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).

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

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

Sponsor protocol code	110474

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

Notes:

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:

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:

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:

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:

Country: Number of subjects enrolled	Germany: 301
Worldwide total number of subjects	301
EEA total number of subjects	301

Notes:

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

Recruitment details: -

Screening details:

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

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

	Group Engerix

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)

	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"

Reporting group title	Overall Study

Reporting group description: -

	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	

Reporting group title	Group Engerix

Reporting group description:

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

End point title	Number of participants with anti-hepatitis B surface antigen (HBs) antibody concentrations above the cut-off value[1]

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

	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	280			
Units: Subjects				
anti-(HB)s	275			

No statistical analyses for this end point

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

	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			

No statistical analyses for this end point

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.	

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

No statistical analyses for this end point

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.	

	Group Engerix			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
(SAE)	1			

No statistical analyses for this end point

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

Dictionary name	MedDRA
Dictionary version	11.0

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

	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 %

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

Were there any global substantial amendments to the protocol? Yes

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:

Were there any global interruptions to the trial? No

None reported