



## Clinical trial results:

**An open, phase IV, multicentre study to assess the long-term persistence of antibodies against hepatitis B and the immune response to a hepatitis B vaccine challenge in healthy children 4-6 years old, previously vaccinated with 4 doses of GlaxoSmithKline (GSK) Biologicals' DTPa-HBV-IPV/Hib vaccine, in clinical trials conducted by GSK Biologicals.**

### Summary

EudraCT number	2006-000553-22
Trial protocol	DE
Global end of trial date	27 April 2007

### Results information

Result version number	v2 (current)
This version publication date	31 July 2016
First version publication date	10 December 2014
Version creation reason	• Correction of full data set Data (typos) were corrected.

### Trial information

#### Trial identification

Sponsor protocol code	106745
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00335881
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	09 May 2007
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 April 2007
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the anti-HBs antibody response to a challenge dose of HBV vaccine in subjects aged 4-6 years, previously primed and boosted with 4 doses of Infanrix hexa in the first two years of life.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always 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	02 June 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 203
Worldwide total number of subjects	203
EEA total number of subjects	203

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)	0
Children (2-11 years)	203
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	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Arm title	Engerix-B Kinder Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Engerix™-B Kinder
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects previously vaccinated with 4 doses of Infanrix hexa™ vaccine in the first 2 years of life received a dose of Engerix™-B Kinder.

Number of subjects in period 1	Engerix-B Kinder Group
Started	203
Completed	201
Not completed	2
Consent withdrawn by subject	1
Unspecified	1

## Baseline characteristics

### Reporting groups

Reporting group title	Engerix-B Kinder Group
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Reporting group description: -

Reporting group values	Engerix-B Kinder Group	Total	
Number of subjects	203	203	
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: years			
geometric mean	4.6		
standard deviation	± 0.48	-	
Gender categorical Units: Subjects			
Female	89	89	
Male	114	114	

## End points

### End points reporting groups

Reporting group title	Engerix-B Kinder Group
Reporting group description: -	

### Primary: Number of subjects with anti-HBs antibody concentrations $\geq 100$ mIU/mL

End point title	Number of subjects with anti-HBs antibody concentrations $\geq 100$ mIU/mL <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

1 month after challenge dose of Engerix™-B Kinder vaccine

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: Subjects				
Anti-Hbs 100mIU/mL	173			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations $\geq 10$ mIU/mL

End point title	Number of subjects with anti-HBs antibody concentrations $\geq 10$ mIU/mL
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End point description:

End point type	Secondary
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End point timeframe:

1 month after challenge dose of Engerix™-B Kinder vaccine

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: Subjects				
Anti-HBs 10 mIU/mL	185			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations
End point description:	
End point type	Secondary
End point timeframe:	
1 month after challenge dose of Engerix™-B Kinder vaccine	

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	7981.4 (5693.5 to 11188.7)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations above or equal the set cut-off values

End point title	Number of subjects with anti-HBs antibody concentrations above or equal the set cut-off values
End point description:	
The cut-off values assessed were $\geq 10$ mIU/mL and $\geq 100$ mIU/mL.	
End point type	Secondary
End point timeframe:	
Before challenge dose of Engerix™-B Kinder vaccine	

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Subjects				
Anti-HBs 10 mIU/mL	171			
Anti-HBs 100 mIU/mL	106			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations
End point description:	
End point type	Secondary
End point timeframe:	
Before challenge dose of HBV vaccine	

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs antibody concentrations	110.8 (85.3 to 143.9)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-diphtheria (anti-D) and anti -tetanus (anti-T) antibody concentrations $\geq 0.1$ IU/mL

End point title	Number of subjects with anti-diphtheria (anti-D) and anti -tetanus (anti-T) antibody concentrations $\geq 0.1$ IU/mL
End point description:	
End point type	Secondary

End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Subjects				
Anti-D	136			
Anti-T	148			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-polyribosyl ribitol phosphate (anti-PRP) antibody concentration $\geq 0.15 \mu\text{g/mL}$ and $\geq 1 \mu\text{g/mL}$

End point title	Number of subjects with anti-polyribosyl ribitol phosphate (anti-PRP) antibody concentration $\geq 0.15 \mu\text{g/mL}$ and $\geq 1 \mu\text{g/mL}$
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End point description:

End point type	Secondary
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End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Subjects				
Anti-PRP $\geq 0.15 \mu\text{g/mL}$	194			
Anti-PRP $\geq 1 \mu\text{g/mL}$	140			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-poliovirus types 1, 2 and 3 antibody titres $\geq 8$ .

End point title	Number of subjects with anti-poliovirus types 1, 2 and 3 antibody titres $\geq 8$ .
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End point description:

End point type	Secondary
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End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	187			
Units: Subjects				
Anti-polio 1 (N = 185)	177			
Anti-polio 2 (N = 187)	179			
Anti-polio 3 (N = 174)	170			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentration $\geq 5$ EL.U/mL.

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentration $\geq 5$ EL.U/mL.
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End point description:

End point type	Secondary
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End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Subjects				
Anti-PT (N=197)	50			
Anti-FHA (N=197)	192			
Anti-PRN (N=198)	180			

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of subjects with solicited local symptoms**

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End point title	Number of subjects with solicited local symptoms
End point description: The solicited local symptoms assessed were pain, redness and swelling.	
End point type	Secondary
End point timeframe: During the 4-day (Day 0-3) follow-up period after the challenge dose of Engerix™-B Kinder vaccine	

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<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	202			
Units: Subjects				
Pain	53			
Redness	70			
Swelling	36			

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of subjects with solicited general symptoms**

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End point title	Number of subjects with solicited general symptoms
End point description: The solicited general symptoms assessed were drowsiness, fever (defined as axillary temperature >37.5C), irritability and loss of appetite.	
End point type	Secondary
End point timeframe: During the 4-day (Day 0-3) follow-up period after the challenge dose of Engerix™-B Kinder vaccine	

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<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	202			
Units: Subjects				
Drowsiness	32			
Fever	9			
Irritability	14			
Loss of appetite	19			

## 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).
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End point description:

An unsolicited AE was 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.

End point type	Secondary
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End point timeframe:

During the 31-day (Day 0-30) follow-up period after the challenge dose of Engerix™-B Kinder vaccine

End point values	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	203			
Units: Subjects				
Subjects with any AEs	41			

## 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:

End point type	Secondary
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End point timeframe:

During the entire study period (from Day 0 to Day 30).

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	203			
Units: Subjects				
Subjects with any SAEs	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-D and anti-T antibody concentrations.

End point title	Anti-D and anti-T antibody concentrations.
End point description:	
Concentrations were expressed as geometric mean concentrations (GMCs) in IU/mL.	
End point type	Secondary
End point timeframe:	
Before challenge dose of Engerix™-B Kinder vaccine	

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	0.189 (0.158 to 0.225)			
Anti-T	0.196 (0.168 to 0.229)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentration.

End point title	Anti-PRP antibody concentration.
End point description:	
Concentrations were expressed as geometric mean concentrations (GMCs) in µg/mL.	
End point type	Secondary
End point timeframe:	
Before challenge dose of Engerix™-B Kinder vaccine	

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	1.813 (1.514 to 2.17)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations.

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations.
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End point description:

Concentrations were expressed as geometric mean concentrations (GMCs) in EL.U/mL.

End point type	Secondary
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End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=197)	3.7 (3.3 to 4.1)			
Anti-FHA (N=197)	49.6 (40.8 to 60.3)			
Anti-PRN (N=198)	20.6 (17.5 to 24.3)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-poliovirus types 1, 2 & 3 antibody titres.

End point title	Anti-poliovirus types 1, 2 & 3 antibody titres.
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End point description:

Titres (anti-polio) were expressed as geometric mean titres (GMTs).

End point type	Secondary
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End point timeframe:

Before challenge dose of Engerix™-B Kinder vaccine

<b>End point values</b>	Engerix-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	187			
Units: titres				
geometric mean (confidence interval 95%)				
Anti-polio 1 (N=185)	87.2 (72 to 105.7)			
Anti-polio 2 (N=187)	84.5 (70.5 to 101.3)			
Anti-polio 3 (N=174)	158.7 (128.5 to 195.9)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 4-day follow-up period after vaccination (Day 0 - Day 3); Unsolicited AEs: 31-day follow-up period after vaccination (Day 0 - Day 30); SAEs: during the entire study period.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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### Reporting groups

Reporting group title	Engerix-B Kinder Group
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Reporting group description: -

Serious adverse events	Engerix-B Kinder Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 202 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Engerix-B Kinder Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 202 (34.65%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	53 / 202 (26.24%)		
occurrences (all)	53		
Redness			
subjects affected / exposed	70 / 202 (34.65%)		
occurrences (all)	70		
Swelling			
subjects affected / exposed	36 / 202 (17.82%)		
occurrences (all)	36		
Drowsiness			

subjects affected / exposed	32 / 202 (15.84%)		
occurrences (all)	32		
Irritability			
subjects affected / exposed	14 / 202 (6.93%)		
occurrences (all)	14		
Loss of appetite			
subjects affected / exposed	19 / 202 (9.41%)		
occurrences (all)	19		

## **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