Clinical trial results:
A phase IV, partially double-blind, multicentre study to assess the immunogenicity and reactogenicity of GlaxoSmithKline (GSK) Biologicals' combined DTPa-HBV-IPV/Hib vaccine (new formulation) as compared with GSK Biologicals' combined DTPa-HBV-IPV/Hib vaccine (current formulation) when administered as a booster dose to children aged 18-23 months, previously primed with the same vaccines in primary vaccination study DTPa-HBV-IPV-109 (105910). The immunogenicity and reactogenicity of a booster dose of the DTPa-HBV-IPV vaccine will be evaluated in a third group of subjects who had received this vaccine in the primary study.

Summary

EudraCT number	2012-002428-34
Trial protocol	Outside EU/EEA
Global end of trial date	25 June 2008

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	29 May 2015

Trial information

Trial identification

Sponsor protocol code	110478

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00611559
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 Biolgicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biolgicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 June 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 June 2008
Global end of trial reached?	Yes
Global end of trial date	25 June 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of the DTPa-HBV-IPV/Hib vaccine (new formulation) in terms of response to all vaccine antigens is non-inferior to that of the DTPa-HBV-IPV/Hib vaccine (current formulation), one month after the booster dose.

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 vaccine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2008
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	Russian Federation: 283
Worldwide total number of subjects	283
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)	283
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Partially double-blind study. The study was double-blind for the two groups receiving current formulation or new formulation i.e. the investigator and parents/guardians of the subjects were unaware of the treatment administered. The study was open for the Penta Group i.e. the vaccine GSK Biologicals' Infanrix™ penta (DTPa-HBV-IPV) administered to the subjects in this group was known to the investigator and to the parents/guardians of the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	Infanrix hexa preservative-free formulation Group

Arm description:

Subjects received a booster dose of the preservative-free formulation of Infanrix™ hexa.

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

Dosage and administration details:

Subjects received a booster dose.

Arm title	Infanrix hexa Preservative-Containing Formulation Group

Arm description:

Subjects received a booster dose of the preservative-containing formulation of Infanrix™ hexa.

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

Dosage and administration details:

Subjects received a booster dose.

Arm title	Infanrix penta Preservative-Free Formulation Group

Arm description:

Subjects received a booster dose of the preservative-free formulation of Infanrix™ penta.

Arm type	Active comparator

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a booster dose.

Number of subjects in period 1	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group
Started	111	115	57
Completed	110	114	56
Not completed	1	1	1
Lost to follow-up	-	1	-
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix hexa preservative-free formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-free formulation of Infanrix™ hexa.	
Reporting group title	Infanrix hexa Preservative-Containing Formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-containing formulation of Infanrix™ hexa.	
Reporting group title	Infanrix penta Preservative-Free Formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-free formulation of Infanrix™ penta.	

Reporting group values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group
Number of subjects	111	115	57
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	21.2	21.3	21.2
standard deviation	± 1.61	± 1.57	± 1.62
Gender categorical Units: Subjects			
Female	56	46	35
Male	55	69	22

Reporting group values	Total		
Number of subjects	283		
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	137		
Male	146		

End points

End points reporting groups

Reporting group title	Infanrix hexa preservative-free formulation Group
Reporting group description: Subjects received a booster dose of the preservative-free formulation of Infanrix™ hexa.	
Reporting group title	Infanrix hexa Preservative-Containing Formulation Group
Reporting group description: Subjects received a booster dose of the preservative-containing formulation of Infanrix™ hexa.	
Reporting group title	Infanrix penta Preservative-Free Formulation Group
Reporting group description: Subjects received a booster dose of the preservative-free formulation of Infanrix™ penta.	

Primary: Number of subjects with anti-hepatitis B (HB) antibody concentrations above the cut-off one month after the booster dose.

End point title	Number of subjects with anti-hepatitis B (HB) antibody concentrations above the cut-off one month after the booster dose.
End point description: Anti-HB antibodies cut-off value assessed was ≥ 10 milli-international units per milliliter (mIU/mL).	
End point type	Primary
End point timeframe: One month after the booster dose.	

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	92	48	
Units: Subjects				
Anti-HBs (N=91; 92; 48)	88	92	48	

Statistical analyses

Statistical analysis title	Non-inferiority in terms of vaccine response to HB
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group

Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in seroprotection rate
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	9.27

Notes:

[1] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to hepatitis B, standardized asymptotic 95% CI for the groups 'difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Primary: Number of subjects with anti-polyribosyl-ribitol-phosphate (PRP) antibodies concentrations above the cut-off one month after the booster dose.

End point title	Number of subjects with anti-polyribosyl-ribitol-phosphate (PRP) antibodies concentrations above the cut-off one month after the booster dose.

End point description:

Anti-PRP antibodies cut-off value assessed was ≥ 0.15 microgram per milliliter (µg/mL).

End point type	Primary

End point timeframe:

One month after the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	79	42	
Units: Subjects				
Anti-PRP (N=76; 79; 42)	74	78	27	

Statistical analyses

Statistical analysis title	Non-inferiority - vaccine response to PRP
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in seroprotection rate
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.49
upper limit	8.01

Notes:

[2] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to PRP, standardized asymptotic 95% CI for the groups'difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed. Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Primary: Number of subjects with anti-diphtheria and anti-tetanus antibodies concentration above the cut-off one month after the booster dose.

End point title	Number of subjects with anti-diphtheria and anti-tetanus antibodies concentration above the cut-off one month after the booster dose.

End point description:

Anti-diphtheria and anti-tetanus antibodies cut-off value assessed was ≥ 0.1 international units per milliliter (IU/mL).

End point type	Primary

End point timeframe:

One month after the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	79	42	
Units: Subjects				
Anti-D	76	76	40	
Anti-T	76	78	42	

Statistical analyses

Statistical analysis title	Non-inferiority in terms of vaccine response to D
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group

Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in seroprotection rate
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.48
upper limit	3.62

Notes:

[3] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to diphtheria, standardized asymptotic 95% CI for the groups'difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Statistical analysis title	Non-inferiority in terms of vaccine response to T
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in seroprotection rate
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.68
upper limit	5.88

Notes:

[4] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to tetanus, standardized asymptotic 95% CI for the groups'difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Primary: Number of subjects with anti-poliovirus antibodies concentration above the cut-off one month after the booster dose.

End point title	Number of subjects with anti-poliovirus antibodies concentration above the cut-off one month after the booster dose.

End point description:

Anti-poliovirus antibodies cut-off value assessed was ≥ 8 effective dose 50 (ED50).

End point type	Primary

End point timeframe:

One month after the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	52	31	
Units: Subjects				
Anti-polivirus 1 (N=55; 51; 31)	55	51	31	
Anti-polivirus 2 (N=55; 51; 31)	55	51	30	
Anti-polivirus 3 (N=55; 52; 31)	55	52	29	

Statistical analyses

Statistical analysis title	Non-inferiority - vaccine response to polio-1
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.07
upper limit	6.59

Notes:

[5] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to poliovirus type 1, standardized asymptotic 95% CI for the groups' difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed. Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Statistical analysis title	Non-inferiority - vaccine response to polio-2
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.07
upper limit	6.59

Notes:

[6] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to poliovirus type 2, standardized asymptotic 95% CI for the groups' difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed. Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Statistical analysis title	Non-inferiority - vaccine response to polio-3
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.94
upper limit	6.59

Notes:

[7] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to poliovirus type 3, standardized asymptotic 95% CI for the groups' difference (Infanrix hexa preservative-containing formulation Group minus Infanrix hexa preservative-free formulation Group) was computed. Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 10%.

Primary: Number of subjects with anti-pertussis toxoid (PT), anti-filamentous haemagglutinin (FHA) and anti-pertactin (PRN) antibodies concentration above the cut-off one month after the booster dose.

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

End point description:

Concentration of anti-PT, ant-FHA and anti-PRN antibodies given as geometric mean concentration (GMC) in Enzyme-Linked Immuno Sorbent Assay (ELISA) unit per milliliter (EL.U/mL).

End point type	Primary

End point timeframe:

One month after the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	77	41	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=84; 70; 33)	65.5 (49.8 to 86.3)	84.2 (61.5 to 115.4)	43.9 (22.4 to 85.8)	
Anti-FHA (N=86; 69; 38)	476.6 (369.7 to 614.4)	428.3 (311.2 to 589.5)	221.1 (120.3 to 406.6)	
Anti-PRN (N=89; 77; 41)	418.1 (303.2 to 576.6)	384.1 (271.3 to 544)	251.6 (143.9 to 439.7)	

Statistical analyses

Statistical analysis title	Non-inferiority in terms of vaccine response to PT
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Risk ratio (RR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.94

Notes:

[8] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to pertussis toxoid.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 1.5.

Statistical analysis title	Non-inferiority - vaccine response to FHA
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Risk ratio (RR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.34

Notes:

[9] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to filamentous haemagglutinin.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 1.5.

Statistical analysis title	Non-inferiority - vaccine response to PRN
Comparison groups	Infanrix hexa preservative-free formulation Group v Infanrix hexa Preservative-Containing Formulation Group
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Risk ratio (RR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.47

Notes:

[10] - To assess the Non-inferiority of the Infanrix hexa preservative-free formulation Group compared to the Infanrix hexa preservative-containing formulation Group in terms of vaccine response to pertactin.
Objective of non-inferiority was met since the LL of the 95% CI was below the predefined limit of 1.5.

Secondary: Number of subjects with anti-hepatitis B (HB) antibody concentrations above the cut-off before and one month after the booster dose.

End point title	Number of subjects with anti-hepatitis B (HB) antibody concentrations above the cut-off before and one month after the booster dose.

End point description:

Anti-HB antibodies cut-off value assessed were ≥ 10 mIU/mL and ≥ 100 mIU/mL. Number of subjects with cut-off ≥ 10 mIU/mL one month after the booster dose was already presented in the primary outcomes.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	93	48	
Units: Subjects				
≥ 10 mIU/mL Pre (N=93, 93,47)	87	86	44	
≥ 100 mIU/mL Pre (N=93, 93,47)	57	57	35	
≥ 100 mIU/mL Post (N=91, 92,48)	85	87	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HB antibodies concentration.

End point title	Anti-HB antibodies concentration.

End point description:

Concentration of anti-HB antibodies given as GMC in mIU/mL.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	93	48	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Pre (N=93,93,47)	163.5 (114.3 to 233.7)	161.2 (111.5 to 232.9)	196.9 (124.2 to 312.2)	
Post (N=91,92,48)	4668 (2861.4 to 7615.3)	4962.3 (3289.7 to 7485.4)	3867.8 (1751.4 to 8541.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibodies concentrations above the cut-off before and one month after the booster dose.

End point title	Number of subjects with anti-PRP antibodies concentrations above the cut-off before and one month after the booster dose.

End point description:

Anti-PRP antibodies cut-off value assessed were ≥ 0.15 µg/mL and ≥ 1.0 µg/mL. Number of subjects with cut-off ≥ 0.15 µg/mL one month after the booster dose was already presented in the primary outcomes.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	79	42	
Units: Subjects				
≥ 0.15 µg/mL Pre (N=75,72,42)	55	55	23	
≥ 1.0 µg/mL Pre (N=75,72,42)	12	14	7	
≥ 1.0 µg/mL Post (N=76,79,42)	69	74	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibodies concentration.

End point title	Anti-PRP antibodies concentration.

End point description:

Concentration of anti-PRP antibodies given as GMC in µg/mL.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	79	42	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Pre (N=75,72,42)	0.3 (0.2 to 0.4)	0.4 (0.3 to 0.5)	0.2 (0.1 to 0.4)	
Post (N=76,79,42)	25.3 (16 to 40)	34.7 (22.9 to 52.7)	0.4 (0.2 to 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria and anti-tetanus antibodies concentration above the cut-off before the booster dose.

End point title	Number of subjects with anti-diphtheria and anti-tetanus antibodies concentration above the cut-off before the booster dose.

End point description:

Anti-diphtheria and anti-tetanus antibodies cut-off value assessed was ≥ 0.1 IU/mL.

End point type	Secondary

End point timeframe:

Before the booster dose administration (at baseline).

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	72	42	
Units: Subjects				
Anti-diphtheria	45	47	23	
Anti-tetanus	69	62	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria and anti-tetanus antibodies concentration.

End point title	Anti-diphtheria and anti-tetanus antibodies concentration.

End point description:

Concentration of anti-diphtheria and anti-tetanus antibodies given as GMC in IU/mL.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	79	42	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria Pre (N=75,72,42)	0.2 (0.1 to 0.2)	0.2 (0.1 to 0.3)	0.1 (0.1 to 0.2)	
Anti-diphtheria Post (N=77,79,42)	2.7 (1.9 to 3.7)	3.4 (2.5 to 4.5)	2.2 (1.4 to 3.5)	
Anti-tetanus Pre (N=75,72,42)	0.5 (0.3 to 0.6)	0.5 (0.3 to 0.7)	0.3 (0.2 to 0.4)	
Anti-tetanus Post (N=77,79,42)	4.9 (3.6 to 6.7)	6.9 (5.3 to 9)	4.5 (2.8 to 7.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies concentration above the cut-off before and one month after the booster dose.

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibodies concentration above the cut-off before and one month after the booster dose.

End point description:

Anti-PT, anti-FHA and anti-PRN antibodies cut-off value assessed were ≥ 5 EL.U/mL.

End point type	Secondary

End point timeframe:

Before (Pre) and one month after (Post) the booster dose.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	77	42	
Units: Subjects				
Anti-PT Pre (N=83,78,42)	45	43	26	
Anti-PT Post (N=84,70,33)	79	66	25	
Anti-FHA Pre (N=85,77,42)	77	68	39	
Anti-FHA Post (N=86,69,38)	86	69	37	
Anti-PRN Pre (N=85,84,43)	75	67	35	
Anti-PRN Post (N=89,77,41)	88	77	40	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA, and anti-PRN antibodies concentration before the booster dose.

End point title	Anti-PT, anti-FHA, and anti-PRN antibodies concentration before the booster dose.

End point description:

Concentration of anti-PT, anti-FHA and anti-PRN antibodies given as GMC in EL.U/mL.

End point type	Secondary

End point timeframe:

Before the booster dose administration (at baseline).

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	84	43	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=83,78,42)	6.6 (5.2 to 8.4)	6.2 (5 to 7.8)	7.1 (5.3 to 9.4)	
Anti-FHA (N=85,77,42)	24.5 (18.4 to 32.6)	22.1 (16.3 to 30)	23.8 (17.3 to 32.6)	
Anti-PRN (N=85,84,43)	17.5 (13.4 to 23)	13.7 (10.3 to 18.1)	15 (10.3 to 21.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-poliovirus antibodies concentration above the cut-off before the booster dose.

End point title	Number of subjects with anti-poliovirus antibodies concentration above the cut-off before the booster dose.
End point description:	
Anti-poliovirus antibodies cut-off value assessed was ≥ 8 ED50.	
End point type	Secondary
End point timeframe:	
Before the booster dose.	

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	51	27	
Units: Subjects				
Anti-poliovirus type 1 (N=49,50,26)	46	47	24	
Anti-poliovirus type 2 (N=49,50,27)	46	48	26	
Anti-poliovirus type 3 (N=49,51,27)	47	48	23	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus antibodies titer.

End point title	Anti-poliovirus antibodies titer.
End point description:	
Concentration of anti-poliovirus antibodies given as geometric mean titers (GMT).	
End point type	Secondary
End point timeframe:	
Before (Pre) and one month after (Post) the booster dose.	

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	51	31	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-poliovirus type 1 Pre (N=49,50,26)	106.5 (67.9 to 167)	120.4 (76.9 to 188.4)	85.9 (47.1 to 156.5)	
Anti-poliovirus type 1 Post (N=55,51,31)	1237.1 (940.7 to 1626.9)	1939.8 (1465.1 to 2568.2)	979.5 (539.4 to 1778.8)	
Anti-poliovirus type 2 Pre (N=49,50,27)	144.4 (96.9 to 215.2)	102.5 (68.2 to 154.2)	95.3 (56.3 to 161.1)	
Anti-poliovirus type 2 Post (N=55,51,31)	1412 (1096.4 to 1818.5)	1900.6 (1399.7 to 2580.7)	916.3 (498.1 to 1685.5)	
Anti-poliovirus type 3 Pre (N=49,51,27)	98.7 (68 to 143.2)	68.9 (47 to 101.1)	77.5 (41.9 to 143.4)	
Anti-poliovirus type 3 Post (N=49,51,27)	1485.9 (1041.4 to 2120.3)	1828.7 (1303.8 to 2565.1)	605.6 (264 to 1389.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited symptoms.

End point title	Number of subjects reporting solicited symptoms.

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Solicited general symptoms assessed include drowsiness, fever, irritability, and loss of appetite.

End point type	Secondary

End point timeframe:

Within the 4-day (Day 0-3) post-vaccination period.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	115	57	
Units: Subjects				
Pain	35	36	14	
Redness	54	54	22	
Swelling	39	45	19	
Drowsiness	21	18	8	
Fever	18	15	6	

Irritability	21	21	4	
Loss of appetite	22	14	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AE).

End point title	Number of subjects reporting unsolicited adverse events (AE).

End point description:

An AE is 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.

End point type	Secondary

End point timeframe:

Within the 31-day (Day 0-30) post-vaccination period.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	115	57	
Units: Subjects				
Any AE(s)	8	9	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAE).

End point title	Number of subjects reporting serious adverse events (SAE).

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Up to one month after the booster dose administration.

End point values	Infanrix hexa preservative-free formulation Group	Infanrix hexa Preservative-Containing Formulation Group	Infanrix penta Preservative-Free Formulation Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	115	57	
Units: Subjects				
Any SAE(s)	0	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 (Day 0-3) follow-up period after booster vaccination.
Unsolicited symptoms: during the 31-day (Day 0-30) follow-up period after booster vaccination.
(SAEs): following booster vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Infanrix hexa preservative-free formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-free formulation of Infanrix™ hexa	
Reporting group title	Infanrix hexa preservative-containing formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-containing formulation of Infanrix™ hexa	
Reporting group title	Infanrix penta preservative-free formulation Group
Reporting group description:	
Subjects received a booster dose of the preservative-free formulation of Infanrix™ penta	

Serious adverse events	Infanrix hexa preservative-free formulation Group	Infanrix hexa preservative-containing formulation Group	Infanrix penta preservative-free formulation Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 111 (0.00%)	0 / 115 (0.00%)	0 / 57 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Infanrix hexa preservative-free formulation Group	Infanrix hexa preservative-containing formulation Group	Infanrix penta preservative-free formulation Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 111 (48.65%)	54 / 115 (46.96%)	22 / 57 (38.60%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			

subjects affected / exposed	35 / 111 (31.53%)	36 / 115 (31.30%)	14 / 57 (24.56%)
occurrences (all)	35	36	14
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 111 (48.65%)	54 / 115 (46.96%)	22 / 57 (38.60%)
occurrences (all)	54	54	22
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	39 / 111 (35.14%)	45 / 115 (39.13%)	19 / 57 (33.33%)
occurrences (all)	39	45	19
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 111 (18.92%)	18 / 115 (15.65%)	8 / 57 (14.04%)
occurrences (all)	21	18	8
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 111 (16.22%)	15 / 115 (13.04%)	6 / 57 (10.53%)
occurrences (all)	18	15	6
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 111 (18.92%)	21 / 115 (18.26%)	4 / 57 (7.02%)
occurrences (all)	21	21	4
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 111 (19.82%)	14 / 115 (12.17%)	5 / 57 (8.77%)
occurrences (all)	22	14	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported