Clinical trial results:
Comparative study of the immunogenicity and protective efficacy of GlaxoSmithKline Biologicals' rec-DNA Hepatitis B vaccine (10µg) with or without Hepatitis B immunoglobulin (HBIG) in newborns of Hepatitis B envelope antigen positive (HBeAg+) mothers

Summary

EudraCT number	2011-004879-36
Trial protocol	Outside EU/EEA
Global end of trial date	18 March 2010

Results information

Result version number	v1 (current)
This version publication date	22 April 2016
First version publication date	22 July 2015

Trial information

Trial identification

Sponsor protocol code	100450

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00240526
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 November 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2010
Global end of trial reached?	Yes
Global end of trial date	18 March 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the anti-HBs persistence up to Year 20 after the first vaccine dose of the primary vaccination.
• To evaluate the prevalence and incidence of other hepatitis B markers (HBsAg, anti-HBc, HBeAg, anti-HBe) up to Year 20 after the first vaccine dose of the primary vaccination.
• To evaluate the clinical significance of the HBsAg positive and anti-HBc positive cases observed during the long-term follow-up of this study.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination 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. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 October 2003
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	Thailand: 79
Worldwide total number of subjects	79
EEA total number of subjects	0

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)	30

Adults (18-64 years)	49
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The baseline characteristics are given for the Year 15 time point. Therefore the number of participants in the Engerix-3D Group is 21, as in the Year 15 participant flow data.

Period 1

Period 1 title	At Year 15 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Engerix 4D + HBIg Group

Arm description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.

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

Dosage and administration details:

3 (Groups A and C) or 4 (Groups B and D) intramuscular injections during the primary study.

Investigational medicinal product name	Hepatitis B immunoglobulin (HBIg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 intramuscular injections at birth (primary study).

Arm title	Engerix 3D + HBIg Group

Arm description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.

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

Dosage and administration details:

3 (Groups A and C) or 4 (Groups B and D) intramuscular injections during the primary study.

Investigational medicinal product name	Hepatitis B immunoglobulin (HBIg)
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 intramuscular injections at birth (primary study).

Arm title	Engerix 4D

Arm description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60.

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

Dosage and administration details:

3 (Groups A and C) or 4 (Groups B and D) intramuscular injections during the primary study.

Arm title	Engerix 3D Group

Arm description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6.

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

Dosage and administration details:

3 (Groups A and C) or 4 (Groups B and D) intramuscular injections during the primary study.

Number of subjects in period 1[1]	Engerix 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D
Started	19	19	14
Completed	19	19	14

Number of subjects in period 1[1]	Engerix 3D Group
Started	21
Completed	21

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: The baseline characteristics are given for subjects who came back at Year 15 time-point of the study.

Baseline characteristics

Reporting groups	
Reporting group title	Engerix 4D + HBIg Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.	
Reporting group title	Engerix 3D + HBIg Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.	
Reporting group title	Engerix 4D
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60.	
Reporting group title	Engerix 3D Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6.	

Reporting group values	Engerix 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D
Number of subjects	19	19	14
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	14.5	14.7	14.6
standard deviation	± 0.51	± 0.45	± 0.5
Gender categorical			
Units: Subjects			
Female	12	7	6
Male	7	12	8

Reporting group values	Engerix 3D Group	Total	
Number of subjects	21	73	
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	14.5		
standard deviation	± 0.51	-	
Gender categorical			
Units: Subjects			
Female	10	35	
Male	11	38	

End points

End points reporting groups

Reporting group title	Engerix 4D + HBIg Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.	
Reporting group title	Engerix 3D + HBIg Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.	
Reporting group title	Engerix 4D
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60.	
Reporting group title	Engerix 3D Group
Reporting group description:	
Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6.	

Primary: Anti-hepatitis B Surface Antigen (Anti-HBs) Antibody Concentration as measured by Enzyme-Linked Immunosorbent Assay (ELISA).

End point title	Anti-hepatitis B Surface Antigen (Anti-HBs) Antibody Concentration as measured by Enzyme-Linked Immunosorbent Assay (ELISA).[1]
End point description:	
Concentrations given as GMC expressed as milli-international unit per millilitre (mIU/mL). Note: At Year 15 and 16, a commercial ELISA was used. From Year 17 to Year 20, anti-HBs antibody concentrations were tested with a validated in-house assay with cut-off 3.3mIU/mL.	
End point type	Primary
End point timeframe:	
At Years 15, 16, 17, 18, 19 and 20	

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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	12	17
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Year 15 (N=17;15;12;17)	118.6 (53.4 to 263.1)	14.8 (6.8 to 32)	142.8 (30.4 to 669.4)	24.2 (10 to 58.7)
Year 16 (N=15;13;12;16)	119.3 (50 to 284.7)	14.1 (6.8 to 29.4)	134.3 (30.1 to 599.8)	22.9 (9.7 to 54.1)
Year 17 (N=17;13;11;13)	140 (67.2 to 291.9)	8.2 (3.9 to 17.1)	70.2 (14.3 to 344.1)	17 (6.7 to 43.3)
Year 18 (N=14;14;10;13)	82.3 (32.1 to 211.3)	10.8 (6.5 to 17.9)	56.5 (11.7 to 271.8)	26.1 (10.7 to 63.3)
Year 19 (N=13;12;8;11)	103.3 (38.9 to 274.7)	9.5 (4 to 22.8)	84.9 (12 to 600.2)	19.9 (7.4 to 53.7)

Year 20 (N=13;13;6;12)	73.9 (26.6 to 205.4)	14.3 (6.7 to 30.6)	297.1 (46 to 1919.5)	16.3 (7.2 to 36.9)

Statistical analyses

No statistical analyses for this end point

Primary: Anti-hepatitis B Surface Antigen (Anti-HBs) Antibody Concentration as measured by ChemiLuminescence ImmunoAssay (CLIA).

End point title	Anti-hepatitis B Surface Antigen (Anti-HBs) Antibody Concentration as measured by ChemiLuminescence ImmunoAssay (CLIA).[2]

End point description:

Concentrations given as GMC expressed as milli-international unit per millilitre (mIU/mL). Note: There was a change of assay kit at Year 19 time-point, thus for the sake of bridging, blood samples corresponding to Year 19 were re-tested with new CLIA. At Year 19 and 20, anti-HBs antibody concentrations tested with the CLIA with cut-off 6.2 mIU/mL.

End point type	Primary

End point timeframe:

At Years 19 and 20

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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	13	7	13
Units: mIU/mL				
geometric mean (confidence interval 95%)				
YEAR 19 (N=14;12;6;11)	60.1 (26.7 to 135.5)	5.8 (3.3 to 10)	159 (32.6 to 776.5)	11.7 (5 to 27.4)
YEAR 20 (N=16;13;7;13)	44 (18.3 to 105.9)	5.1 (3.1 to 8.6)	83.5 (16.2 to 431.7)	9.5 (4.3 to 21.2)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-hepatitis B surface antigen (anti-HBs) Antibody Concentrations Above Pre-defined Cut-off Values Enzyme-Linked Immunosorbent Assay (ELISA).

End point title	Number of Subjects With Anti-hepatitis B surface antigen (anti-HBs) Antibody Concentrations Above Pre-defined Cut-off Values Enzyme-Linked Immunosorbent Assay (ELISA).[3]

End point description:

Anti-hepatitis B surface antigen (anti-HBs) antibody cut-off values assessed include 1.0 and 10 mIU/mL.

End point type	Primary

End point timeframe:

At Years 15, 16, 17, 18, 19 and 20

Notes:

[3] - 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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	12	17
Units: Subjects				
Year 15 (≥ 1.0 mIU/mL) (N=17;15;12;17)	17	7	10	11
Year 15 (≥ 10 mIU/mL) (N=17;15;12;17)	16	4	9	7
Year 16 (≥ 1.0 mIU/mL) (N=15;13;12;16)	15	9	12	11
Year 16 (≥ 10 mIU/mL) (N=15;13;12;16)	14	6	10	8
Year 17 (≥ 1.0 mIU/mL) (N=17;13;11;13)	15	7	11	10
Year 17 (≥ 10 mIU/mL) (N=17;13;11;13)	15	2	9	5
Year 18 (≥ 1.0 mIU/mL) (N=14;14;10;13)	14	7	10	8
Year 18 (≥ 10 mIU/mL) (N=14;14;10;13)	13	3	7	7
Year 19 (≥ 1.0 mIU/mL) (N=14;12;8;11)	13	7	8	8
Year 19 (≥ 10 mIU/mL) (N=14;12;8;11)	12	3	6	6
Year 20 (≥ 1.0 mIU/mL) (N=13;13;6;12)	13	9	5	10
Year 20 (≥ 10 mIU/mL) (N=13;13;6;12)	11	5	5	6

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-hepatitis B surface antigen (anti-HBs) Antibody Concentrations Above Pre-defined Cut-off Values as measured by ChemiLuminescence ImmunoAssay (CLIA)

End point title	Number of Subjects With Anti-hepatitis B surface antigen (anti-HBs) Antibody Concentrations Above Pre-defined Cut-off Values as measured by ChemiLuminescence ImmunoAssay (CLIA)[4]

End point description:

Anti-hepatitis B surface antigen (anti-HBs) antibody cut-off values assessed include 1.0 and 10 mIU/mL.

End point type	Primary

End point timeframe:

At Years 19 and 20

Notes:

[4] - 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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	13	7	13
Units: Subjects				
number (not applicable)				
Year 19 (≥ 1.0 mIU/mL) (N=14;12;6;11)	13	4.2	6	7
Year 19 (≥ 10 mIU/mL) (N=14;12;6;11)	12	3.9	5	4
Year 20 (≥ 1.0 mIU/mL) (N=16;13;7;13)	13.1	5.4	6	6.3
Year 20 (≥ 10 mIU/mL) (N=16;13;7;13)	12.2	2.1	5	5.8

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with positive results for serological markers for hepatitis B infection

End point title	Number of subjects with positive results for serological markers for hepatitis B infection[5]

End point description:

Serological markers for hepatitis B infection assessed are hepatitis B surface antigen (HBsAg), antibodies to hepatitis B core antigen (anti-HBc), hepatitis B e antigen (HBeAg) and antibodies to hepatitis B e antigen (anti-HBe).

End point type	Primary

End point timeframe:

At Years 15, 16, 17, 18, 19 and 20

Notes:

[5] - 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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	14	21
Units: Subjects				
Year 15 HBsAg (N=19;19;14;21)	0	1	0	3
Year 15 Anti-HBc (N=19;19;14;21)	4	7	1	9
Year 15 HBeAg (N=4;7;1;8)	0	1	0	1
Year 15 Anti-HBe (N=4;7;1;8)	1	1	0	3
Year 16 HBsAg (N=16;17;16;22)	2	0	2	5
Year 16 Anti-HBc (N=16;17;16;22)	4	5	1	9
Year 16 HBeAg (N=6;5;3;11)	1	1	0	3

Year 16 Anti-HBe (N=6;5;3;11)	0	1	0	2
Year 17 HBsAg (N=19;17;13;19)	6	0	3	6
Year 17 Anti-HBc (N=19;17;13;20)	5	5	1	8
Year 17 HBeAg (N=9;5;4;10)	0	0	0	1
Year 17 Anti-HBe (N=9;5;4;10)	1	0	0	3
Year 18 HBsAg (N=16;17;14;20)	3	1	3	5
Year 18 Anti-HBc (N=16;17;14;20)	5	6	1	8
Year 18 HBeAg (N=8;7;4;10)	0	0	0	1
Year 18 Anti-HBe (N=8;7;4;10)	1	1	0	2
Year 19 HBsAg (N=17;16;12;18)	4	3	3	5
Year 19 Anti-HBc (N=17;16;12;18)	4	5	2	9
Year 19 HBeAg (N=8;7;5;10)	0	0	0	2
Year 19 Anti-HBe (N=8;7;5;10)	1	1	0	3
Year 20 HBsAg (N=19;17;12;20)	6	5	4	12
Year 20 Anti-HBc (N=19;17;12;20)	5	7	2	8
Year 20 HBeAg (N=8;7;6;14)	1	0	0	1
Year 20 Anti-HBe (N=10;9;6;15)	1	0	0	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with different hepatitis B infection statuses

End point title	Number of subjects with different hepatitis B infection

End point description:

Categories hepatitis B (HB) infection: 1) Chronic infection: HBsAg and anti-HBc pos (pos) in more than two consecutive samples 2) False positive: single HB marker (HBsAg, HBeAg, anti-HBc) pos + all other markers negative (neg) in one sample. Consecutive time points all neg. 3) Possible subclinical breakthrough infection: One or more HB markers pos in one or more consecutive samples. 4) Isolated natural booster: >4-fold increase of anti-HBs concentrations if <100 mIU/mL at previous sample OR >2-fold increase of anti-HBs concentrations if >=100 mIU/mL at previous sample + other markers neg

End point type	Primary

End point timeframe:

Over the entire follow up period (Final assessment of clinical significance was analyzed after the Year 20 time point)

Notes:

[6] - 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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D	Engerix 3D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	14	21
Units: Subjects				
Chronic HB infection	0	0	0	4
False positive	5	5	9	10
Possible subclinical breakthrough HB infection	9	12	4	10
Isolated natural booster	8	8	9	7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

No SAEs were reported from Year 15 to Year 20.

Adverse event reporting additional description:

As no adverse events data were collected during this study the number of participants at risk is 0 for all groups.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Engerix 4D + HBIg Group

Reporting group description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.

Reporting group title	Engerix 3D + HBIg Group

Reporting group description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6 with hepatitis B immunoglobulins (HBIg) administered concomitantly at birth in the opposite arm.

Reporting group title	Engerix 4D

Reporting group description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, 6 and 60.

Reporting group title	Engerix 3D Group

Reporting group description:

Subjects received Engerix™ (hepatitis B vaccine [HBV]) at Month 0, 1, and 6.

Serious adverse events	Engerix 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Engerix 3D Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (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 4D + HBIg Group	Engerix 3D + HBIg Group	Engerix 4D
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)

Non-serious adverse events	Engerix 3D Group		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 21 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: As no adverse events data were collected during this study the number of participants at risk is 0 for all groups.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2003	The protocol was amended to further extend the follow-up period up to Year 20 after the first vaccine dose (with a blood sample taken at yearly intervals), to evaluate the anti-HBs persistence and to further investigate the prevalence and incidence of other hepatitis B markers (HBsAg, anti-HBc, HBeAg, anti-HBe, ALT/AST), and the clinical significance of the HBsAg and anti-HBc positive cases observed during the long-term follow-up of this study. These additional data was important to determine the long-term booster policy in subjects born from HBsAg+ mothers. Moreover, if subjects developed clinical signs possibly related to hepatitis B or have significantly high AST/ALT serum concentrations, additional medical tests were performed by the investigator, according to good medical practices.
05 April 2007	The protocol was amended to state that from Year 16 onwards to Year 20 time points, only subjects who test positive for HBsAg or anti-HBc antibodies were tested for HBeAg and anti-HBe antibodies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported