Clinical trial results:
An Open-label, randomised, controlled, multi-centre study of the immunogenicity and safety of a booster dose of two different Hepatitis B vaccines to explore the anamnestic immune response in healthy 4 to 7 year-old children previously vaccinated at about 3, 5 and 11 to 13 months of age with either HEXAVAC or INFANRIX-HEXA

Summary

EudraCT number	2007-005168-29
Trial protocol	IT
Global end of trial date	04 January 2010

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	HXV01C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00693186
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur MSD S.N.C.
Sponsor organisation address	162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367
Public contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.com
Scientific contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.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	04 January 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 January 2010
Global end of trial reached?	Yes
Global end of trial date	04 January 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity: To describe in subjects vaccinated with 3 doses of HEXAVAC® or 3 doses of INFANRIX-HEXA® during the first 2 years of life the percentage of subjects with an anti-HBs antibody titre ≥10 mIU/mL (i.e. seroprotection rate) 1 month after a booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO® 5 µg (modified process) or ENGERIX-B® 10 µg.
Note: "HBVaxPRO® 5 µg (modified process)" was referred to "HBVaxPRO" and "ENGERIX-B® 10 µg" was referred to "ENGERIX-B" to facilitate reading.

Protection of trial subjects:

Healthy subjects with known sensitivity and/or allergy to any component of the study vaccine were not vaccinated.
Vaccines were administered by qualified study personnel.
After each vaccination, subjects were kept under observation for at least 20 minutes to ensure their safety.

Background therapy:

Subjects were previously vaccinated with 3 doses of HEXAVAC or 3 doses of INFANRIX-HEXA during their first 2 years of life (at about 3, 5, and 11 to 13 months of age).

Evidence for comparator:

This study was designed to explore the immune memory against Hepatitis B in healthy 4 to 7 year-old children previously vaccinated with HEXAVAC or INFANRIX-HEXA as part as the routine immunisation program. Two different Hepatitis B vaccines were used for this purpose: HBVaxPRO (namely study product) and ENGERIX-B (namely study comparator). ENGERIX-B was used as it was the one licensed for children and adolescents from birth to 15 years of age at the time the study started.

Note: The lot of HBVaxPRO used in the study expired on 14 March 2009. Consequently, the study was continued with ENGERIX-B only for all subjects from 11 March 2009.

Actual start date of recruitment	27 October 2008
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	Italy: 410
Worldwide total number of subjects	410
EEA total number of subjects	410

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)	410
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:

Study subjects were enrolled in 5 active centres in Italy.

Pre-assignment

Screening details:

410 subjects were included and vaccinated during Part I of the study (period 1: booster dose).
405 subjects completed period 1.
15 subjects were vaccinated during Part II of the study: all received 1 extra-dose of Hepatitis B vaccine and 3 of them also received a 2nd extra-dose (period 2: extra-doses).

Period 1

Period 1 title	Booster dose
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable as this study was open-label.
For immunogenicity data, serology tests were performed by laboratory staffs which were blinded to the previous hexavalent vaccine history and to which study vaccine each subject received.

Arms

Are arms mutually exclusive?	Yes
Arm title	HEXAVAC / HBVaxPRO (period 1)

Arm description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Arm type	Experimental
Investigational medicinal product name	HBVaxPRO® 5 µg (modified process)
Investigational medicinal product code	
Other name	HBVaxPRO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 dose at 4 to 7 years of age.

Arm title	HEXAVAC / ENGERIX-B (period 1)

Arm description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Arm type	Active comparator
Investigational medicinal product name	ENGERIX-B® 10 µg
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 dose at 4 to 7 years of age.

Arm title	INFANRIX-HEXA / HBVaxPRO (period 1)

Arm description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Arm type	Experimental
Investigational medicinal product name	HBVaxPRO® 5 µg (modified process)
Investigational medicinal product code	
Other name	HBVaxPRO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 dose at 4 to 7 years of age.

Arm title	INFANRIX-HEXA / ENGERIX-B (period 1)

Arm description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Arm type	Active comparator
Investigational medicinal product name	ENGERIX-B® 10 µg
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 dose at 4 to 7 years of age.

Number of subjects in period 1	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)
Started	34	167	28
Completed	33	164	28
Not completed	1	3	0
Consent withdrawn by subject	1	-	-
Lost to follow-up	-	3	-

Number of subjects in period 1	INFANRIX-HEXA / ENGERIX-B (period 1)
Started	181

Completed	180
Not completed	1
Consent withdrawn by subject	1
Lost to follow-up	-

Period 2

Period 2 title	Extra-doses
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable as this study was open-label.
For immunogenicity data, serology tests were performed by laboratory staffs which were blinded to the previous hexavalent vaccine history and to which study vaccine each subject received.

Arms

Are arms mutually exclusive?	Yes
Arm title	HEXAVAC / HBVaxPRO (period 2)

Arm description:

Subject previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=1, Local Italian Laboratory) received 1 extra-dose of HBVaxPRO by intramuscular route 2 months after the booster dose.
Blood sample was collected 1 month (D28 to D42) after the extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2 additional doses.

Arm type	Experimental
Investigational medicinal product name	HBVaxPRO® 5 µg (modified process)
Investigational medicinal product code	
Other name	HBVaxPRO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 extra-dose 2 months after the booster dose.

Arm title	HEXAVAC / ENGERIX-B (period 2)

Arm description:

Subjects previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=13, Local Italian laboratory) received 1 extra-dose of ENGERIX-B by intramuscular route 2 months after the booster dose.
Out of these 13 subjects, 3 with post-extra-dose 1 anti-HBs Ab titre <10 mIU/mL (local Italian laboratory) received a 2nd extra-dose of ENGERIX-B 6 months after the booster dose.
Blood samples were collected 1 month (D28 to D42) after each extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2 additional doses.

Arm type	Active comparator

Investigational medicinal product name	ENGERIX-B® 10 µg
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1st extra-dose 2 months after the booster dose, 2nd extra-dose 6 months after the booster dose.

Arm title	INFANRIX-HEXA / ENGERIX-B (period 2)

Arm description:

Subject previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=1, Local Italian Laboratory) received 1 extra-dose of ENGERIX-B by intramuscular route 2 months after the booster dose.
Blood sample was collected 1 month (D28 to D42) after the extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2 additional doses.

Arm type	Active comparator
Investigational medicinal product name	ENGERIX-B® 10 µg
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (deltoid muscle), 1 extra-dose 2 months after the booster dose.

Number of subjects in period 2[1]	HEXAVAC / HBVaxPRO (period 2)	HEXAVAC / ENGERIX-B (period 2)	INFANRIX-HEXA / ENGERIX-B (period 2)
Started	1	13	1
Completed	1	13	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: For subjects' follow-up, only subjects of period 1 with post-booster anti-HBs antibody titre <10 mIU/mL and anti-HBc antibody titre test negative as measured at the local Italian laboratory were proposed 1 or 2 extra-doses of a Hepatitis B vaccine respectively 2 and 6 months after the booster dose of either HBVaxPRO or ENGERIX-B.
Thus, only 15 subjects continued in period 2 of the study.

Baseline characteristics

Reporting groups	
Reporting group title	HEXAVAC / HBVaxPRO (period 1)
Reporting group description:	
# Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age. # Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.	
Reporting group title	HEXAVAC / ENGERIX-B (period 1)
Reporting group description:	
# Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age. # Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.	
Reporting group title	INFANRIX-HEXA / HBVaxPRO (period 1)
Reporting group description:	
# Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age. # Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.	
Reporting group title	INFANRIX-HEXA / ENGERIX-B (period 1)
Reporting group description:	
# Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age. # Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.	

Reporting group values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)
Number of subjects	34	167	28
Age categorical			
Age (years) at booster dose.			
Units: Subjects			
Children (2-11 years)	34	167	28
Age continuous			
Age at booster dose, Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.			
Units: years			
arithmetic mean	6.6	5.7	5.9
standard deviation	± 0.9	± 0.9	± 0.7
Gender categorical			
Units: Subjects			
Female	12	88	15
Male	22	79	13

Reporting group values	INFANRIX-HEXA / ENGERIX-B (period 1)	Total	

Number of subjects	181	410	
Age categorical			
Age (years) at booster dose.			
Units: Subjects			
Children (2-11 years)	181	410	
Age continuous			
Age at booster dose, Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.			
Units: years			
arithmetic mean	5.7		
standard deviation	± 0.7	-	
Gender categorical			
Units: Subjects			
Female	89	204	
Male	92	206	

End points

End points reporting groups

Reporting group title	HEXAVAC / HBVaxPRO (period 1)

Reporting group description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Reporting group title	HEXAVAC / ENGERIX-B (period 1)

Reporting group description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Reporting group title	INFANRIX-HEXA / HBVaxPRO (period 1)

Reporting group description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Reporting group title	INFANRIX-HEXA / ENGERIX-B (period 1)

Reporting group description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Blood samples were collected on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.

Reporting group title	HEXAVAC / HBVaxPRO (period 2)

Reporting group description:

Subject previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=1, Local Italian Laboratory) received 1 extra-dose of HBVaxPRO by intramuscular route 2 months after the booster dose.
Blood sample was collected 1 month (D28 to D42) after the extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2 additional doses.

Reporting group title	HEXAVAC / ENGERIX-B (period 2)

Reporting group description:

Subjects previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=13, Local Italian laboratory) received 1 extra-dose of ENGERIX-B by intramuscular route 2 months after the booster dose.
Out of these 13 subjects, 3 with post-extra-dose 1 anti-HBs Ab titre <10 mIU/mL (local Italian laboratory) received a 2nd extra-dose of ENGERIX-B 6 months after the booster dose.
Blood samples were collected 1 month (D28 to D42) after each extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2 additional doses.

Reporting group title	INFANRIX-HEXA / ENGERIX-B (period 2)

Reporting group description:

Subject previously vaccinated as planned during period 1 with post-booster anti-HBs Ab titre <10 mIU/mL (N=1, Local Italian Laboratory) received 1 extra-dose of ENGERIX-B by intramuscular route 2 months after the booster dose.
Blood sample was collected 1 month (D28 to D42) after the extra-dose.
Note: Local Italian laboratory (Laboratorio Epatite, Università degli Studi di Milano) was used to obtain results on an ongoing basis in order to invite children to continue in part II of the study to receive 1 or 2

additional doses.

Primary: Seroprotection rate: percentage of subjects with an anti-Hepatitis B surface (anti-HBs) antibody titre ≥10 mIU/mL 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point title	Seroprotection rate: percentage of subjects with an anti-Hepatitis B surface (anti-HBs) antibody titre ≥10 mIU/mL 1 month after the booster dose of either HBVaxPRO or ENGERIX-B[1]

End point description:

Percentage of subjects with an anti-HBs titre ≥10 mIU/mL measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA, 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.
Analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.

End point type	Primary

End point timeframe:

1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

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: Objectives were only descriptive. Thus no formal statistical hypothesis was tested in this study.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	160	27	171
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-HBs ≥10 mIU/mL	90.9 (75.7 to 98.1)	91.3 (85.8 to 95.1)	100 (87.2 to 100)	97.7 (94.1 to 99.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with an anti-Hepatitis B surface (anti-HBs) antibody titre # ≥5 mIU/mL, # ≥10 mIU/mL, and # ≥100 mIU/mL pre-booster and 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point title	Percentage of subjects with an anti-Hepatitis B surface (anti-HBs) antibody titre # ≥5 mIU/mL, # ≥10 mIU/mL, and # ≥100 mIU/mL pre-booster and 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point description:

Percentage of subjects with an anti-HBs titre # ≥5 mIU/mL, # ≥10 mIU/mL, and # ≥100 mIU/mL measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA, on Day 0 (D0) before booster dose (pre-booster) and 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B (post-booster).
Analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.

End point type	Secondary

End point timeframe:

Pre-booster: Day 0 (D0) before booster dose.
Post-booster: 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	160	27	171
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre-booster anti-HBs ≥5 mIU/mL	63.6 (45.1 to 79.6)	44.7 (36.8 to 52.7)	77.8 (57.7 to 91.4)	84.8 (78.5 to 89.8)
Post-booster anti-HBs ≥5 mIU/mL	97 (84.2 to 99.9)	91.3 (85.8 to 95.1)	100 (87.2 to 100)	98.2 (95 to 99.6)
Pre-booster anti-HBs ≥10 mIU/mL	57.6 (39.2 to 74.5)	35.8 (28.4 to 43.8)	77.8 (57.7 to 91.4)	81.9 (75.3 to 87.3)
Post-booster anti-HBs ≥10 mIU/mL	90.9 (75.7 to 98.1)	91.3 (85.8 to 95.1)	100 (87.2 to 100)	97.7 (94.1 to 99.4)
Pre-booster anti-HBs ≥100 mIU/mL	9.1 (1.9 to 24.3)	5.7 (2.6 to 10.5)	40.7 (22.4 to 61.2)	43.3 (35.7 to 51.1)
Post-booster anti-HBs ≥100 mIU/mL	90.9 (75.7 to 98.1)	81.3 (74.3 to 87)	96.3 (81 to 99.9)	95.3 (91 to 98)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMT) of anti-HBs antibodies pre-booster and 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point title	Geometric Mean Titres (GMT) of anti-HBs antibodies pre-booster and 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point description:

Study participants were blood sampled on Day 0 (D0) before booster dose (pre-booster) and 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B (post-booster).
Anti-HBs antibody titres expressed in mIU/mL were measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA.
Analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.

End point type	Secondary

End point timeframe:

Pre-booster: Day 0 (D0) before booster dose.
Post-booster: 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	160	27	171
Units: Titres				
geometric mean (confidence interval 95%)				
Pre-booster anti-HBs GMT	13 (7 to 22)	8 (6 to 10)	50 (23 to 109)	61 (45 to 82)
Post-booster anti-HBs GMT	1255 (554 to 2846)	878 (581 to 1327)	6564 (2917 to 14772)	7420 (5227 to 10531)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres Ratios (GMTR) of individual post-/pre-booster anti-HBs antibody titres 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point title	Geometric Mean Titres Ratios (GMTR) of individual post-/pre-booster anti-HBs antibody titres 1 month after the booster dose of either HBVaxPRO or ENGERIX-B

End point description:

Study participants were blood sampled on Day 0 (D0) before booster dose (pre-booster) and 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B (post-booster).
Anti-HBs antibody titres were measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA.
Individual post- (1 month) / pre-booster (D0) anti-HBs titres ratios were measured.
Analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.

End point type	Secondary

End point timeframe:

1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	160	27	171
Units: Not applicable				
geometric mean (confidence interval 95%)				
Anti-HBs GMTR	100 (57 to 175)	111 (80 to 154)	131 (83 to 205)	122 (96 to 155)

Statistical analyses

No statistical analyses for this end point

Secondary: Global summary of safety from D0 to D14 after the booster dose of either HBVaxPRO or ENGERIX-B

End point title	Global summary of safety from D0 to D14 after the booster dose of either HBVaxPRO or ENGERIX-B

End point description:

Adverse events (AEs) occurring after injection of the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B were recorded as follows.
1/ From D0 to D4: # solicited injection-site adverse reactions (ISRs) (erythema, pain, and swelling), and # solicited systemic AE (pyrexia),
2/ From D0 to D14: # unsolicited ISRs, and # unsolicited systemic AEs.
AEs at injection sites were always considered as related to vaccine (ISRs). The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.
Analysis was done on the Safety Analysis Set (N=407), i.e. all subjects who received at least 1 of the booster study vaccines and who had safety follow-up data.

End point type	Secondary

End point timeframe:

Day 0 (D0) to D14 after injection of the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	164	28	181
Units: Percentage of subjects				
number (confidence interval 95%)				
At least 1 ISR or systemic AE (D0-D14)	47.1 (29.8 to 64.9)	38.4 (30.9 to 46.3)	35.7 (18.6 to 55.9)	45.9 (38.4 to 53.4)
At least 1 ISR (D0-D14)	20.6 (8.7 to 37.9)	24.4 (18 to 31.7)	28.6 (13.2 to 48.7)	38.1 (31 to 45.6)
At least 1 solicited ISR (D0-D4)	20.6 (8.7 to 37.9)	24.4 (18 to 31.7)	28.6 (13.2 to 48.7)	37.6 (30.5 to 45.1)
Injection-site erythema (D0-D4)	0 (0 to 10.3)	1.2 (0.1 to 4.3)	3.6 (0.1 to 18.3)	8.8 (5.1 to 14)
Injection-site pain (D0-D4)	20.6 (8.7 to 37.9)	23.2 (16.9 to 30.4)	25 (10.7 to 44.9)	32.6 (25.8 to 39.9)
Injection-site swelling (D0-D4)	0 (0 to 10.3)	1.8 (0.4 to 5.3)	7.1 (0.9 to 23.5)	7.2 (3.9 to 12)
At least 1 systemic AE (D0-D14)	29.4 (15.1 to 47.5)	18.3 (12.7 to 25.1)	17.9 (6.1 to 36.9)	20.4 (14.8 to 27.1)
At least 1 solicited systemic AE: pyrexia (D0-D4)	8.8 (1.9 to 23.7)	3.7 (1.4 to 7.8)	3.6 (0.1 to 18.3)	2.8 (0.9 to 6.3)
At least 1 vaccine-related pyrexia (D0-D4)	0 (0 to 10.3)	1.8 (0.4 to 5.3)	3.6 (0.1 to 18.3)	1.7 (0.3 to 4.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Individual anti-HBs antibody titres 1 month after each extra-dose as

measured at PPD Vaccines and Biologics LLC, USA

End point title	Individual anti-HBs antibody titres 1 month after each extra-dose as measured at PPD Vaccines and Biologics LLC, USA

End point description:

Study participants were blood sampled 1 month after each extra-dose of either HBVaxPRO or ENGERIX-B.
Individual post extra-doses anti-HBs Ab titres expressed in mIU/mL were measured by the Ortho enhanced chemiluminescence (ECi) assay at the USA laboratory in 15 subjects 1 month after extra-dose 1, and in 3 subjects 1 month after extra-dose 2 of either HBVaxPRO or ENGERIX-B.
Note: "0" means not applicable, "2.5" means anti-HBs titre <5 mIU/mL.

End point type	Secondary

End point timeframe:

1 month after each extra-dose of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 2)	HEXAVAC / ENGERIX-B (period 2)	INFANRIX-HEXA / ENGERIX-B (period 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	13	1	
Units: Titres (mIU/mL)				
number (not applicable)				
Subject 04005 extra-dose 1	19.8	0	0	
Subject 04012 extra-dose 1	0	401	0	
Subject 04029 extra-dose 1	0	2.5	0	
Subject 04029 extra-dose 2	0	52.8	0	
Subject 04037 extra-dose 1	0	15.8	0	
Subject 04051 extra-dose 1	0	2.5	0	
Subject 04051 extra-dose 2	0	269	0	
Subject 04056 extra-dose 1	0	190	0	
Subject 04059 extra-dose 1	0	237	0	
Subject 04063 extra-dose 1	0	680	0	
Subject 04080 extra-dose 1	0	154	0	
Subject 04086 extra-dose 1	0	11.5	0	
Subject 04114 extra-dose 1	0	36.9	0	
Subject 04136 extra-dose 1	0	2.5	0	
Subject 04136 extra-dose 2	0	2.5	0	
Subject 05049 extra-dose 1	0	93.3	0	
Subject 07026 extra-dose 1	0	6.5	0	
Subject 01031 extra-dose 1	0	0	383	

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of subjects with an anti-HBs antibody titre ≥10 mIU/mL and ≥100 mIU/mL 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres (<10 mIU/mL or ≥10 mIU/mL)

End point title	Percentage of subjects with an anti-HBs antibody titre ≥10 mIU/mL and ≥100 mIU/mL 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres (<10 mIU/mL or ≥10 mIU/mL)

End point description:

Percentage of subjects with an anti-HBs titre # ≥10 mIU/mL and # ≥100 mIU/mL measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA, 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B, according to the pre-booster anti-HBs antibody titres (<10 mIU/mL or ≥10 mIU/mL).
Post-hoc analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.
Note: (N=***, ***, ***, ***) represents the number of assessed subjects in the HEXAVAC / HBVaxPRO, HEXAVAC / ENGERIX-B, INFANRIX-HEXA / HBVaxPRO, and INFANRIX-HEXA / ENGERIX-B groups, respectively.

End point type	Post-hoc

End point timeframe:

1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	159[2]	27	171
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre- <10, post-booster ≥10 (N=14, 102, 6, 31)	78.6 (49.2 to 95.3)	86.3 (78 to 92.3)	100 (54.1 to 100)	90.3 (74.2 to 98)
Pre- <10, post-booster ≥100 (N=14, 102, 6, 31)	78.6 (49.2 to 95.3)	70.6 (60.7 to 79.2)	83.3 (35.9 to 99.6)	77.4 (58.9 to 90.4)
Pre- ≥10, post-booster ≥10 (N=19, 57, 21, 140)	100 (82.4 to 100)	100 (93.7 to 100)	100 (83.9 to 100)	99.3 (96.1 to 100)
Pre- ≥10, post-booster ≥100 (N=19, 57, 21, 140)	100 (82.4 to 100)	100 (93.7 to 100)	100 (83.9 to 100)	99.3 (96.1 to 100)

Notes:

[2] - 1 pre-booster missing data

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric Mean Titres (GMT) of anti-HBs antibodies 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres

End point title	Geometric Mean Titres (GMT) of anti-HBs antibodies 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres

End point description:

Study participants were blood sampled on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.
Anti-HBs antibody titres expressed in mIU/mL were measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA.
Post-hoc analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.
Note: (N=***, ***, ***, ***) represents the number of assessed subjects in the HEXAVAC / HBVaxPRO, HEXAVAC / ENGERIX-B, INFANRIX-HEXA / HBVaxPRO, and INFANRIX-HEXA / ENGERIX-B groups, respectively.

End point type	Post-hoc

End point timeframe:

Pre-booster: Day 0 (D0) before booster dose.
Post-booster: 1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	159[3]	27	171
Units: Titres				
geometric mean (confidence interval 95%)				
Pre- <10, pre-booster GMT (N=14, 102, 6, 31)	3 (2 to 4)	3 (3 to 3)	3 (3 to 3)	3 (3 to 3)
Pre- <10, post-booster GMT (N=14, 102, 6, 31)	239 (60 to 944)	291 (178 to 476)	564 (104 to 3054)	307 (141 to 665)
Pre- ≥10, pre-booster GMT (N=19, 57, 21, 140)	36 (21 to 62)	48 (34 to 68)	118 (67 to 207)	119 (92 to 153)
Pre- ≥10, post-booster GMT (N=19, 57, 21, 140)	4266 (2297 to 7921)	6372 (4257 to 9538)	13233 (6447 to 27162)	15023 (11327 to 19925)

Notes:

[3] - 1 pre-booster missing data

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric Mean Titres Ratios (GMTR) of individual post-/pre-booster anti-HBs antibody titres 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres

End point title	Geometric Mean Titres Ratios (GMTR) of individual post-/pre-booster anti-HBs antibody titres 1 month after the booster dose of either HBVaxPRO or ENGERIX-B according to the pre-booster anti-HBs antibody titres

End point description:

Study participants were blood sampled on Day 0 (D0) before booster dose (pre-booster) and 1 month (D28 to D42) after the booster dose.
Anti-HBs antibody titres were measured by the Ortho enhanced chemiluminescence (ECi) assay at PPD Vaccines and Biologics LLC, USA.
Individual post- (D28-D42) / pre-booster (D0) anti-HBs titres ratios were calculated.
Post-hoc analysis was done on the Per Protocol Set (PPS), i.e. all randomised subjects without protocol violation which may interfere with the immunogenicity evaluation.
Note: (N=***, ***, ***, ***) represents the number of assessed subjects in the HEXAVAC / HBVaxPRO, HEXAVAC / ENGERIX-B, INFANRIX-HEXA / HBVaxPRO, and INFANRIX-HEXA / ENGERIX-B groups, respectively.

End point type	Post-hoc

End point timeframe:

1 month after the booster dose (4th dose of a Hepatitis B vaccine) of either HBVaxPRO or ENGERIX-B.

End point values	HEXAVAC / HBVaxPRO (period 1)	HEXAVAC / ENGERIX-B (period 1)	INFANRIX-HEXA / HBVaxPRO (period 1)	INFANRIX-HEXA / ENGERIX-B (period 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	159[4]	27	171
Units: Not applicable				
geometric mean (confidence interval 95%)				
Pre-booster <10 mIU/mL, GMTR (N=14, 102, 6, 31)	80 (23 to 279)	100 (62 to 161)	226 (42 to 1222)	104 (49 to 221)
Pre-booster ≥10 mIU/mL, GMTR (N=19, 57, 21, 140)	117 (72 to 191)	133 (92 to 193)	112 (72 to 173)	127 (99 to 162)

Notes:

[4] - 1 pre-booster missing data

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited non-serious adverse events (AEs) were collected from D0 to D14 after booster dose.
Serious AEs were collected through period 1.
Deaths and vaccine-related serious AEs were collected throughout the study.

Adverse event reporting additional description:

Analysis of AEs was performed on the Safety Analysis Set, i.e. all randomised subjects who received at least 1 vaccination and who had safety follow-up (N=407).
Unsolicited non-serious systemic AEs (vaccine-related or not) with incidence ≥1% in at least 1 reporting group are presented hereafter.
None of the serious AEs were vaccine-related.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	HBVaxPRO (HEXAVAC)

Reporting group description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
Respectively, 8 (23.5%) subjects reported at least 1 non-serious systemic AE and 1 (2.9%) subject reported 1 vaccine-related non-serious systemic AE within 14 days after booster dose.

Reporting group title	HBVaxPRO (INFANRIX-HEXA)

Reporting group description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of HBVaxPRO (Hepatitis B virus surface antigen, recombinant 5 µg, adsorbed on amorphous aluminium hydroxyphosphate sulphate 0.25 mg) by intramuscular route at 4 to 7 years of age.
5 (17.9%) subjects reported at least 1 non-serious systemic AE within 14 days after booster dose. No vaccine-related non-serious systemic AE was reported in this reporting group.

Reporting group title	ENGERIX-B (HEXAVAC)

Reporting group description:

Subjects previously vaccinated with 3 doses of HEXAVAC (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Respectively, 26 (15.9%) subjects reported at least 1 non-serious systemic AE and 2 (1.2%) subjects reported at least 1 vaccine-related non-serious systemic AE within 14 days after booster dose.

Reporting group title	ENGERIX-B (INFANRIX-HEXA)

Reporting group description:

Subjects previously vaccinated with 3 doses of INFANRIX-HEXA (at 3, 5, and 11 to 13 months of age) received 1 booster dose of ENGERIX-B (Hepatitis B virus surface antigen (rDNA) 10 µg, adsorbed on amorphous aluminium oxide hydrated 0.25 mg) by intramuscular route at 4 to 7 years of age.
Respectively, 34 (18.8%) subjects reported at least 1 non-serious systemic AE and 6 (3.3%) subjects reported at least 1 vaccine-related non-serious systemic AE within 14 days after booster dose.

Serious adverse events	HBVaxPRO (HEXAVAC)	HBVaxPRO (INFANRIX-HEXA)	ENGERIX-B (HEXAVAC)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	3 / 164 (1.83%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infectious mononucleosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis mycoplasmal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	0 / 164 (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

Serious adverse events	ENGERIX-B (INFANRIX-HEXA)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 181 (0.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 181 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Infectious mononucleosis			
subjects affected / exposed	0 / 181 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parotitis			
subjects affected / exposed	0 / 181 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis mycoplasmal			
subjects affected / exposed	0 / 181 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	HBVaxPRO (HEXAVAC)	HBVaxPRO (INFANRIX-HEXA)	ENGERIX-B (HEXAVAC)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 34 (23.53%)	5 / 28 (17.86%)	26 / 164 (15.85%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 34 (2.94%)	0 / 28 (0.00%)	0 / 164 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 34 (2.94%)	1 / 28 (3.57%)	9 / 164 (5.49%)
occurrences (all)	1	1	9
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	1 / 34 (2.94%)	0 / 28 (0.00%)	2 / 164 (1.22%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 34 (2.94%)	1 / 28 (3.57%)	1 / 164 (0.61%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	2 / 164 (1.22%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 34 (2.94%)	1 / 28 (3.57%)	2 / 164 (1.22%)
occurrences (all)	1	1	2
Oropharyngeal pain			
subjects affected / exposed	2 / 34 (5.88%)	0 / 28 (0.00%)	0 / 164 (0.00%)
occurrences (all)	2	0	0
Productive cough			
subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	0 / 164 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 34 (0.00%)	2 / 28 (7.14%)	1 / 164 (0.61%)
occurrences (all)	0	3	1
Influenza			
subjects affected / exposed	1 / 34 (2.94%)	0 / 28 (0.00%)	0 / 164 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	1 / 28 (3.57%)	0 / 164 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 28 (3.57%)	2 / 164 (1.22%)
occurrences (all)	0	1	2
Rhinitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 28 (3.57%)	0 / 164 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			

subjects affected / exposed	0 / 34 (0.00%)	0 / 28 (0.00%)	1 / 164 (0.61%)
occurrences (all)	0	0	1

Non-serious adverse events	ENGERIX-B (INFANRIX-HEXA)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 181 (18.78%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 181 (1.10%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	12 / 181 (6.63%)		
occurrences (all)	12		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 181 (1.10%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 181 (3.31%)		
occurrences (all)	6		
Oropharyngeal pain			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	2 / 181 (1.10%)		
occurrences (all)	2		
Infections and infestations			

Ear infection			
subjects affected / exposed	6 / 181 (3.31%)		
occurrences (all)	7		
Influenza			
subjects affected / exposed	0 / 181 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 181 (1.10%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	4 / 181 (2.21%)		
occurrences (all)	4		
Rhinitis			
subjects affected / exposed	1 / 181 (0.55%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	2 / 181 (1.10%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2008	Continuation of the study with ENGERIX-B for all subjects from 11 March 2009 due to expiration of the lot of HBVaxPRO used in the study on 14 March 2009.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported