



## Clinical trial results:

**A phase I/II, double-blind, randomized, multicentre study to evaluate the safety and immunogenicity of new formulations of GlaxoSmithKline Biologicals' DTPa-HBV-IPV/Hib vaccine when administered to healthy infants as a primary vaccination course at 2, 3 and 4 months of age.**

### Summary

EudraCT number	2010-021569-58
Trial protocol	FI
Global end of trial date	05 January 2012

### Results information

Result version number	v1
This version publication date	19 April 2016
First version publication date	02 July 2015

### Trial information

#### Trial identification

Sponsor protocol code	113948
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01248884
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 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 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 January 2012
Global end of trial reached?	Yes
Global end of trial date	05 January 2012
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of at least one DTPa-HBVIPV/Hib formulation is non-inferior to the licensed formulation in terms of seroprotection rates to diphtheria, tetanus, hepatitis B and PRP antigens and in terms of antibody geometric mean concentrations (GMCs) for pertussis antigens one month after the third dose of the primary vaccination.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccine remained under medical supervision for 30 minutes after vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 December 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 456
Country: Number of subjects enrolled	Dominican Republic: 265
Worldwide total number of subjects	721
EEA total number of subjects	456

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)	721
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
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## Subject disposition

### Recruitment

Recruitment details:

A total of 721 subjects were enrolled in the study.

### 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:

This study is a double-blind study in which the parent(s)/LAR(s) and investigators were unaware of the treatment administered.

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	GSK217744 Group 1

Arm description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation A vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

Investigational medicinal product name	GSK217744
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses, intramuscular into left thigh

<b>Arm title</b>	GSK217744 Group 2
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Arm description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation B vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Arm type	Experimental
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Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 co-administered doses, intramuscular into right thigh	
Investigational medicinal product name	GSK217744
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses, intramuscular into left thigh	
<b>Arm title</b>	Infanrix hexa Group

Arm description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of **Infanrix hexa™** vaccine, co-administered with **Prevenar 13®** at 2, 3 and 4 months of age. The **Infanrix hexa™** and **Prevenar 13®** vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses, intramuscular into left thigh	
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

<b>Number of subjects in period 1</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Started	240	242	239
Completed	238	239	238
Not completed	2	3	1
Consent withdrawn by subject	1	3	1
Adverse event, non-fatal	1	-	-

## Baseline characteristics

### Reporting groups

Reporting group title	GSK217744 Group 1
Reporting group description:	
Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation A vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.	
Reporting group title	GSK217744 Group 2
Reporting group description:	
Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation B vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.	
Reporting group title	Infanrix hexa Group
Reporting group description:	
Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of Infanrix hexa™ vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.	

Reporting group values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Number of subjects	240	242	239
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	9.7	9.8	9.7
standard deviation	± 1.36	± 1.29	± 1.21
Gender categorical			
Units: Subjects			
Female	119	138	99
Male	121	104	140

Reporting group values	Total		
Number of subjects	721		
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	356		
Male	365		

## End points

### End points reporting groups

Reporting group title	GSK217744 Group 1
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation A vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Reporting group title	GSK217744 Group 2
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation B vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Reporting group title	Infanrix hexa Group
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of Infanrix hexa™ vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

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

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.
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End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-D and anti-T antibody concentrations  $\geq 0.1$  international units per milliliter (IU/mL).

End point type	Primary
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End point timeframe:

At Months 0 and 3

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	214	217	219	
Units: Subjects				
Anti-D at Month 0 [N=200;210;211]	154	165	160	
Anti-D at Month 3 [N=214;217;219]	214	217	219	
Anti-T at Month 0 [N=200;210;211]	197	206	209	
Anti-T at Month 3 [N=214;217;219]	214	217	219	

### Statistical analyses



<b>Statistical analysis title</b>	Immune response non-inferiority - anti-D (ELISA)
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.25
upper limit	2.3

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-T
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.25
upper limit	2.3

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-D (ELISA)
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.25
upper limit	2.27

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-T
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group

Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.25
upper limit	2.27

### **Primary: Concentrations for anti-pertussis toxoid (anti-PT) and anti-pertactin (anti-PRN) antibodies.**

End point title	Concentrations for anti-pertussis toxoid (anti-PT) and anti-pertactin (anti-PRN) antibodies.
End point description:	Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was $\geq 5$ enzyme-linked immunosorbent assay (ELISA) units per milliliters (EL.U/mL).
End point type	Primary
End point timeframe:	At Months 0 and 3.

<b>End point values</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	215	217	219	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT at Month 0 [N=199;210;210]	3.3 (3 to 3.6)	3.4 (3.1 to 3.7)	3.1 (2.9 to 3.4)	
Anti-PT at Month 3 [N=215;217;218]	57.7 (52.9 to 62.9)	57.5 (53.1 to 62.4)	73.2 (67.7 to 79.2)	
Anti-PRN at Month 0 [N=200;210;210]	5.1 (4.5 to 5.9)	4.9 (4.3 to 5.5)	4.9 (4.3 to 5.7)	
Anti-PRN at Month 3 [N=214;215;219]	76.6 (68.1 to 86.3)	65.7 (58.9 to 73.3)	106.6 (96.6 to 117.8)	

### **Statistical analyses**

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PT
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group

Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	1.26
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.11
upper limit	1.44

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PRN
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	1.33
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.14
upper limit	1.54

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PT
Comparison groups	Infanrix hexa Group v GSK217744 Group 2
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	1.25
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.1
upper limit	1.43

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PRN
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group

Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	1.58
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.37
upper limit	1.84

**Primary: Number of seroprotected subjects for anti-polyribosyl-ribitol-phosphate (anti-PRP) antibodies.**

End point title	Number of seroprotected subjects for anti-polyribosyl-ribitol-phosphate (anti-PRP) antibodies.
End point description:	
A seroprotected subject was defined as a vaccinated subject who had anti-PRP antibody concentrations $\geq 0.15$ micrograms per milliliter ( $\mu\text{g/mL}$ ).	
End point type	Primary
End point timeframe:	
At Month 3.	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	214	216	218	
Units: Subjects				
Anti-PRP	197	190	193	

**Statistical analyses**

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PRP
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	-3.52
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-10.19
upper limit	3

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-PRP
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0.57
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-6.53
upper limit	7.7

**Primary: Number of subjects with anti-hepatitis B (anti-HBs) antibody concentration equal to or above ( $\geq$ ) 10 and 100 milli-International units per milliliter (mIU/mL).**

End point title	Number of subjects with anti-hepatitis B (anti-HBs) antibody concentration equal to or above ( $\geq$ ) 10 and 100 milli-International units per milliliter (mIU/mL).
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End point description:

A decrease in the specificity of the anti-HB enzyme-linked immunosorbent assay (ELISA) had been observed in some studies for low levels of antibody (10-100 mIU/mL). All the available blood samples initially tested with ELISA were re-tested using the Chemi Luminescence Immuno Assay (CLIA) approved by the US Food and Drug Administration (FDA). The table shows updated results following partial or complete retesting/reanalysis.

End point type	Primary
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End point timeframe:

At Month 3.

<b>End point values</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	202	205	209	
Units: Subjects				
Anti-HBs $\geq$ 10 mIU/mL	197	203	205	
Anti-HBs $\geq$ 100 mIU/mL	184	183	196	

**Statistical analyses**

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-HBs(ELISA)
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group

Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0.56
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.27
upper limit	4.63

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-HBs(ELISA)
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	-0.94
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.57
upper limit	2.36

### Primary: Concentrations for anti-HBs antibodies $\geq 10$ and 100 mIU/mL.

End point title	Concentrations for anti-HBs antibodies $\geq 10$ and 100 mIU/mL.
End point description:	A decrease in the specificity of the anti-HB enzyme-linked immunosorbent assay (ELISA) had been observed in some studies for low levels of antibody (10-100 mIU/mL). All the available blood samples initially tested with ELISA were re-tested using the Chemi Luminescence Immuno Assay (CLIA) approved by the US Food and Drug Administration (FDA). The table shows updated results following partial or complete retesting/reanalysis. Concentrations were expressed as geometric mean concentrations (GMCs) in milli-International units per milliliter (mIU/mL).
End point type	Primary
End point timeframe:	
At Month 3.	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	202	205	209	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	639.5 (523.6 to 781.2)	602.6 (492.1 to 737.9)	799 (662.2 to 964)	

## Statistical analyses

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-HBs
Comparison groups	GSK217744 Group 1 v Infanrix hexa Group
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	-0.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.62
upper limit	3.8

<b>Statistical analysis title</b>	Immune response non-inferiority - anti-HBs
Comparison groups	GSK217744 Group 2 v Infanrix hexa Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	-0.92
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-5.07
upper limit	3.02

## 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.
End point description: Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.1 IU/mL.	
End point type	Secondary
End point timeframe: At Months 0 and 3.	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	214	217	219	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D at Month 0 [N=200;210;211]	0.292 (0.247 to 0.347)	0.281 (0.238 to 0.332)	0.29 (0.245 to 0.343)	
Anti-D at Month 3 [N=214;217;219]	1.499 (1.367 to 1.644)	1.704 (1.564 to 1.856)	1.839 (1.686 to 2.005)	
Anti-T at Month 0 [N=200;210;211]	0.936 (0.832 to 1.053)	0.92 (0.822 to 1.029)	0.907 (0.812 to 1.013)	
Anti-T at Month 3 [N=214;217;219]	1.761 (1.624 to 1.91)	1.726 (1.597 to 1.865)	1.947 (1.818 to 2.085)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT) and anti-pertactin (anti-PRN) antibodies.

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT) and anti-pertactin (anti-PRN) antibodies.
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End point description:

A seropositive subject was defined as a vaccinated subject who had anti-PT and anti-PRN antibody concentrations  $\geq 5$  EL.U/mL.

End point type	Secondary
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End point timeframe:

At Months 0 and 3.

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	214	217	219	
Units: Subjects				
Anti-PT at Month 0 [N=200;210;211]	33	38	31	
Anti-PT at Month 3 [N=214;217;219]	215	217	218	
Anti-PRN at Month 0 [N=200;210;211]	84	89	76	
Anti-PRN at Month 3 [N=214;217;219]	214	215	219	

### Statistical analyses



No statistical analyses for this end point

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

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

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was  $\geq 0.15$   $\mu\text{g/mL}$ .

End point type	Secondary
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End point timeframe:

At Month 3.

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	214	216	218	
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP	0.951 (0.793 to 1.142)	0.73 (0.606 to 0.88)	1.082 (0.884 to 1.324)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.

End point title	Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.
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End point description:

A seropositive subject was defined as a vaccinated subject who had anti- pneumococcal antibody concentrations  $\geq 0.15$  micrograms per milliliter ( $\mu\text{g/mL}$ ). The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

End point type	Secondary
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End point timeframe:

At Month 3.

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	112	114	
Units: Subjects				
Anti- PNE 1 [N=107;112;112]	107	112	111	
Anti- PNE 3 [N=106;105;107]	106	105	107	

Anti- PNE 4 [N=108;112;114]	108	112	114	
Anti- PNE 5 [N=108;111;112]	107	109	109	
Anti- PNE 6A [N=108;112;114]	108	111	112	
Anti- PNE 6B [N=107;112;113]	97	104	102	
Anti- PNE 7F [N=108;112;114]	107	111	114	
Anti- PNE 9V [N=108;112;114]	107	112	113	
Anti- PNE 14 [N=108;112;114]	108	112	114	
Anti- PNE 18C [N=108;112;113]	106	112	109	
Anti- PNE 19A [N=106;112;114]	106	112	114	
Anti- PNE 19F [N=108;112;114]	107	111	114	
Anti- PNE 23F [N=108;112;114]	103	104	108	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations for anti-PNE antibodies.

End point title	Concentrations for anti-PNE antibodies.
End point description:	
Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity cut-off of the assay was 0.15 µg /mL. The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.	
End point type	Secondary
End point timeframe:	
At Month 3.	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	112	114	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti- PNE 1 [N=107;112;112]	1.61 (1.42 to 1.83)	1.48 (1.32 to 1.67)	1.58 (1.38 to 1.81)	
Anti- PNE 3 [N=106;105;107]	0.91 (0.8 to 1.03)	0.91 (0.82 to 1.01)	0.94 (0.84 to 1.05)	
Anti- PNE 4 [N=108;112;114]	1.8 (1.61 to 2.03)	1.62 (1.47 to 1.8)	1.69 (1.5 to 1.9)	
Anti- PNE 5 [N=108;111;112]	0.79 (0.69 to 0.89)	0.77 (0.69 to 0.87)	0.82 (0.72 to 0.93)	
Anti- PNE 6A [N=108;112;114]	1.63 (1.39 to 1.91)	1.43 (1.23 to 1.66)	1.52 (1.3 to 1.79)	
Anti- PNE 6B [N=107;112;113]	0.66 (0.53 to 0.82)	0.64 (0.52 to 0.78)	0.69 (0.56 to 0.85)	
Anti- PNE 7F [N=108;112;114]	2.18 (1.91 to 2.49)	2.3 (2.05 to 2.59)	2.48 (2.2 to 2.79)	
Anti- PNE 9V [N=108;112;114]	1.12 (0.97 to 1.28)	1.11 (0.99 to 1.25)	1.16 (1.02 to 1.32)	

Anti- PNE 14 [N=108;112;114]	7.47 (6.33 to 8.81)	7.8 (6.79 to 8.96)	8.03 (6.81 to 9.48)	
Anti- PNE 18C [N=108;112;113]	1.56 (1.33 to 1.84)	1.55 (1.39 to 1.74)	1.56 (1.33 to 1.82)	
Anti- PNE 19A [N=106;112;114]	2.7 (2.35 to 3.09)	2.75 (2.4 to 3.15)	2.68 (2.38 to 3.03)	
Anti- PNE 19F [N=108;112;114]	2.55 (2.16 to 3)	2.53 (2.19 to 2.92)	2.79 (2.44 to 3.18)	
Anti- PNE 23F [N=108;112;114]	0.89 (0.73 to 1.09)	0.83 (0.69 to 1.01)	0.91 (0.75 to 1.1)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with a vaccine response to PT and PRN.

End point title	Number of subjects with a vaccine response to PT and PRN.
End point description:	
Vaccine response defined as: for initially seronegative subjects, antibody concentration $\geq 5$ EL.U/mL at 1 month post primary vaccination (Month 3); for initially seropositive subjects, antibody concentration at 1 month post primary vaccination (Month 3) $\geq 1$ fold the pre-vaccination antibody concentration.	
End point type	Secondary
End point timeframe:	
At Month 3.	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	199	210	210	
Units: Subjects				
Anti- PT [N=199;210;209]	195	204	207	
Anti- PRN 3 [N=199;208;210]	181	194	198	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any solicited local symptoms.

End point title	Number of subjects reporting any solicited local symptoms.
End point description:	
Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade.	
End point type	Secondary
End point timeframe:	
During the 8-day (Days 0-7).	

<b>End point values</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	240	240	238	
Units: Subjects				
Any pain	190	183	155	
Any redness	151	140	128	
Any swelling	124	122	115	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any solicited general symptoms.

End point title	Number of subjects reporting any solicited general symptoms.
End point description: Solicited local symptoms assessed were drowsiness, irritability, loss of appetite and fever [axillary temperature above ( $\geq$ ) 37.5 degrees Celsius ( $^{\circ}$ C)]. Any = occurrence of any local symptom regardless of intensity grade.	
End point type	Secondary
End point timeframe: During the 8-day (Days 0-7).	

<b>End point values</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	240	240	238	
Units: Subjects				
Any drowsiness	188	185	171	
Any irritability	197	205	191	
Any loss of appetite	135	127	112	
Any fever	180	173	140	

### Statistical analyses

No statistical analyses for this end point

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

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

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 = occurrence of an AE regardless of intensity grade or relationship to study vaccination.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) follow up period after vaccination.

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	240	242	239	
Units: Subjects				
Any AEs	153	165	159	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any serious adverse events (SAEs).

End point title	Number of subjects reporting any serious adverse events (SAEs).
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End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Any SAE = any SAE regardless of assessment of relationship to study vaccination.

End point type	Secondary
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End point timeframe:

During the entire study period (Month 0 to Month 3).

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	240	242	239	
Units: Subjects				
Any SAEs	9	5	4	

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 8-day follow-up period after vaccination; unsolicited AEs: 31-day follow-up period after vaccination; SAEs: during the entire study period (Months 0-3).

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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### Reporting groups

Reporting group title	GSK217744 Group 1
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation A vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Reporting group title	GSK217744 Group 2
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of GSK217744 formulation B vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Reporting group title	Infanrix hexa Group
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Reporting group description:

Subjects aged between and including 60 and 90 days of age at the time of first vaccination received 3 doses of Infanrix hexa™ vaccine, co-administered with Prevenar 13® at 2, 3 and 4 months of age. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the left and right sides of the thigh, respectively.

Serious adverse events	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 240 (3.75%)	5 / 242 (2.07%)	4 / 239 (1.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	0 / 240 (0.00%)	1 / 242 (0.41%)	0 / 239 (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
Congenital, familial and genetic disorders			
Scaphocephaly			

subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 240 (0.00%)	1 / 242 (0.41%)	0 / 239 (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
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Bronchospasm			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Interstitial lung disease			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Respiratory tract congestion			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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			
Bronchiolitis			
subjects affected / exposed	4 / 240 (1.67%)	0 / 242 (0.00%)	3 / 239 (1.26%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 240 (0.42%)	1 / 242 (0.41%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Amoebiasis			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Pyelonephritis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 242 (0.41%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 242 (0.00%)	0 / 239 (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
Tonsillitis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 242 (0.41%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	197 / 240 (82.08%)	205 / 242 (84.71%)	191 / 239 (79.92%)
General disorders and administration site conditions			
Injection site induration			
subjects affected / exposed	22 / 240 (9.17%)	14 / 242 (5.79%)	25 / 239 (10.46%)
occurrences (all)	22	14	25
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	190 / 240 (79.17%)	183 / 242 (75.62%)	155 / 239 (64.85%)
occurrences (all)	190	183	155
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	151 / 240 (62.92%)	140 / 242 (57.85%)	128 / 239 (53.56%)
occurrences (all)	151	140	128



Swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all)	124 / 240 (51.67%) 124	122 / 242 (50.41%) 122	115 / 239 (48.12%) 115
Drowsiness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	188 / 240 (78.33%) 188	185 / 242 (76.45%) 185	171 / 239 (71.55%) 171
Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	197 / 240 (82.08%) 197	205 / 242 (84.71%) 205	191 / 239 (79.92%) 191
Loss of appetite alternative assessment type: Systematic subjects affected / exposed occurrences (all)	135 / 240 (56.25%) 135	127 / 242 (52.48%) 127	112 / 239 (46.86%) 112
Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)	180 / 240 (75.00%) 180	173 / 242 (71.49%) 173	140 / 239 (58.58%) 140
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	8 / 240 (3.33%) 8	7 / 242 (2.89%) 7	14 / 239 (5.86%) 14
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	13 / 240 (5.42%) 13	13 / 242 (5.37%) 13	21 / 239 (8.79%) 21
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 240 (2.92%) 7	14 / 242 (5.79%) 14	8 / 239 (3.35%) 8
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	53 / 240 (22.08%) 53	64 / 242 (26.45%) 64	51 / 239 (21.34%) 51

Upper respiratory tract infection subjects affected / exposed occurrences (all)	14 / 240 (5.83%) 14	21 / 242 (8.68%) 21	15 / 239 (6.28%) 15
Rhinitis subjects affected / exposed occurrences (all)	18 / 240 (7.50%) 18	14 / 242 (5.79%) 14	8 / 239 (3.35%) 8

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2011	<p>Due to slow recruitment, the study from now on will also be conducted in countries outside Europe.</p> <p>In order to allow recruitment in other countries, hepatitis b vaccination at birth will now be allowed and preferred route for recording temperature in this study will be axillary or rectal.</p> <p>In countries outside Finland, Prevenar 13 will not be associated with any clinical endpoints.</p> <p>Due to the multi-country approach, one of the statistical methods has been updated.</p>
19 September 2011	<p>The protocol is being amended to allow a preliminary descriptive analysis of the available immunogenicity data. In order to ensure validity of the study results and integrity of data, the preliminary analysis will be performed by a statistician not otherwise involved with the conduct of the study, and results will be shared only with a restricted group of individuals within GSK Biologicals. The study team and the investigators will remain blinded until the study end.</p> <p>The 95% confidence interval (CI) criteria in the primary objectives have been updated to 97.5% CI to reflect the adjustment for multiplicity planned in the sample size consideration and to align to the wording used in the Booster DTPAHBV-IPV-125 (114843) protocol.</p> <p>A sequential list will be generated to allocate treatment numbers to the Prevenar 13 doses. The same has been reflected in the Randomization of supplies section.</p> <p>At the discretion of GSK Biologicals, pneumococcal testing may be done at a GSK Biologicals laboratory or the World Health Organisation (WHO) reference laboratory. Since the 22F-inhibition ELISA assay used at the WHO reference laboratory has a different assay cut-off, different thresholds are mentioned in the statistical analysis description. The threshold for the 22F-inhibition non-GSK ELISA assay performed at the WHO reference laboratory is 0.35 µg/ml.</p>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported