 4 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Investigational medicinal product name	Poliorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3, 4 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Arm title	Infanrix+Hib/Poliorix 2 Group

Arm description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4 and 5 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Arm type	Experimental

Investigational medicinal product name	Infanrix+Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4, 5 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Investigational medicinal product name	Poliorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4, 5 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Arm title	Control Group

Arm description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix+Hib and of Poliorix vaccines at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

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

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix+Hib vaccine at 2, 3, 4 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Investigational medicinal product name	Poliorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects primed with 3 doses of the Infanrix+Hib vaccine at 2, 3, 4 months of age in the primary 112584 study, received 1 dose of Poliorix and of Infanrix+Hib vaccines at 18-24 months of age. The Poliorix and Infanrix+Hib vaccines were administered as an intramuscular (IM) injection into the upper sides of the left and right thighs, respectively.

Number of subjects in period 1	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group
Started	272	273	280
Completed	270	273	279
Not completed	2	0	1
Consent withdrawn by subject	-	-	1
Migrated/moved from study area	1	-	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix+Hib/Poliorix 1 Group
Reporting group description:	
Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.	
Reporting group title	Infanrix+Hib/Poliorix 2 Group
Reporting group description:	
Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4 and 5 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.	
Reporting group title	Control Group
Reporting group description:	
Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix+Hib and of Poliorix vaccines at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.	

Reporting group values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group
Number of subjects	272	273	280
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: months			
arithmetic mean	19.5	19.4	19.5
standard deviation	± 0.93	± 0.91	± 0.97
Gender categorical Units: Subjects			
Female	131	126	120
Male	141	147	160
Race/Ethnicity Units: Subjects			
Asian-Chinese heritage	272	273	280

Reporting group values	Total		
Number of subjects	825		
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: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	377		
Male	448		
Race/Ethnicity Units: Subjects			
Asian-Chinese heritage	825		

End points

End points reporting groups

Reporting group title	Infanrix+Hib/Poliorix 1 Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Reporting group title	Infanrix+Hib/Poliorix 2 Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4 and 5 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Reporting group title	Control Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix+Hib and of Poliorix vaccines at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Primary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations

End point title	Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations[1]

End point description:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seroprotection cut-off of ≥ 0.1 IU/mL. The analysis was performed on the ATP cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	279	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria [N=271;272;279]	0.175 (0.163 to 0.188)	0.189 (0.176 to 0.202)	0.154 (0.142 to 0.166)	
Anti-tetanus [N=272;273;278]	0.45 (0.423 to 0.478)	0.509 (0.481 to 0.54)	0.38 (0.359 to 0.404)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of seroprotected subjects against polyribosyl-ribitol-phosphate (Anti-PRP)[2]

End point description:

A seroprotected subject was defined as a vaccinated subject with Anti-PRP antibody concentration ≥ 0.15 microgram per milliliter (µg/mL). The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: Subjects				
Anti-PRP [N=272;273;280]	226	234	241	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations[3]

End point description:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seroprotection cut-off of ≥ 0.15 µg/mL. The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP [N=272;273;280]	2.275 (1.856 to 2.788)	2.674 (2.193 to 3.26)	2.413 (2.006 to 2.904)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polio type 1, 2 and 3

End point title	Number of seroprotected subjects for anti-polio type 1, 2 and

End point description:

The Anti-Polivirus cut-off value was defined as greater than or equal to 8 Estimated Dose 50% (ED50). ED50 is the estimated serum dilution reducing the signal generated by viral infection, by 50%. The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: Subjects				
Anti-Polio 1	259	267	270	
Anti-Polio 2	248	261	250	
Anti-Polio 3	254	259	257	

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-polio type 1, 2 and 3 antibody titers[5]

End point description:

Titers were expressed as Geometric Mean Titers (GMTs) for the seroprotection cut-off of ≥ 8. The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1	72.3 (62.4 to 83.7)	95.7 (82.5 to 111)	77.2 (67 to 89)	
Anti-Polio 2	57.3 (47 to 70)	63.6 (53.5 to 75.5)	42.6 (35.7 to 50.8)	
Anti-Polio 3	71.3 (60.1 to 84.7)	79.9 (66.4 to 96.2)	60.6 (51.2 to 71.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[6]

End point description:

A seropositive subject was defined as a vaccinated subject with Anti-PT, Anti-FHA and Anti-PRN antibody concentration ≥ 5 (ELISA) units per milliliter (EL.U/ml). The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: Subjects				
Anti-PT	260	263	260	
Anti-FHA	262	267	262	
Anti-PRN	260	265	267	

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:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seropositivity cut-off of ≥ 5 EL.U/ml. The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: EL.U/ml				
geometric mean (confidence interval 95%)				
Anti-PT	10.3 (9.6 to 11.1)	12.2 (11.3 to 13.1)	10.4 (9.6 to 11.2)	
Anti-FHA	12.8 (11.9 to 13.7)	14.3 (13.4 to 15.2)	12.4 (11.5 to 13.4)	
Anti-PRN	9.2 (8.8 to 9.7)	9.7 (9.2 to 10.1)	9 (8.5 to 9.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-diphtheria (Anti-D) and

anti-tetanus toxoids (Anti-T)

End point title	Number of seroprotected subjects against anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T)[8]

End point description:

A seroprotected subject was defined as a vaccinated subject with Anti-D and Anti-T antibody concentrations ≥ 0.1 international units per milliliter (IU/mL). The analysis was performed on the According-to-Protocol (ATP) cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[8] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	272	
Units: Subjects				
Anti-diphteria [N=265;268;270]	265	268	270	
Anti-tetanus [N=266;268;272]	266	268	272	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations

End point title	Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations[9]

End point description:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seroprotection cut-off of ≥ 0.1 IU/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

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

End point values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	272	
Units: IU/mL				
geometric mean (confidence interval 95%)				

Anti-diphteria [N=265;267;272]	0.174 (0.162 to 0.187)	0.189 (0.176 to 0.202)	0.154 (0.142 to 0.166)	
Anti-tetanus [N=266;268;271]	0.455 (0.429 to 0.483)	0.511 (0.482 to 0.542)	0.38 (0.357 to 0.403)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-polyribosylribitol phosphate (Anti-PRP)

End point title	Number of seroprotected subjects against anti-polyribosylribitol phosphate (Anti-PRP)[10]

End point description:

A seroprotected subject was defined as a vaccinated subject with Anti-PRP antibody concentration ≥ 0.15 microgram per milliliter (µg/mL). The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[10] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects	221	229	234	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations[11]

End point description:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seroprotection cut-off of ≥ 0.15 µg/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[11] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: µg/mL				
geometric mean (confidence interval 95%)	2.308 (1.878 to 2.836)	2.743 (2.245 to 3.352)	2.407 (1.993 to 2.908)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polio type 1, 2 and 3

End point title	Number of seroprotected subjects for anti-polio type 1, 2 and

End point description:

The Anti-Polivirus cut-off value was defined as greater than or equal to 8 Estimated Dose 50% (ED50). ED50 is the estimated serum dilution reducing the signal generated by viral infection, by 50%. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[12] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects				
Anti-Polio 1	253	262	263	
Anti-Polio 2	243	256	244	
Anti-Polio 3	249	254	250	

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-polio type 1, 2 and 3 antibody titers[13]

End point description:

Titers were expressed as Geometric Mean Titers (GMTs) for the seroprotection cut-off of ≥ 8. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[13] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1	72 (62 to 83.7)	96.3 (82.8 to 112)	75.9 (65.7 to 87.6)	
Anti-Polio 2	56.5 (46.2 to 69)	64.1 (53.8 to 76.4)	41.9 (35 to 50)	
Anti-Polio 3	72.6 (61.1 to 86.3)	79.4 (65.8 to 95.8)	60.3 (50.8 to 71.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[14]

End point description:

A seropositive subject was defined as a vaccinated subject with Anti-PT, Anti-FHA and Anti-PRN antibody concentration ≥ 5 (ELISA) units per millilitre (EL.U/ml). The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[14] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects				
Anti-PT	254	258	253	
Anti-FHA	256	262	255	
Anti-PRN	254	260	260	

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[15]

End point description:

Concentrations were expressed as Geometric Mean Concentrations (GMCs) for the seropositivity cut-off of ≥ 5 EL.U/ml. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[15] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: EL.U/ml				
geometric mean (confidence interval 95%)				
Anti-PT	10.3 (9.5 to 11.1)	12.2 (11.3 to 13.1)	10.3 (9.5 to 11.2)	
Anti-FHA	12.7 (11.8 to 13.6)	14.3 (13.4 to 15.2)	12.3 (11.4 to 13.3)	
Anti-PRN	9.2 (8.7 to 9.6)	9.7 (9.2 to 10.2)	9 (8.5 to 9.5)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with a booster response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[16]

End point description:

Booster response defined as the 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. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[16] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects				
Anti-PT	266	268	272	
Anti-FHA	266	268	272	
Anti-PRN	239	230	244	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T)

End point title	Number of seroprotected subjects against anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T)[17]

End point description:

A seroprotected subject was defined as a vaccinated subject with anti-D and anti-T antibody concentrations greater than or equal to (≥) 0.1 IU/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[17] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	272	
Units: Subjects				
Anti-diphteria [N=265;267;272]	235	245	228	
Anti-tetanus [N=266;268;271]	264	266	268	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations

End point title	Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-T) antibody concentrations[18]

End point description:

Antibody concentrations were presented as GMCs for the seroprotection cut-off of ≥ 0.1 IU/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[18] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	272	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphteria [N=265;268;270]	1.341 (1.239 to 1.451)	1.504 (1.377 to 1.643)	1.227 (1.134 to 1.326)	
Anti-tetanus [N=266;268;272]	4.862 (4.614 to 5.124)	4.927 (4.693 to 5.173)	4.371 (4.161 to 4.591)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against anti-polyribosylribitol phosphate (Anti-PRP)

End point title	Number of seroprotected subjects against anti-polyribosylribitol phosphate (Anti-PRP)[19]

End point description:

A seroprotected subject was defined as a vaccinated subject with anti-PRP antibody concentrations ≥ 0.15 µg/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[19] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects	264	268	271	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations[20]

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs) for the seroprotection cut-off of ≥ 0.15 µg/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[20] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: µg/mL				
geometric mean (confidence interval 95%)	35.178 (30.617 to 40.418)	49.023 (43.649 to 55.058)	27.682 (24.251 to 31.598)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polio type 1, 2 and 3

End point title	Number of seroprotected subjects for anti-polio type 1, 2 and

End point description:

A seroprotected subject was defined as a vaccinated subject with anti-polivirus antibody concentrations ≥ 8 ED50. ED50 is the estimated serum dilution reducing the signal generated by viral infection with 50%. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[21] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	265	268	273	
Units: Subjects				
Anti-Polio 1	265	268	273	
Anti-Polio 2	265	268	273	
Anti-Polio 3	265	268	273	

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-polio type 1, 2 and 3 antibody titers[22]

End point description:

Titers were expressed as Geometric Mean Titers (GMTs) for the seroprotection cut-off of ≥ 8. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[22] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	265	268	273	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1	3512.2 (3159.7 to 3904.1)	3410.9 (3081.7 to 3775.4)	3386.8 (3078 to 3726.6)	

Anti-Polio 2	1931.2 (1721.7 to 2166.2)	2237.9 (2001.6 to 2502.1)	1886.1 (1679.6 to 2117.9)	
Anti-Polio 3	5237.8 (4671.8 to 5872.3)	5438.5 (4846.8 to 6102.4)	5141.2 (4650.1 to 5684.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[23]

End point description:

A seropositive subject was defined as a vaccinated subject with Anti-PT, Anti-FHA and Anti-PRN antibody concentration ≥ 5 (ELISA) units per millilitre (EL.U/ml). The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[23] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: Subjects				
Anti-PT	266	268	273	
Anti-FHA	266	268	273	
Anti-PRN	266	268	273	

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[24]

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs) for the seropositivity cut-off of ≥ 5 EL.U/mL. The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay

results for antibodies against at least one study vaccine antigen component after vaccination were available.

End point type	Primary

End point timeframe:

One month after the booster vaccination (At Month 1)

Notes:

[24] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	266	268	273	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	138.5 (132 to 145.3)	146.2 (139.7 to 153)	126.8 (120.4 to 133.5)	
Anti-FHA	124.6 (119.2 to 130.2)	124 (119.2 to 129)	120.8 (115.3 to 126.6)	
Anti-PRN	57.3 (55.6 to 59.1)	59.9 (58.1 to 61.8)	57.2 (55.3 to 59.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against diphtheria (D) and tetanus (T) toxoids

End point title	Number of seroprotected subjects against diphtheria (D) and tetanus (T) toxoids[25]

End point description:

A seroprotected subject was defined as a vaccinated subject with anti-D and anti-T antibody concentrations greater than or equal to (≥) 0.1 international units per milliliter (IU/mL). The analysis was performed on the According-to-Protocol (ATP) cohort for analysis of antibody persistence, which included all subjects who have completed their full three-dose primary vaccination course in the DTPA-IPV-056 study and for whom serological results were available at the persistence time point.

End point type	Primary

End point timeframe:

Before the booster vaccination (At Day 0)

Notes:

[25] - 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+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	279	
Units: Subjects				
Anti-diphteria [N=271;272;279]	241	250	234	
Anti-tetanus [N=272;273;278]	269	271	275	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms

End point title	Number of subjects with any solicited local symptoms

End point description:

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

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	270	273	279	
Units: subjects				
Any Pain	73	74	76	
Any Redness	19	15	19	
Any Swelling	16	10	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms

End point title	Number of subjects with any solicited general symptoms

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as axillary temperature equal to or above 37.1 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade and relationship to vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	270	273	279	
Units: subjects				
Any Drowsiness	38	50	38	
Any Irritability	78	81	72	
Any Loss of appetite	67	73	69	
Any Fever	102	105	91	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited AEs

End point title	Number of subjects with unsolicited 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 (Days 0-30) post-vaccination period

End point values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: subjects				
Any AEs	16	13	21	

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:

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 1)

End point values	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	272	273	280	
Units: subjects				
Any SAEs	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 4-day (Days 0-3) post-vaccination period. AEs: within the 31-day (Days 0-30) period following booster vaccination. SAEs: throughout the entire study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Infanrix+Hib/Poliorix 1 Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Reporting group title	Infanrix+Hib/Poliorix 2 Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix-IPV/Hib vaccine at 3, 4 and 5 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Reporting group title	Control Group

Reporting group description:

Healthy male or female children between, and including, 18 and 24 months of age at the time of booster vaccination, who were primed with 3 doses of the Infanrix+Hib and of Poliorix vaccines at 2, 3 and 4 months of age in the DTPA-IPV-056 (112584) primary study, additionally received 1 dose of Poliorix and of Infanrix+Hib vaccines, administered intramuscularly into the upper sides of the left and right thighs, respectively.

Serious adverse events	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 280 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 280 (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
Infections and infestations			
Bronchopneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 280 (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

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

Non-serious adverse events	Infanrix+Hib/Poliorix 1 Group	Infanrix+Hib/Poliorix 2 Group	Control Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 272 (57.72%)	164 / 273 (60.07%)	158 / 280 (56.43%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	73 / 270 (27.04%)	74 / 273 (27.11%)	76 / 279 (27.24%)
occurrences (all)	73	74	76
Redness			
subjects affected / exposed[2]	19 / 270 (7.04%)	15 / 273 (5.49%)	16 / 279 (5.73%)
occurrences (all)	19	15	16
Swelling			
subjects affected / exposed[3]	16 / 270 (5.93%)	10 / 273 (3.66%)	14 / 279 (5.02%)
occurrences (all)	16	10	14
Drowsiness			
subjects affected / exposed[4]	38 / 270 (14.07%)	50 / 273 (18.32%)	38 / 279 (13.62%)
occurrences (all)	38	50	38
Irritability			
subjects affected / exposed[5]	78 / 270 (28.89%)	81 / 273 (29.67%)	72 / 279 (25.81%)
occurrences (all)	78	81	72
Loss of appetite			
subjects affected / exposed[6]	67 / 270 (24.81%)	73 / 273 (26.74%)	69 / 279 (24.73%)
occurrences (all)	67	73	69
Fever			
subjects affected / exposed[7]	102 / 270 (37.78%)	105 / 273 (38.46%)	91 / 279 (32.62%)
occurrences (all)	102	105	91

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
12 July 2011	Due to significant revisions to the Chinese Pharmacopeia, the DTPa-IPV/Hib vaccine can currently not be locally retested and released in that country. The study design is therefore being modified to boost all subjects with the DTPa/Hib (Infanrix Hib) and IPV (Poliorix) vaccines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported