



## Clinical trial results:

**A randomised, open-label study to assess the immunogenicity and safety of GSK Biologicals' DTPa-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2-3-4 or 3-4-5 months of age in healthy infants in China.**

### Summary

EudraCT number	2011-005868-25
Trial protocol	Outside EU/EEA
Global end of trial date	19 November 2010

### Results information

Result version number	v3 (current)
This version publication date	13 May 2018
First version publication date	24 June 2015
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set</li><li>Minor corrections of the full study results.</li></ul>

### Trial information

#### Trial identification

Sponsor protocol code	112584
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01086423
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	26 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2010
Global end of trial reached?	Yes
Global end of trial date	19 November 2010
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

To demonstrate that the immunogenicity of DTPa-IPV/Hib vaccine administered at 2, 3 and 4 months of age (DTPa Combo-1 Group) was non-inferior to that of the concomitant administration of DTPa/Hib and IPV vaccines at the same age (Control Group), in terms of immune response to all vaccine antigens, one month after the third vaccine dose.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects****Subjects enrolled per country**

Country: Number of subjects enrolled	China: 984
Worldwide total number of subjects	984
EEA total number of subjects	0

Notes:

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**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)	984
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:

Out of the 985 subjects originally enrolled in the study, 984 subjects were vaccinated with at least one dose of the study vaccine.

### 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
<b>Arm title</b>	Infanrix-IPV+Hib 1 Group

Arm description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right thigh.

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

Dosage and administration details:

Subjects received 3 doses of Infanrix-IPV+Hib vaccine intramuscularly, in the upper side of the right thigh at 2, 3 and 4 months of age.

<b>Arm title</b>	Infanrix-IPV+Hib 2 Group
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Arm description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 3, 4 and 5 months of age, administered intramuscularly in the upper side of the right thigh.

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

Dosage and administration details:

Subjects received 3 doses of Infanrix-IPV+Hib vaccine intramuscularly in the upper side of the right thigh at 3, 4 and 5 months of age.

<b>Arm title</b>	Infanrix-Hib + Poliorix Group
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Arm description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-Hib vaccine co-administered with Poliorix vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right or left thigh, respectively.

Arm type	Active comparator
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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 received 3 doses of Infanrix-Hib vaccine intramuscularly in the upper side of the right thigh at 2, 3 and 4 months of age.

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

Dosage and administration details:

Subjects received 3 doses of Poliorix vaccine intramuscularly in the upper side of the left thigh at 2, 3 and 4 months of age.

<b>Number of subjects in period 1</b>	<b>Infanrix-IPV+Hib 1 Group</b>	<b>Infanrix-IPV+Hib 2 Group</b>	<b>Infanrix-Hib + Poliorix Group</b>
Started	330	324	330
Completed	320	321	321
Not completed	10	3	9
Adverse event, serious fatal	1	1	-
Consent withdrawn by subject	5	1	3
Adverse event, non-fatal	2	1	-
Protocol violation	-	-	1
Migrated/moved from study area	2	-	4
Lost to follow-up	-	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Infanrix-IPV+Hib 1 Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right thigh.

Reporting group title	Infanrix-IPV+Hib 2 Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 3, 4 and 5 months of age, administered intramuscularly in the upper side of the right thigh.

Reporting group title	Infanrix-Hib + Poliorix Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-Hib vaccine co-administered with Poliorix vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right or left thigh, respectively.

Reporting group values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group
Number of subjects	330	324	330
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: weeks			
arithmetic mean	9.9	14.3	9.9
standard deviation	± 1.12	± 1.14	± 1.17
Gender categorical Units: Subjects			
Female	155	147	141
Male	175	177	189
Race/Ethnicity Units: Subjects			
Asian-Chinese heritage	330	324	330

Reporting group values	Total		
Number of subjects	984		

Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: weeks			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	443		
Male	541		
Race/Ethnicity			
Units: Subjects			
Asian-Chinese heritage	984		

## End points

### End points reporting groups

Reporting group title	Infanrix-IPV+Hib 1 Group
Reporting group description: Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right thigh.	
Reporting group title	Infanrix-IPV+Hib 2 Group
Reporting group description: Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 3, 4 and 5 months of age, administered intramuscularly in the upper side of the right thigh.	
Reporting group title	Infanrix-Hib + Poliorix Group
Reporting group description: Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-Hib vaccine co-administered with Poliorix vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right or left thigh, respectively.	

### Primary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antigens

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antigens
End point description: A seroprotected subject was defined as a subject with anti-D and anti-T antibody concentrations greater than or equal to ( $\geq$ ) 0.1 international units per milliliter (IU/mL).	
End point type	Primary
End point timeframe: At Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group)	

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	156	147	
Units: Subjects				
Anti-D	146	156	147	
Anti-T	147	156	147	

### Statistical analyses

Statistical analysis title	Difference in seroprotection rates for anti-D
Statistical analysis description: To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of	

immune response to anti-diphtheria, one month after the third vaccine dose.

Comparison groups	Infanrix-Hib + Poliorix Group v Infanrix-IPV+Hib 1 Group
Number of subjects included in analysis	294
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	3.76

Notes:

[1] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

<b>Statistical analysis title</b>	Difference in seroprotection rates for anti-T
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Statistical analysis description:

To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-tetanus, one month after the third vaccine dose.

Comparison groups	Infanrix-Hib + Poliorix Group v Infanrix-IPV+Hib 1 Group
Number of subjects included in analysis	294
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.56
upper limit	2.56

Notes:

[2] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

### **Primary: Number of seroprotected subjects for anti-poly-ribosyl-ribitol phosphate (anti-PRP) antigens**

End point title	Number of seroprotected subjects for anti-poly-ribosyl-ribitol phosphate (anti-PRP) antigens
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End point description:

A seroprotected subject was defined as a subject with anti-PRP antibody concentrations  $\geq 0.15$  micrograms per milliliter ( $\mu\text{g/mL}$ )

End point type	Primary
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End point timeframe:

At Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group)



End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	150	
Units: Subjects	142	155	133	

## Statistical analyses

Statistical analysis title	Difference in seroprotection rates for anti-PRP
Statistical analysis description:	
To demonstrate that the immunogenicity of <b>Infanrix™</b> IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of <b>Infanrix™</b> -Hib and <b>Poliorix™</b> vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-PRP antibodies, one month after the third vaccine dose.	
Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	-7.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.44
upper limit	-2.13

Notes:

[3] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

## Primary: Number of seroprotected subjects for anti-poliovirus (anti-polio) types 1, 2 and 3 antigens

End point title	Number of seroprotected subjects for anti-poliovirus (anti-polio) types 1, 2 and 3 antigens
End point description:	
A seroprotected subject was defined as a subject with anti-poliovirus (anti-polio) types 1, 2 and 3 antibody titres $\geq$ the value of 8.	
End point type	Primary
End point timeframe:	
At Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group)	

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	150	
Units: Subjects				
Anti-polio 1	147	157	150	
Anti-polio 2	147	157	150	

Anti-polio 3	147	157	150	
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## Statistical analyses

<b>Statistical analysis title</b>	Seroprotection rates difference for anti-Polio1
Statistical analysis description:	
To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-Polio type 1 antibodies, one month after the third vaccine dose.	
Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	2.56

Notes:

[4] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

<b>Statistical analysis title</b>	Seroprotection rates difference for anti-Polio2
Statistical analysis description:	
To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-Polio type 2 antibodies, one month after the third vaccine dose.	
Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[5]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	2.56

Notes:

[5] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

<b>Statistical analysis title</b>	Seroprotection rates difference for anti-Polio3
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Statistical analysis description:

To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4

months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of **Infanrix™-Hib** and **Poliorix™** vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-Polio type 3 antibodies, one month after the third vaccine dose.

Comparison groups	Infanrix-IPV+Hib 1 Group v <b>Infanrix-Hib + Poliorix Group</b>
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[6]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	2.56

Notes:

[6] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus **Infanrix-IPV+Hib 1 Group**] in percentage of seroprotected subjects  $\leq 10\%$ .

### **Primary: Number of subjects with a vaccine response to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antigens.**

End point title	Number of subjects with a vaccine response to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antigens.
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End point description:

Vaccine response was defined as: For PT and FHA response, antibody concentration  $\geq 20$  enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL) at post-vaccination. For PRN response: for initially seronegative subjects [antibody concentration lower than ( $<$ ) 5 EL.U/mL], post-vaccination antibody concentration  $\geq 20$  EL.U/mL; for initially seropositive subjects (antibody concentration  $\geq 5$  EL.U/mL), at least a 4-fold increase in antibody concentration from pre to post-vaccination.

End point type	Primary
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End point timeframe:

At Month 3 (for **Infanrix-IPV+Hib 1 Group** and **Infanrix-Hib + Poliorix Group**) and Month 4 (for **Infanrix-IPV+Hib 2 Group**).

<b>End point values</b>	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	156	148	
Units: Subjects				
Anti-PT	147	155	147	
Anti-FHA	147	155	144	
Anti-PRN	145	156	145	

### **Statistical analyses**

<b>Statistical analysis title</b>	Difference in vaccine response rates for anti-PT
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Statistical analysis description:

To demonstrate that the immunogenicity of **Infanrix™** IPV/Hib vaccine administered at 2, 3 and 4 months of age (**Infanrix-IPV+Hib 1 Group**) was non-inferior to that of the concomitant administration of

Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-PT antigens, one month after the third vaccine dose.

Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[7]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.74
upper limit	1.89

Notes:

[7] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

<b>Statistical analysis title</b>	Difference in vaccine response rates for anti-FHA
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Statistical analysis description:

To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-FHA antigens, one month after the third vaccine dose.

Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[8]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	-0.11

Notes:

[8] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

<b>Statistical analysis title</b>	Difference in vaccine response rates for anti-PRN
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Statistical analysis description:

To demonstrate that the immunogenicity of Infanrix™ IPV/Hib vaccine administered at 2, 3 and 4 months of age (Infanrix-IPV+Hib 1 Group) was non-inferior to that of the concomitant administration of Infanrix™-Hib and Poliorix™ vaccines at the same age (Infanrix-Hib + Poliorix Group), in terms of immune response to anti-PRN antigens, one month after the third vaccine dose.

Comparison groups	Infanrix-IPV+Hib 1 Group v Infanrix-Hib + Poliorix Group
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[9]</sup>
Parameter estimate	Difference in seroprotection rate
Point estimate	-0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	3.04

Notes:

[9] - The upper limit of the standardized asymptotic 95% confidence interval (CI) on the group difference [Infanrix-Hib + Poliorix Group minus Infanrix-IPV+Hib 1 Group] in percentage of seroprotected subjects  $\leq 10\%$ .

### Secondary: Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point title	Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.
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End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in IU/mL.

End point type	Secondary
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End point timeframe:

At Month 0 [PRE] and Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group) [POST]

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	151	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D PRE [N=147;157;151]	0.052 (0.05 to 0.053)	0.051 (0.05 to 0.052)	0.051 (0.049 to 0.052)	
Anti-D POST [N=147;156;147]	0.719 (0.661 to 0.782)	0.753 (0.699 to 0.812)	0.613 (0.565 to 0.666)	
Anti-T PRE [N=147;157;151]	0.051 (0.05 to 0.052)	0.052 (0.05 to 0.054)	0.05 (0.05 to 0.05)	
Anti-T POST [N=147;156;147]	4.118 (3.779 to 4.488)	4.124 (3.796 to 4.479)	3.618 (3.339 to 3.921)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentrations for anti-poly-ribosyl-ribitol phosphate (anti-PRP) antibodies.

End point title	Concentrations for anti-poly-ribosyl-ribitol phosphate (anti-PRP) antibodies.
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End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in µg/mL.

End point type	Secondary
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End point timeframe:

At Month 0 [PRE] and Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group) [POST]

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	151	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP PRE [N=146;157;151]	0.127 (0.104 to 0.154)	0.135 (0.112 to 0.163)	0.15 (0.122 to 0.185)	
Anti-PRP POST [N=147;157;150]	5.601 (4.676 to 6.709)	9.396 (8.032 to 10.992)	2.826 (2.235 to 3.572)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Titers for anti-poliovirus (anti-polio) types 1, 2 and 3 antibodies.

End point title	Titers for anti-poliovirus (anti-polio) types 1, 2 and 3 antibodies.
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End point description:

Antibody titers were presented as geometric mean titers (GMTs).

End point type	Secondary
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End point timeframe:

At Month 0 [PRE] and Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group) [POST]

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	151	
Units: titres				
geometric mean (confidence interval 95%)				
Anti-polio 1 PRE [N=146;157;151]	9.4 (7.7 to 11.5)	7.1 (6.2 to 8.2)	9.2 (7.7 to 11)	
Anti-polio 1 POST [N=147;157;150]	1143.7 (952.7 to 1372.9)	1328.9 (1137.6 to 1552.4)	533.6 (469.5 to 606.4)	
Anti-polio 2 PRE [N=146;157;151]	6.3 (5.5 to 7.2)	5 (4.6 to 5.5)	6.9 (6 to 8)	
Anti-polio 2 POST [N=147;157;150]	416.2 (344.5 to 502.8)	458.6 (385.6 to 545.5)	186.4 (160.4 to 216.5)	
Anti-polio 3 PRE [N=146;157;151]	5.8 (5 to 6.8)	4.9 (4.3 to 5.6)	5.7 (5.1 to 6.4)	

Anti-polio 3 POST [N=147;157;150]	1478.8 (1210.6 to 1806.5)	1411.6 (1175.3 to 1695.3)	820.7 (820.7 to 964.4)	
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## 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.
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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
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period after each vaccine dose.

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	330	324	330	
Units: Subjects				
Any Pain, D1 [N=330;324;330]	65	64	83	
Any Redness, D1 [N=330;324;330]	16	19	15	
Any Swelling, D1 [N=330;324;330]	8	9	9	
Any Pain, D2 [N=321;321;322]	43	50	58	
Any Redness, D2 [N=321;321;322]	14	19	13	
Any Swelling, D2 [N=321;321;322]	6	8	8	
Any Pain, D3 [N=321;321;321]	39	41	39	
Any Redness, D3 [N=321;321;321]	10	11	8	
Any Swelling, D3 [N=321;321;321]	5	8	6	
Any Pain, Across [N=330;324;330]	90	91	102	
Any Redness, Across [N=330;324;330]	28	34	26	
Any Swelling, Across [N=330;324;330]	14	17	19	

## 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.
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as axillary temperature equal to or above 37.0 degrees Celsius (°C)]. Any = occurrence of the symptom

regardless of intensity grade or relationship to study vaccination.

End point type	Secondary
End point timeframe:	
During the 4-day (Days 0-3) post-vaccination period after each vaccine dose.	

End point values	Infanrix- IPV+Hib 1 Group	Infanrix- IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	330	324	330	
Units: Subjects				
Any Drowsiness, D1 [N=330;324;330]	95	80	69	
Any Irritability, D1 [N=330;324;330]	123	120	116	
Any Loss of appet., D1 [N=330;324;330]	77	86	76	
Any Fever/Axillary, D1 [N=330;324;330]	137	152	103	
Any Drowsiness, D2 [N=321;321;322]	53	47	53	
Any Irritability, D2 [N=321;321;322]	96	100	103	
Any Loss of appet., D2 [N=321;321;322]	69	72	59	
Any Fever/Axillary, D2 [N=321;321;322]	131	144	102	
Any Drowsiness, D3 [N=321;321;321]	43	32	28	
Any Irritability, D3 [N=321;321;321]	77	70	61	
Any Loss of appet., D3 [N=321;321;321]	65	57	36	
Any Fever/Axillary, D3 [N=321;321;321]	93	82	75	
Any Drowsiness, Across [N=330;324;330]	124	102	99	
Any Irritability, Across [N=330;324;330]	171	166	163	
Any Loss of appet., Across [N=330;324;330]	131	136	114	
Any Fever/Axillary, Across [N=330;324;330]	217	217	183	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with unsolicited adverse events (AEs).

End point title	Number of subjects with unsolicited adverse events (AEs).
End point description:	
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 after any dose.

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	330	324	330	
Units: Subjects				
AEs	98	114	110	

### 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).
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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
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End point timeframe:

During the entire study period (from Month 0 to Month 4/5)

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	330	324	330	
Units: Subjects				
SAEs	6	3	4	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentrations of antibodies against anti-PT, anti-FHA and anti-PRN antigens

End point title	Concentrations of antibodies against anti-PT, anti-FHA and anti-PRN antigens
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End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in EL.U/mL.

End point type	Secondary
End point timeframe:	
At Month 0 [PRE] and Month 3 (for Infanrix-IPV+Hib 1 Group and Infanrix-Hib + Poliorix Group) and Month 4 (for Infanrix-IPV+Hib 2 Group) [POST]	

End point values	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	157	151	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, PRE [N=147;157;151]	2.9 (2.8 to 3.1)	2.7 (2.6 to 2.8)	2.8 (2.6 to 2.9)	
Anti-PT, POST [N=147;156;148]	108.7 (99.2 to 119.1)	114.7 (105.4 to 124.8)	97.1 (88.3 to 106.8)	
Anti-FHA, PRE [N=147;157;151]	2.9 (2.7 to 3.1)	2.6 (2.5 to 2.7)	2.9 (2.7 to 3.1)	
Anti-FHA, POST [N=147;156;148]	87.7 (79.9 to 96.3)	87.6 (79.6 to 96.4)	76.3 (68.5 to 85)	
Anti-PRN, PRE [N=147;157;151]	2.6 (2.5 to 2.7)	2.6 (2.5 to 2.6)	2.5 (2.5 to 2.6)	
Anti-PRN, POST [N=147;156;148]	44.8 (42 to 47.9)	43.7 (41.3 to 46.3)	43.2 (39.8 to 47)	

## 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. Unsolicited AEs: during the 31-day (Days 0-30) post-vaccination period. SAEs: during the entire study period (from Month 0 up to Month 4/5).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

### Reporting groups

Reporting group title	Infanrix-IPV+Hib 1 Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right thigh.

Reporting group title	Infanrix-IPV+Hib 2 Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-IPV+Hib vaccine at 3, 4 and 5 months of age, administered intramuscularly in the upper side of the right thigh.

Reporting group title	Infanrix-Hib + Poliorix Group
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Reporting group description:

Healthy male or female infants, between and including 60 and 90 days of age at the time of the first study visit, received 3 doses of Infanrix-Hib vaccine co-administered with Poliorix vaccine at 2, 3 and 4 months of age, administered intramuscularly in the upper side of the right or left thigh, respectively.

Serious adverse events	Infanrix-IPV+Hib 1 Group	Infanrix-IPV+Hib 2 Group	Infanrix-Hib + Poliorix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 330 (1.82%)	3 / 324 (0.93%)	4 / 330 (1.21%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 330 (0.30%)	1 / 324 (0.31%)	0 / 330 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 330 (0.00%)	0 / 324 (0.00%)	1 / 330 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Hepatitis neonatal			
subjects affected / exposed	0 / 330 (0.00%)	1 / 324 (0.31%)	0 / 330 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	3 / 330 (0.91%)	2 / 324 (0.62%)	1 / 330 (0.30%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 330 (0.61%)	0 / 324 (0.00%)	0 / 330 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 330 (0.00%)	0 / 324 (0.00%)	1 / 330 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 330 (0.00%)	0 / 324 (0.00%)	1 / 330 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 330 (0.30%)	0 / 324 (0.00%)	0 / 330 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 330 (0.30%)	0 / 324 (0.00%)	0 / 330 (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
Malnutrition			
subjects affected / exposed	1 / 330 (0.30%)	0 / 324 (0.00%)	0 / 330 (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 %

<b>Non-serious adverse events</b>	<b>Infanrix-IPV+Hib 1 Group</b>	<b>Infanrix-IPV+Hib 2 Group</b>	<b>Infanrix-Hib + Poliorix Group</b>
Total subjects affected by non-serious adverse events			
subjects affected / exposed	279 / 330 (84.55%)	277 / 324 (85.49%)	272 / 330 (82.42%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	19 / 330 (5.76%)	24 / 324 (7.41%)	17 / 330 (5.15%)
occurrences (all)	19	24	17
Nasopharyngitis			
subjects affected / exposed	42 / 330 (12.73%)	46 / 324 (14.20%)	50 / 330 (15.15%)
occurrences (all)	42	46	50
Pain			
subjects affected / exposed	90 / 330 (27.27%)	91 / 324 (28.09%)	102 / 330 (30.91%)
occurrences (all)	90	91	102
Redness			
subjects affected / exposed	28 / 330 (8.48%)	34 / 324 (10.49%)	26 / 330 (7.88%)
occurrences (all)	28	34	26
Swelling			
subjects affected / exposed	14 / 330 (4.24%)	17 / 324 (5.25%)	19 / 330 (5.76%)
occurrences (all)	14	17	19
Drowsiness			
subjects affected / exposed	124 / 330 (37.58%)	102 / 324 (31.48%)	99 / 330 (30.00%)
occurrences (all)	124	102	99
Irritability			
subjects affected / exposed	171 / 330 (51.82%)	166 / 324 (51.23%)	163 / 330 (49.39%)
occurrences (all)	171	166	163
Loss of appetite			
subjects affected / exposed	131 / 330 (39.70%)	136 / 324 (41.98%)	114 / 330 (34.55%)
occurrences (all)	131	136	114
Fever (Axillary)			

subjects affected / exposed occurrences (all)	217 / 330 (65.76%) 217	217 / 324 (66.98%) 217	183 / 330 (55.45%) 183
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	23 / 330 (6.97%) 23	22 / 324 (6.79%) 22	33 / 330 (10.00%) 33

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported