



## Clinical trial results:

**An open, phase IV, single-group, multicentre study to assess the long-term persistence of antibodies against hepatitis B and the immune response to a hepatitis B (HBV) vaccine challenge in adolescents 12-13 years of age who were vaccinated in infancy with GSK Biologicals' HBV vaccine (Engerix™-B).**

### Summary

EudraCT number	2009-012117-21
Trial protocol	DE
Global end of trial date	07 April 2010

### Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	28 February 2015

### Trial information

#### Trial identification

Sponsor protocol code	112682
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00984139
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	25 October 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 April 2010
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 (Engerix-B Kinder) in subjects 12-13 years of age, vaccinated with three doses of Engerix-B in infancy.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis following the administration of the vaccine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2009
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: 306
Worldwide total number of subjects	306
EEA total number of subjects	306

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)	306
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 Group
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Arm description:

Subjects who were vaccinated with 3 doses of Engerix-B in infancy and who received a single challenge dose of Engerix-B , intramuscularly in the deltoid region of the non-dominant arm, at 12-13 years of age (Day 0).

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

Dosage and administration details:

All subjects received a single-dose of HBV vaccine at 12-13 years of age (Day 0). The vaccine was administered as an intramuscular injection into the deltoid region of the non-dominant arm.

<b>Number of subjects in period 1</b>	Engerix-B Group
Started	306
Completed	306

## Baseline characteristics

### Reporting groups

Reporting group title	Engerix-B Group
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Reporting group description:

Subjects who were vaccinated with 3 doses of Engerix-B in infancy and who received a single challenge dose of Engerix-B , intramuscularly in the deltoid region of the non-dominant arm, at 12-13 years of age (Day 0).

Reporting group values	Engerix-B Group	Total	
Number of subjects	306	306	
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	12.4		
standard deviation	± 0.49	-	
Gender categorical Units: Subjects			
Female	152	152	
Male	154	154	

## End points

### End points reporting groups

Reporting group title	Engerix-B Group
Reporting group description: Subjects who were vaccinated with 3 doses of Engerix-B in infancy and who received a single challenge dose of Engerix-B , intramuscularly in the deltoid region of the non-dominant arm, at 12-13 years of age (Day 0).	

### Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations as measured by ELISA equal to or above cut-off value

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations as measured by ELISA equal to or above cut-off value <sup>[1]</sup>
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End point description:

The cut-off value was defined as 100 milli-international units per milliliter (mIU/mL).

End point type	Primary
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End point timeframe:

One month after the challenge dose (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 Group			
Subject group type	Reporting group			
Number of subjects analysed	284			
Units: Subjects				
post challenge dose 100 mIU/mL [Units:subjects]	266			

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations as measured by ChemiLuminescence ImmunoAssay (CLIA) equal to or above cut-off value.

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations as measured by ChemiLuminescence ImmunoAssay (CLIA) equal to or above cut-off value. <sup>[2]</sup>
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End point description:

The cut-off value was defined as 100 milli-international units per milliliter (mIU/mL).

End point type	Primary
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End point timeframe:

One month after the challenge dose (Month 1)

Notes:

[2] - 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 Group			
Subject group type	Reporting group			
Number of subjects analysed	276			
Units: Subjects				
post challenge dose 100 mIU/mL [Units:Subjects]	257			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations as measured by ELISA equal to or above cut-off values

End point title	Number of subjects with anti-HBs antibody concentrations as measured by ELISA equal to or above cut-off values
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End point description:

The cut-off values were defined as 3.3 mIU/mL, 10 mIU/mL and 100 mIU/mL. Note: the number of subjects with anti-HBs antibody concentrations equal to or above 100 mIU/mL on month post-challenge dose data are presented as a primary outcome measure.

End point type	Secondary
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End point timeframe:

Before (Day 0) and one month (Month 1) after the challenge dose

End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	284			
Units: Subjects				
pre challenge dose 3.3 mIU/mL (N=282)	259			
post challenge dose 3.3 mIU/mL (N=284)	283			
pre challenge dose 10 mIU/mL (N=282)	220			
post challenge dose 10 mIU/mL (N=284)	281			
pre challenge dose 100 mIU/mL (N=282)	70			

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of subjects with anti-HBs antibody concentrations as measured by CLIA equal to or above cut-off values**

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End point title	Number of subjects with anti-HBs antibody concentrations as measured by CLIA equal to or above cut-off values
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End point description:

The cut-off values were defined as 6.2 mIU/mL, 10 mIU/mL and 100 mIU/mL. Note: the number of subjects with anti-HBs antibody concentrations equal to or above 100 mIU/mL on month post-challenge dose data are presented as a primary outcome measure.

End point type	Secondary
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End point timeframe:

Before (Day 0) and one month (Month 1) after the challenge dose

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End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: Subjects				
pre challenge dose 6.2 mIU/mL (N=279)	201			
post challenge dose 6.2 mIU/mL (N=276)	271			
pre challenge dose 10 mIU/mL (N=279)	181			
post challenge dose 10 mIU/mL (N=276)	271			
pre challenge dose 100 mIU/mL (N=279)	67			

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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 local and general symptoms**

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End point title	Number of subjects with solicited local and general symptoms
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End point description:

Solicited local symptoms were pain, redness and swelling. Solicited general symptoms were fatigue, gastrointestinal symptoms, headache and fever. Fever was defined as axillary temperature greater than or equal to 37.5 degrees Celsius.

End point type	Secondary
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End point timeframe:

During the 4-day (Day 0-3) follow-up period following the challenge dose vaccination

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End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	306			
Units: Subjects				
pain	104			
redness	56			
swelling	26			
fatigue	63			
gastrointestinal symptoms	14			
headache	56			
fever	9			

## 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)
End point description:	
SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.	
End point type	Secondary
End point timeframe:	
After the challenge dose of the vaccine (Day 0) up to the study end (Month 1)	

End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	306			
Units: Subjects				
Number of subjects with serious adverse events [Un	0			

## 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:	
Unsolicited AE covers any AE 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



End point timeframe:

During the 31-day (Day 0-30) follow-up period following the challenge dose vaccination

End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	306			
Units: Subjects				
Number of subjects with unsolicited adverse events	64			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anamnestic response to the challenge dose as measured by ELISA.

End point title	Number of subjects with anamnestic response to the challenge dose as measured by ELISA.
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End point description:

Anamnestic response was defined as: - At least (i.e. greater than or equal to) a 4-fold rise in post-challenge vaccine dose anti-HBs antibody concentrations in subjects seropositive (i.e. with anti-HBs antibody concentration equal to or greater than 3.3 mIU/mL) at the pre-challenge dose time point. - Post-challenge dose anti-HBs antibody concentrations equal to or greater than 10 mIU/mL in subjects seronegative (i.e. with anti-HBs antibody concentrations less than 3.3 mIU/mL) at the pre-challenge dose time point.

End point type	Secondary
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End point timeframe:

One month after the challenge dose (Month 1)

End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	282			
Units: Subjects				
post challenge dose 3.3 mIU/mL [Units:subjects]	274			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anamnestic response to the challenge dose as measured by CLIA.

End point title	Number of subjects with anamnestic response to the challenge dose as measured by CLIA.
End point description:	
Anamnestic response was defined as: - At least (i.e. greater than or equal to) a 4-fold rise in post-challenge vaccine dose anti-HBs antibody concentrations in subjects seropositive (i.e. with anti-HBs antibody concentration $\geq 6.2$ mIU/mL) at the pre-challenge dose time point. - Post-challenge dose anti-HBs antibody concentrations equal to or greater than 10 mIU/mL in subjects seronegative (i.e. with anti-HBs antibody concentrations $< 6.2$ mIU/mL) at the pre-challenge dose time point.	
End point type	Secondary
End point timeframe:	
One month after the challenge dose (Month 1)	

End point values	Engerix-B Group			
Subject group type	Reporting group			
Number of subjects analysed	271			
Units: Subjects				
post challenge dose 6.2 mIU/mL [Units:Subjects]	267			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms = During the 4-day (Day 0 to Day 3) post-vaccination period.

Unsolicited AEs = During the 31-day (Day 0-30) follow-up period after the HBV challenge dose.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, number of participants at risk included those from Total Vaccinated cohort who had the symptom sheet completed.

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

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	13
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### Reporting groups

Reporting group title	Engerix-B Group
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Reporting group description:

Subjects who were vaccinated with 3 doses of Engerix-B in infancy and who received a single challenge dose of Engerix-B , intramuscularly in the deltoid region of the non-dominant arm, at 12-13 years of age (Day 0).

Serious adverse events	Engerix-B Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 306 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Engerix-B Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 306 (33.99%)		
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	104 / 306 (33.99%)		
occurrences (all)	104		
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	56 / 306 (18.30%)		
occurrences (all)	56		
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 306 (8.50%)		
occurrences (all)	26		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	63 / 306 (20.59%)		
occurrences (all)	63		
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	56 / 306 (18.30%)		
occurrences (all)	56		

## **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