Clinical trial results:
A Study to Assess the Safety, Tolerability, and Immunogenicity of 2 Antigen Doses of Recombinant Hepatitis B Vaccine Manufactured With a Modified Process Administered to Healthy Infants at 2, 4, and 6 Months of Age

Summary

EudraCT number	2006-001638-42
Trial protocol	NO FI
Global end of trial date	24 October 2007

Results information

Result version number	v1 (current)
This version publication date	03 February 2017
First version publication date	03 February 2017

Trial information

Trial identification

Sponsor protocol code	V232-057

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00414050
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	24 October 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 October 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to demonstrate that at 1 month after the third dose of vaccine, either the modified process hepatitis B vaccine at 5 µg or RECOMBIVAX HB™ will induce adequate seroprotection rates (SPR).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 October 2006
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	Finland: 1688
Country: Number of subjects enrolled	Norway: 30
Worldwide total number of subjects	1718
EEA total number of subjects	1718

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)	1718
Children (2-11 years)	0
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:

15-Nov-2006 (first participant enrolled in study) to 24-Oct-2007 (last participant had their last visit). Last participant completed follow-up: 16-Oct-2007. This study was conducted at 15 sites; 14 in Finland and 1 in Norway.

Pre-assignment

Screening details:

Participants include healthy infants approximately 2 months of age.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Modified Process Hepatitis B vaccine 5 µg

Arm description:

Infants received a primary series of 3 doses of experimental vaccine (5 µg per dose) at 2, 4 and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	Modified Process Hepatitis B vaccine
Investigational medicinal product code	
Other name	V232
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

5 µg/0.5mL IM injection

Arm title	RECOMBIVAX™ Hepatitis B Vaccine

Arm description:

Infants received a primary series of 3 doses of currently licensed vaccine (5 µg per dose) at 2, 4 and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	Hepatitis B Vaccine (Recombinant)
Investigational medicinal product code	
Other name	RECOMBIVAX HB™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

5 µg/0.5mL IM injection

Arm title	Modified Process Hepatitis B vaccine 10 µg

Arm description:

Infants received a primary series of 3 doses of experimental vaccine (10 µg per dose) at 2, 4 and 6 months of age.

Arm type	Experimental

Investigational medicinal product name	Modified Process Hepatitis B vaccine
Investigational medicinal product code	
Other name	V232
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10 µg/0.5mL IM injection

Arm title	ENGERIX-B™

Arm description:

Infants received a primary series of 3 doses of currently licensed vaccine (10 µg per dose) at 2, 4 and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	Hepatitis B Vaccine (Recombinant)
Investigational medicinal product code	
Other name	ENGERIX-B™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10 µg/0.5mL IM injection

Number of subjects in period 1	Modified Process Hepatitis B vaccine 5 µg	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg
Started	431	427	429
Received Vaccination 1	431	426	429
Received Vaccination 2	425	421	425
Received Vaccination 3	424	419	425
Completed	422	419	423
Not completed	9	8	6
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	5	3	2
Adverse event, non-fatal	1	-	1
Subject discontinued for other reason	1	2	2
Lost to follow-up	2	2	1
Subject Moved	-	-	-

Number of subjects in period 1	ENGERIX-B™
Started	431
Received Vaccination 1	431
Received Vaccination 2	425
Received Vaccination 3	424
Completed	423
Not completed	8
Adverse event, serious fatal	-

Consent withdrawn by subject	4
Adverse event, non-fatal	1
Subject discontinued for other reason	1
Lost to follow-up	1
Subject Moved	1

Baseline characteristics

Reporting groups	
Reporting group title	Modified Process Hepatitis B vaccine 5 µg
Reporting group description:	
Infants received a primary series of 3 doses of experimental vaccine (5 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	RECOMBIVAX™ Hepatitis B Vaccine
Reporting group description:	
Infants received a primary series of 3 doses of currently licensed vaccine (5 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	Modified Process Hepatitis B vaccine 10 µg
Reporting group description:	
Infants received a primary series of 3 doses of experimental vaccine (10 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	ENGERIX-B™
Reporting group description:	
Infants received a primary series of 3 doses of currently licensed vaccine (10 µg per dose) at 2, 4 and 6 months of age.	

Reporting group values	Modified Process Hepatitis B vaccine 5 µg	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg
Number of subjects	431	427	429
Age categorical Units: Subjects			
Age Continuous | Units: days			
arithmetic mean	63.2	62.9	63.3
standard deviation	± 10.18	± 10.15	± 9.83
Gender, Male/Female Units: participants			
Female	190	217	208
Male	241	210	221

Reporting group values	ENGERIX-B™	Total	
Number of subjects	431	1718	
Age categorical Units: Subjects			
Age Continuous | Units: days			
arithmetic mean	62.8		
standard deviation	± 9.81	-	
Gender, Male/Female Units: participants			
Female	201	816	
Male	230	902	

End points

End points reporting groups

Reporting group title	Modified Process Hepatitis B vaccine 5 µg
Reporting group description:	
Infants received a primary series of 3 doses of experimental vaccine (5 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	RECOMBIVAX™ Hepatitis B Vaccine
Reporting group description:	
Infants received a primary series of 3 doses of currently licensed vaccine (5 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	Modified Process Hepatitis B vaccine 10 µg
Reporting group description:	
Infants received a primary series of 3 doses of experimental vaccine (10 µg per dose) at 2, 4 and 6 months of age.	
Reporting group title	ENGERIX-B™
Reporting group description:	
Infants received a primary series of 3 doses of currently licensed vaccine (10 µg per dose) at 2, 4 and 6 months of age.	

Primary: The Percentage of Seroresponders to the Modified Process Hepatitis B Vaccine (5 µg and 10 µg dose), RECOMBIVAX HB™ Hepatitis B Vaccine (Currently Licensed Vaccine), and ENGERIX-B

End point title	The Percentage of Seroresponders to the Modified Process Hepatitis B Vaccine (5 µg and 10 µg dose), RECOMBIVAX HB™ Hepatitis B Vaccine (Currently Licensed Vaccine), and ENGERIX-B[1]

End point description:

The percentage of participants as measured by Seroresponse. Seroresponse was defined as anti-hepatitis B surface antibodies greater than or equal to 10 milli-International Units (mIU)/mL. Success on the primary immunogenicity hypothesis required demonstrating an adequate anti-HBs seroprotection rate response for either modified process hepatitis B 5 µg vaccine or RECOMBIVAX HB. Specifically, the lower bound of the multiplicity adjusted 95% CI on the seroprotection rate for either vaccine was required to be above 90.0%.
Analysis population: per-protocol population is defined as the participants able to complete the study as defined by the protocol.

End point type	Primary

End point timeframe:

7 months of age (1 month after 3 doses)

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: No betweengroup statistical analyses were planned or performed for this endpoint.

End point values	Modified Process Hepatitis B vaccine 5 µg	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg	ENGERIX-B™
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	405	406	398	400
Units: Percentage of participants				
number (confidence interval 95%)	99.3 (98.3 to 100)	98.5 (97.2 to 99.8)	100 (99.9 to 100)	99.5 (98.7 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody to Hepatitis B Surface Antigen Geometric Mean Titer (anti-HBs GMT) Responses for Modified Process Vaccine (5 µg and 10 µg), RECOMBIVAX Hepatitis B (Currently Licensed Vaccine), and ENGERIX-B

End point title	Antibody to Hepatitis B Surface Antigen Geometric Mean Titer (anti-HBs GMT) Responses for Modified Process Vaccine (5 µg and 10 µg), RECOMBIVAX Hepatitis B (Currently Licensed Vaccine), and ENGERIX-B

End point description:

Geometric Mean Titer - Antibody titer is a laboratory test that measures the presence and amount of antibodies in blood. Analysis population: per-protocol population is defined as the participants able to complete the study as defined by the protocol.

End point type	Secondary

End point timeframe:

7 months of age (1 month after 3 doses)

End point values	Modified Process Hepatitis B vaccine 5 µg	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg	ENGERIX-B™
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	405	406	398	400
Units: mIU/mL				
geometric mean (confidence interval 95%)	748.2 (672 to 833.1)	376.8 (331.4 to 428.5)	981.5 (891 to 1081.2)	556.6 (491.8 to 629.9)

Statistical analyses

Statistical analysis title	Non-inferiority of Geometric Mean Titers Ratio

Statistical analysis description:

Comparison of Induced (effected) Geometric Mean Titer for the Modified Hepatitis B Process Vaccine and RECOMBIVAX Hepatitis B vaccine.

Comparison groups	Modified Process Hepatitis B vaccine 5 µg v RECOMBIVAX™ Hepatitis B Vaccine
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of geometric means
Point estimate	1.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.69
upper limit	2.35

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs): up to 5 months (entire study period);
Systemic non-serious adverse events (NSAEs): up to 14 days after any vaccination;
Injection-site NSAEs: up to 5 days after any vaccination

Adverse event reporting additional description:

All randomized participants with follow-up who received at least one dose of study vaccine. Below tables exclude one RECOMBIVAX HB participant who received 2 doses of RECOMBIVAX HB and 1 dose of modified process hepatitis B vaccine 10 µg, and one ENGERIX-B participant who received 2 doses of ENGERIX-B and 1 dose of RECOMBIVAX HB.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Modified Process Hepatitis B vaccine, 5 µg (micrograms)

Reporting group description:

Infants received a primary series of 3 doses of experimental vaccine (5 µg per dose) at 2, 4 and 6 months of age.

Reporting group title	RECOMBIVAX™ Hepatitis B Vaccine

Reporting group description:

Infants received a primary series of 3 doses of currently licensed vaccine (5 µg per dose) at 2, 4 and 6 months of age. Population also includes 1 participant randomized to ENGERIX-B but inadvertently received 1 dose of RECOMBIVAX HB.

Reporting group title	Modified Process Hepatitis B vaccine 10 µg (micrograms)

Reporting group description:

Infants received a primary series of 3 doses of experimental vaccine (10 µg per dose) at 2, 4 and 6 months of age. Population also includes 1 participant randomized to ENGERIX-B but inadvertently received 1 dose of modified process hepatitis B vaccine 10 µg.

Reporting group title	ENGERIX-B

Reporting group description:

Infants received a primary series of 3 doses of currently licensed vaccine (10 µg per dose) at 2, 4 and 6 months of age.

Serious adverse events	Modified Process Hepatitis B vaccine, 5 µg (micrograms)	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg (micrograms)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 430 (2.56%)	2 / 424 (0.47%)	6 / 429 (1.40%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Nutritional condition abnormal			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	0 / 430 (0.00%)	1 / 424 (0.24%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Epididymitis			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			

subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	1 / 429 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Crying			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	2 / 429 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	1 / 429 (0.23%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	2 / 430 (0.47%)	0 / 424 (0.00%)	1 / 429 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 430 (0.00%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	2 / 429 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 430 (0.23%)	1 / 424 (0.24%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 430 (0.23%)	0 / 424 (0.00%)	0 / 429 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ENGERIX-B		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 428 (1.87%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Nutritional condition abnormal			

subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 428 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sudden infant death syndrome			
subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Epididymitis			
subjects affected / exposed	0 / 428 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis chronic				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Crying				
subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bacterial infection				
subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 428 (0.47%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 428 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Malnutrition				
subjects affected / exposed	0 / 428 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Modified Process Hepatitis B vaccine, 5 µg (micrograms)	RECOMBIVAX™ Hepatitis B Vaccine	Modified Process Hepatitis B vaccine 10 µg (micrograms)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	308 / 430 (71.63%)	294 / 424 (69.34%)	276 / 429 (64.34%)
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	114 / 430 (26.51%)	109 / 424 (25.71%)	91 / 429 (21.21%)
occurrences (all)	169	157	138
Pyrexia			
subjects affected / exposed	62 / 430 (14.42%)	57 / 424 (13.44%)	56 / 429 (13.05%)
occurrences (all)	78	65	68
Injection-site erythema			
subjects affected / exposed	128 / 430 (29.77%)	117 / 424 (27.59%)	116 / 429 (27.04%)
occurrences (all)	169	160	153
Injection-site induration			
subjects affected / exposed	25 / 430 (5.81%)	15 / 424 (3.54%)	24 / 429 (5.59%)
occurrences (all)	29	19	26
Injection-site pain			
subjects affected / exposed	79 / 430 (18.37%)	73 / 424 (17.22%)	60 / 429 (13.99%)
occurrences (all)	117	96	90
Injection-site swelling			
subjects affected / exposed	78 / 430 (18.14%)	85 / 424 (20.05%)	87 / 429 (20.28%)
occurrences (all)	109	111	110
Eye disorders			
Conjunctivitis			
subjects affected / exposed	9 / 430 (2.09%)	14 / 424 (3.30%)	10 / 429 (2.33%)
occurrences (all)	11	14	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	30 / 430 (6.98%)	26 / 424 (6.13%)	26 / 429 (6.06%)
occurrences (all)	37	36	31
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 430 (4.88%)	15 / 424 (3.54%)	17 / 429 (3.96%)
occurrences (all)	21	18	19
Psychiatric disorders			

Crying			
subjects affected / exposed	41 / 430 (9.53%)	39 / 424 (9.20%)	39 / 429 (9.09%)
occurrences (all)	51	49	48
Infections and infestations			
Rhinitis			
subjects affected / exposed	53 / 430 (12.33%)	47 / 424 (11.08%)	59 / 429 (13.75%)
occurrences (all)	57	54	68
Upper respiratory tract infection			
subjects affected / exposed	32 / 430 (7.44%)	26 / 424 (6.13%)	25 / 429 (5.83%)
occurrences (all)	35	27	25

Non-serious adverse events	ENGERIX-B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	288 / 428 (67.29%)		
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	107 / 428 (25.00%)		
occurrences (all)	139		
Pyrexia			
subjects affected / exposed	53 / 428 (12.38%)		
occurrences (all)	65		
Injection-site erythema			
subjects affected / exposed	94 / 428 (21.96%)		
occurrences (all)	124		
Injection-site induration			
subjects affected / exposed	8 / 428 (1.87%)		
occurrences (all)	9		
Injection-site pain			
subjects affected / exposed	66 / 428 (15.42%)		
occurrences (all)	92		
Injection-site swelling			
subjects affected / exposed	65 / 428 (15.19%)		
occurrences (all)	98		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	22 / 428 (5.14%)		
occurrences (all)	23		

Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 18 / 428 (4.21%) 26		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 25 / 428 (5.84%) 26		
Psychiatric disorders Crying subjects affected / exposed occurrences (all)	 41 / 428 (9.58%) 48		
Infections and infestations Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 51 / 428 (11.92%) 57 23 / 428 (5.37%) 25		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported