

**Clinical trial results:**

**Persistence of hepatitis B antibodies, immunogenicity and safety of GSK Biologicals' hepatitis B vaccine Engerix<sup>TM</sup>-B Kinder (SKF103860) challenge dose in adolescents vaccinated with four doses of Infanrix<sup>TM</sup> hexa (SB217744) during infancy.**

**Summary**

EudraCT number	2013-002821-41
Trial protocol	DE
Global end of trial date	23 September 2014

**Results information**

Result version number	v2 (current)
This version publication date	20 November 2018
First version publication date	10 July 2015
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Results have been amended to account for consistency with other registries.

**Trial information****Trial identification**

Sponsor protocol code	106793
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02052661
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?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2014
Global end of trial reached?	Yes
Global end of trial date	23 September 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the anti-HBs antibody response, in terms of subjects with antibody concentrations  $\geq 100$  mIU/ml, to a single challenge dose of HBV vaccine (Engerix-B Kinder) in subjects 12–13 years of age, previously vaccinated with four doses of Infanrix hexa in the first two years of life.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2014
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: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	0
Adolescents (12-17 years)	300
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

<b>Arm title</b>	Engerix™-B Kinder Group
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Arm description:

Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Kinder
Investigational medicinal product code	
Other name	HBV vaccine, GlaxoSmithKline (GSK) Biologicals' recombinant hepatitis B vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose of HBV vaccine, administered intramuscularly into the deltoid of the non-dominant arm.

<b>Number of subjects in period 1</b>	Engerix™-B Kinder Group
Started	300
Completed	300

## Baseline characteristics

### Reporting groups

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

Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

Reporting group values	Engerix™-B Kinder Group	Total	
Number of subjects	300	300	
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			
arithmetic mean	12.3		
standard deviation	± 0.5	-	
Gender categorical Units: Subjects			
Female	150	150	
Male	150	150	

## End points

### End points reporting groups

Reporting group title	Engerix™-B Kinder Group
Reporting group description: Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm.	

### Primary: Anti-HBs immune response.

End point title	Anti-HBs immune response. <sup>[1]</sup>
End point description: Anti-HBs immune response was defined as the number of subjects with Anti-HBs antibody concentrations $\geq$ 100 mIU/ml.	
End point type	Primary
End point timeframe: One month after the single challenge dose of Engerix™-B Kinder vaccine (Month 1)	

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	289			
Units: Subjects				
Anti-HBs	272			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib.

End point title	Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib.
End point description: Concentrations were expressed as geometric mean concentrations (GMCs) for the seropositivity cut-off of 6.2 mIU/ml.	
End point type	Secondary
End point timeframe: Before (PRE) and 1 month after (POST) the single 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	293			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE [N=293]	22.7 (18.5 to 27.9)			
Anti-HBs, POST [N=289]	3502.6 (2672 to 4591.5)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml, $\geq 10$ mIU/ml, 10 to $< 100$ mIU/ml and $\geq 100$ mIU/ml

End point title	Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml, $\geq 10$ mIU/ml, 10 to $< 100$ mIU/ml and $\geq 100$ mIU/ml
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End point description:

A seropositive subject was defined as a subject with anti-HBs antibody concentrations  $\geq 6.2$  milli-international units per milliliter (mIU/ml). A seroprotected subjects was defined as a subject with anti-HBs antibody concentrations  $\geq 10$  mIU/ml.

End point type	Secondary
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End point timeframe:

Before the single 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	293			
Units: Subjects				
Anti-HBs $\geq 6.2$ mIU/ml	205			
Anti-HBs $\geq 10$ mIU/ml	178			
Anti-HBs 10 to $< 100$ mIU/ml	116			
Anti-HBs $\geq 100$ mIU/ml	62			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml and $\geq 10$ mIU/ml

End point title	Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml and $\geq 10$ mIU/ml
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End point description:

A seropositive subject was defined as a subject with anti-HBs antibody concentrations  $\geq 6.2$  mIU/ml. A seroprotected subjects was defined as a subject with anti-HBs antibody concentrations  $\geq 10$  mIU/ml.

End point type Secondary

End point timeframe:

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

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Subjects				
Anti-HBs $\geq 6.2$ mIU/ml	283			
Anti-HBs $\geq 10$ mIU/ml	282			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine.

End point title Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine.

End point description:

The amnestic response to the challenge dose was defined as: for initially seronegative subjects, antibody concentration  $\geq 10$ mIU/mL; for initially seropositive subjects, antibody concentration at least four times the pre-challenge antibody concentration.

End point type Secondary

End point timeframe:

One month after the single challenge dose of Engerix™-B Kinder vaccine.

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	287			
Units: Subjects				
Anamnestic response	277			

### Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any solicited local symptoms.
End point description: Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.	
End point type	Secondary
End point timeframe: During the 4-day (Day 0–3) follow-up period after the single 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	300			
Units: Subjects				
Pain	132			
Redness	70			
Swelling	29			

### Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any solicited general symptoms.
End point description: Assessed solicited general symptoms were fatigue, gastrointestinal, headache and temperature [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade.	
End point type	Secondary
End point timeframe: During the 4-day (Day 0–3) follow-up period after the single 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	300			
Units: Subjects				
Fatigue	73			
Gastrointestinal	34			
Headache	71			
Temperature/(Axillary)	7			

## Statistical analyses

No statistical analyses for this end point

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

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

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

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Any AEs	44			

## 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:

From Month 0 to Month 1

End point values	Engerix™-B Kinder Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Any SAEs	2			

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4-day (Day 0–3) follow-up period after vaccination

Unsolicited AEs: during the 31-day (Day 0–30) follow-up period after vaccination

SAEs: During the entire study.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

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

Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.

<b>Serious adverse events</b>	Engerix™-B Kinder Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 300 (0.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 300 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Forearm fracture			
subjects affected / exposed	1 / 300 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Engerix™-B Kinder Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 300 (44.00%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	132 / 300 (44.00%)		
occurrences (all)	132		
Redness			
subjects affected / exposed	70 / 300 (23.33%)		
occurrences (all)	70		
Swelling			
subjects affected / exposed	29 / 300 (9.67%)		
occurrences (all)	29		
Fatigue			
subjects affected / exposed	73 / 300 (24.33%)		
occurrences (all)	73		
Gastrointestinal			
subjects affected / exposed	34 / 300 (11.33%)		
occurrences (all)	34		
Headache			
subjects affected / exposed	71 / 300 (23.67%)		
occurrences (all)	71		

## **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