



## 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 children aged 7-8 years of age and previously vaccinated in infancy with GSK Biologicals' HBV vaccine (Engerix™-B).**

### Summary

EudraCT number	2007-002221-76
Trial protocol	DE
Global end of trial date	31 December 2007

### Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	04 December 2014

### Trial information

#### Trial identification

Sponsor protocol code	110474
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00519649
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 December 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2007
Global end of trial reached?	Yes
Global end of trial date	31 December 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 (Engerix-B Kinder) in subjects, 7-8 years of age, previously 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 a rare anaphylactic reaction following the administration of the vaccine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2007
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: 301
Worldwide total number of subjects	301
EEA total number of subjects	301

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)	301
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:

One additional subject, enrolled but not vaccinated, was not included in the number of subjects under "STARTED"

### 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	Group Engerix
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Arm description:

Subjects received a single challenge dose of Engerix™ (hepatitis-B [HBV] vaccine)

Arm type	Experimental
Investigational medicinal product name	Engerix™-B Kinder
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single challenge dose of Engerix™ (hepatitis-B [HBV] vaccine)

Number of subjects in period 1 <sup>[1]</sup>	Group Engerix
Started	300
Completed	299
Not completed	1
Consent withdrawn by subject	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One additional subject, enrolled but not vaccinated, was not included in the number of subjects under "STARTED"

## Baseline characteristics

### Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	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			
geometric mean	7.7		
standard deviation	± 0.46	-	
Gender categorical			
Units: Subjects			
Female	136	136	
Male	164	164	

## End points

### End points reporting groups

Reporting group title	Group Engerix
Reporting group description:	
Subjects received a single challenge dose of Engerix™ (hepatitis-B [HBV] vaccine)	

### Primary: Number of participants with anti-hepatitis B surface antigen (HBs) antibody concentrations above the cut-off value

End point title	Number of participants with anti-hepatitis B surface antigen (HBs) antibody concentrations above the cut-off value <sup>[1]</sup>
End point description:	
Anti-HBs antibody cut-off value assessed was 100 milli-international unit per milliliter (mIU/mL)	
End point type	Primary
End point timeframe:	
One month after the challenge dose of HBV 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	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	280			
Units: Subjects				
anti-(HB)s	275			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with Anti-HBs antibody concentrations above the cut-off value

End point title	Number of participants with Anti-HBs antibody concentrations above the cut-off value
End point description:	
Anti-HBs antibody cut-off values assessed include 3.3, 10 and 100 mIU/mL	
End point type	Secondary
End point timeframe:	
Before challenge dose of HBV vaccine	

End point values	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	282			
Units: Subjects				
>= 3.3 mIU/mL	261			
>= 10 mIU/mL	235			
>= 100 mIU/mL	104			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants reporting Solicited Local Symptoms

End point title	Number of Participants reporting Solicited Local Symptoms
End point description:	
Solicited local symptoms assessed include pain, redness and swelling	
End point type	Secondary
End point timeframe:	
During the 4-day follow-up period after the challenge dose of HBV vaccine.	

End point values	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	299			
Units: Subjects				
Pain	89			
Redness	81			
Swelling	42			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants reporting Solicited General Symptoms

End point title	Number of Participants reporting Solicited General Symptoms
End point description:	
Solicited general symptoms assessed include fatigue, fever, gastrointestinal symptoms, and headache	
End point type	Secondary
End point timeframe:	
During the 4-day follow-up period after the challenge dose of HBV vaccine.	

End point values	Group Egerix			
Subject group type	Reporting group			
Number of subjects analysed	299			
Units: Subjects				
Fatigue	44			
Fever (Axillary)	9			
Gastrointestinal	23			
Headache	40			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants reporting Unsolicited adverse events

End point title	Number of Participants reporting Unsolicited adverse events
End point description: An Adverse Event is 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.	
End point type	Secondary
End point timeframe: During the 31-day follow-up period after the challenge dose of HBV vaccine.	

End point values	Group Egerix			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
Unsolicited adverse events	71			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants reporting serious adverse events (SAE)

End point title	Number of Participants reporting serious adverse events (SAE)
End point description: An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.	
End point type	Secondary
End point timeframe: After the challenge dose of HBV vaccine.	

<b>End point values</b>	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
(SAE)	1			

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse events and Unsolicited Adverse events: During the 31-day follow-up period after HBV challenge dose. Solicited local and general symptoms: During the 4-day follow-up period after the HBV challenge dose.

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	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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### Reporting groups

Reporting group title	Group Engerix
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Reporting group description:

Subjects received a single challenge dose of Engerix™ (hepatitis-B [HBV] vaccine)

Serious adverse events	Group Engerix		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 300 (0.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Concussion			
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 %

Non-serious adverse events	Group Engerix		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 300 (29.67%)		
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			

subjects affected / exposed <sup>[1]</sup>	89 / 299 (29.77%)		
occurrences (all)	89		
Redness			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[2]</sup>	81 / 299 (27.09%)		
occurrences (all)	81		
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[3]</sup>	42 / 299 (14.05%)		
occurrences (all)	42		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[4]</sup>	44 / 299 (14.72%)		
occurrences (all)	44		
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[5]</sup>	23 / 299 (7.69%)		
occurrences (all)	23		
Headache			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[6]</sup>	40 / 299 (13.38%)		
occurrences (all)	40		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: For the solicited local and general symptoms, not all subjects had their symptom sheet completed therefore, the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom sheet completed).

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2007	Protocol Amendment 2 This amendment is being prepared to change the assay cut-off that that was defined as 10 mIU/ml in the original protocol to 3.3 mIU/ml. Additionally the definition of immune memory has also been included to maintain uniformity with other adult studies.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported