Clinical trial results:
Development of read-outs to detect and characterise the early and adaptive immune responses in healthy, hepatitis B virus naive adults vaccinated with the hepatitis B surface antigen in combination with a GSK Biologicals' Adjuvant System

Summary

EudraCT number	2012-001344-22
Trial protocol	BE
Global end of trial date	13 September 2016

Results information

Result version number	v2
This version publication date	14 October 2017
First version publication date	14 September 2017
Version creation reason	• New data added to full data set global end of trial correction

Trial information

Trial identification

Sponsor protocol code	116640

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2016
Global end of trial reached?	Yes
Global end of trial date	13 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To detect and measure soluble mediators from the early immune response in plasma.

Protection of trial subjects:

- All vaccinated subjects were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction. Vaccines/products were administered by qualified and trained personnel. Vaccines/placebos were administered only to eligible subjects that had no contraindications to any components of the vaccines/placebos. Subjects were followed-up for up to one month for adverse events after the last vaccination/placebos administration and during the entire study period for serious adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 February 2013
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	Belgium: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	0
Adults (18-64 years)	81
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subject disposition refers to all subjects included in the Pooling of steps, with at least one vaccine administration documented.

Pre-assignment

Screening details:

During the screening period the following steps occurred: blood samples withdrawals to check eligibility criteria (HBV, hepatitis C virus [HCV], human immunodeficiency virus [HIV], haematology and blood chemistry), blood collection for innate immune assays, adaptive read-outs and urine samples collection

Pre-assignment period milestones

Number of subjects started	81
Number of subjects completed	81

Period 1

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

Blinding implementation details:

Single-blind up to Day 60 in each Step. Subjects were unblinded at the end of their Day 60 visit.

Arms

Are arms mutually exclusive?	Yes
Arm title	HBsAg/AS_1+2 Group

Arm description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30, followed by 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30; and during Step 2 of the study, 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Arm type	Experimental
Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of placebo saline solution was administered intramuscularly into the deltoid region of the non-dominant arm at Day -30 in Step 1 of the study.

Investigational medicinal product name	Adjuvanted Hepatitis B surface antigen (HBsAg) candidate vaccine GSK2231392A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The 2 vaccine doses were administered intramuscularly into the deltoid region of the non-dominant arm at Day 0 and Day 30, in both Step 1 and Step 2 of the study.

Arm title	Engerix-B_1+2 Group

Arm description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30 followed by 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180; and during Step 2 of the study, 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Arm type	Active comparator
Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	HBsAg/Alum
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The 3 doses of active comparator were administered intramuscularly into the deltoid region of the non-dominant arm at Day 0, Day 30 and Day 180, in both Step 1 and Step 2 of the study.

Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of placebo saline solution was administered intramuscularly into the deltoid region of the non-dominant arm at Day -30 in Step 1 of the study.

Number of subjects in period 1	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group
Started	40	41
Completed	36	38
Not completed	4	3
Consent withdrawn by subject	2	2
Unspecified	2	1

Baseline characteristics

Reporting groups	
Reporting group title	HBsAg/AS_1+2 Group
Reporting group description:	
Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30, followed by 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30; and during Step 2 of the study, 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.	
Reporting group title	Engerix-B_1+2 Group
Reporting group description:	
Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30 followed by 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180; and during Step 2 of the study, 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.	

Reporting group values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group	Total
Number of subjects	40	41	81
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39.2	37.5	
standard deviation	± 4.1	± 5.9	-
Gender categorical Units: Subjects			
Female	25	26	51
Male	15	15	30
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	1	0	1
White - Arabic / North African Heritage	1	2	3
White - Caucasian / European Heritage	38	39	77

End points

End points reporting groups

Reporting group title	HBsAg/AS_1+2 Group

Reporting group description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30, followed by 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30; and during Step 2 of the study, 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Reporting group title	Engerix-B_1+2 Group

Reporting group description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30 followed by 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180; and during Step 2 of the study, 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Subject analysis set title	hbsag/as_1 group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30, followed by 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Subject analysis set title	engerix-b_1 group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30 followed by 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Subject analysis set title	hbsag/as_2 group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received, during Step 2 of the study, 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm

Subject analysis set title	engerix-b_2 group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received, during Step 2 of the study, 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Primary: Concentrations of cytokines and chemokines - Step 1

End point title	Concentrations of cytokines and chemokines - Step 1[1]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

At Day -30 prior to product administration

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6000 (4600 to 8300)	6250 (4600 to 7800)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.5)	3.3 (3.3 to 4.1)		
IL-18	198 (148 to 290)	177 (152 to 215)		
IL-2	5.9 (5.9 to 7)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	26000 (20000 to 30000)	22500 (22000 to 30000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.7 (4.2 to 6.6)	5.1 (3.9 to 5.9)		
IP-10	225 (176 to 402)	247.5 (195 to 280)		
MCP-1	107 (89 to 142)	98.5 (83 to 117)		
MCP-2	18 (13 to 25)	19.5 (17 to 26)		
MCP-4	1230 (1070 to 1550)	1170 (1100 to 1600)		
MIG	513 (354 to 682)	435 (285 to 674)		
MIP-1 alpha	20 (18 to 25)	20 (18 to 24)		
MIP-1 beta	190 (162 to 228)	138 (126 to 205)		
MIP-3 alpha	25 (11 to 32)	18 (11 to 28)		
MPIF-1	1600 (1200 to 1800)	1450 (1200 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations - Step 1

End point title	Cytokines and chemokines concentrations - Step 1[2]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 1.5 Hours

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5900 (4100 to 8500)	6450 (4500 to 7600)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.7)	3.3 (3.3 to 3.7)		
IL-18	172 (141 to 225)	179.5 (136 to 215)		
IL-2	5.9 (5.9 to 7)	5.9 (5.9 to 6.3)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	26000 (21000 to 30000)	22000 (19000 to 29000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.2 (3.7 to 4.9)	4.2 (3.2 to 5.3)		
IP-10	220 (183 to 330)	207 (172 to 240)		
MCP-1	79 (58 to 101)	77.5 (63 to 96)		
MCP-2	17 (13 to 24)	19 (14 to 25)		
MCP-4	1300 (933 to 1480)	1190 (896 to 1300)		
MIG	392 (344 to 575)	336 (269 to 487)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 19)		
MIP-1 beta	141 (108 to 191)	124.5 (107 to 151)		
MIP-3 alpha	16 (13 to 27)	16 (13 to 22)		
MPIF-1	1500 (1200 to 1600)	1400 (1000 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines in Step 1

End point title	Concentrations of cytokines and chemokines in Step 1[3]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 3 Hours

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5600 (3800 to 7800)	6300 (4100 to 7600)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.2)	3.3 (3.3 to 3.4)		
IL-18	168 (154 to 283)	173 (142 to 202)		
IL-2	5.9 (5.9 to 7.4)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	28000 (22000 to 34000)	26000 (21000 to 33000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.2 (3.5 to 6.4)	4 (3.2 to 5.3)		
IP-10	223 (169 to 396)	217.5 (175 to 251)		
MCP-1	79 (65 to 92)	64 (48 to 104)		
MCP-2	21 (14 to 27)	20 (18 to 23)		
MCP-4	1170 (951 to 1440)	1175 (1060 to 1310)		
MIG	439 (347 to 558)	343 (285 to 504)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 21)		
MIP-1 beta	163 (120 to 199)	127 (112 to 147)		
MIP-3 alpha	18 (12 to 27)	18 (14 to 22)		
MPIF-1	1600 (1200 to 1900)	1300 (1000 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines during Step 1

End point title	Concentrations of cytokines and chemokines during Step 1[4]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 6 Hours

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5200 (3900 to 8300)	6050 (4200 to 8100)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.6)	3.3 (3.3 to 3.6)		
IL-18	176 (160 to 273)	177.5 (132 to 233)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 2)	1.6 (1.6 to 1.6)		
IL-6r	27000 (21000 to 32000)	24500 (20000 to 33000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.5 (3.7 to 6)	4.5 (3.9 to 5.8)		
IP-10	217 (177 to 400)	218 (174 to 252)		
MCP-1	104 (76 to 119)	101 (76 to 129)		
MCP-2	18 (14 to 24)	20.5 (16 to 23)		

MCP-4	1310 (1030 to 1570)	1245 (1110 to 1490)		
MIG	500 (320 to 614)	378 (313 to 566)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 19)		
MIP-1 beta	166 (140 to 215)	146 (129 to 180)		
MIP-3 alpha	21 (15 to 26)	20 (15 to 24)		
MPIF-1	1500 (1200 to 1800)	1400 (1100 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines - Step 1

End point title	Concentrations of cytokines/chemokines - Step 1[5]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 9 Hours

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5300 (3600 to 7100)	6100 (4600 to 7500)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.8)	3.3 (3.3 to 3.3)		
IL-18	173 (139 to 226)	167.5 (117 to 202)		
IL-2	5.9 (5.9 to 14)	5.9 (5.9 to 7.2)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 2.7)	1.6 (1.6 to 1.6)		

IL-6r	24000 (19000 to 31000)	26000 (19000 to 29000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.9 (3.7 to 6.9)	4.5 (3.6 to 5.3)		
IP-10	210 (162 to 327)	205.5 (159 to 227)		
MCP-1	86 (65 to 104)	81 (61 to 109)		
MCP-2	17 (15 to 24)	17 (15 to 21)		
MCP-4	1310 (1050 to 1610)	1145 (944 to 1400)		
MIG	452 (313 to 610)	327 (244 to 528)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 18)		
MIP-1 beta	131 (111 to 185)	119.5 (102 to 134)		
MIP-3 alpha	19 (11 to 25)	15 (11 to 17)		
MPIF-1	1400 (1100 to 1800)	1200 (1000 to 1400)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines in Step 1

End point title	Concentrations of cytokines/chemokines in Step 1[6]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 12 Hours

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5200 (3500 to 7900)	5600 (4000 to 7800)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.3)	3.3 (3.3 to 3.3)		

IL-18	171 (150 to 244)	180 (131 to 222)		
IL-2	5.9 (5.9 to 6.3)	5.9 (5.9 to 6.3)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	26000 (21000 to 32000)	24000 (21000 to 34000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.6 (3.9 to 5.9)	4.5 (3.9 to 5.8)		
IP-10	217 (160 to 335)	214 (182 to 246)		
MCP-1	117 (79 to 133)	120 (96 to 137)		
MCP-2	18 (14 to 26)	19 (17 to 25)		
MCP-4	1260 (1000 to 1480)	1160 (997 to 1480)		
MIG	460 (344 to 623)	412 (341 to 564)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 21)		
MIP-1 beta	159 (120 to 179)	137 (118 to 167)		
MIP-3 alpha	21 (14 to 26)	22 (17 to 28)		
MPIF-1	1400 (1200 to 1700)	1300 (1000 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines during Step 1

End point title	Concentrations of cytokines/chemokines during Step 1[7]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -30 plus 18 Hours

Notes:

[7] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	11		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	4950 (2900 to 6500)	4200 (2700 to 6300)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.6)	3.3 (3.3 to 3.3)		
IL-18	174 (118 to 267)	142 (81 to 182)		
IL-2	6 (5.9 to 6.3)	5.9 (5.9 to 6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 2.4)		
IL-6r	21500 (18000 to 29000)	21000 (18000 to 28000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.5 (4.6 to 8.2)	6.1 (4.9 to 7.8)		
IP-10	243.5 (174 to 386)	238 (170 to 483)		
MCP-1	98 (76 to 119)	109 (79 to 132)		
MCP-2	18 (12 to 26)	17 (16 to 27)		
MCP-4	1445 (1130 to 1640)	1390 (1140 to 1710)		
MIG	420 (373 to 636)	458 (340 to 811)		
MIP-1 alpha	18 (18 to 26)	18 (18 to 23)		
MIP-1 beta	143.5 (136 to 182)	165 (128 to 216)		
MIP-3 alpha	30 (21 to 34)	20 (17 to 38)		
MPIF-1	1400 (1300 to 1700)	1100 (920 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations in Step 1

End point title	Cytokines and chemokines concentrations in Step 1[8]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -29

Notes:

[8] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5900 (4300 to 8500)	6350 (4500 to 8600)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.5)	3.3 (3.3 to 3.3)		
IL-18	186 (149 to 261)	177.5 (136 to 242)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.7)	1.6 (1.6 to 1.7)		
IL-6r	27000 (19000 to 35000)	26500 (19000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.4 (3.9 to 6.9)	5.2 (4.3 to 6.8)		
IP-10	241 (190 to 345)	244.5 (200 to 307)		
MCP-1	93 (73 to 116)	81.5 (66 to 104)		
MCP-2	19 (15 to 24)	19 (16 to 25)		
MCP-4	1230 (1070 to 1350)	1170 (1020 to 1450)		
MIG	528 (327 to 695)	418.5 (352 to 721)		
MIP-1 alpha	19 (18 to 24)	18 (18 to 21)		
MIP-1 beta	169 (124 to 219)	141.5 (123 to 188)		
MIP-3 alpha	22 (17 to 28)	21 (14 to 28)		
MPIF-1	1700 (1200 to 1900)	1500 (1100 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concetrations during Step 1

End point title	Cytokines and chemokines concetrations during Step 1[9]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -28

Notes:

[9] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5900 (3700 to 7800)	6250 (4300 to 7900)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.9)	3.3 (3.3 to 3.9)		
IL-18	182 (148 to 288)	178.5 (120 to 232)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	27000 (20000 to 35000)	25500 (20000 to 28000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.8 (3.7 to 6.5)	4.9 (3.5 to 6.6)		
IP-10	270 (205 to 381)	228 (186 to 304)		
MCP-1	74 (56 to 112)	73.5 (47 to 90)		
MCP-2	19 (13 to 26)	18.5 (15 to 26)		
MCP-4	1200 (937 to 1530)	1140 (951 to 1340)		
MIG	468 (336 to 568)	397 (292 to 587)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 18)		
MIP-1 beta	174 (141 to 227)	151.5 (113 to 175)		
MIP-3 alpha	20 (15 to 28)	17.5 (11 to 33)		
MPIF-1	1500 (1200 to 1800)	1350 (970 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines/chemokines concentrations in Step 1

End point title	Cytokines/chemokines concentrations in Step 1[10]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -27

Notes:

[10] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6150 (3700 to 8200)	6250 (4000 to 7200)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.4 (3.3 to 4.5)	3.3 (3.3 to 4.2)		
IL-18	183 (157 to 236)	174.5 (139 to 217)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.7)	1.6 (1.6 to 1.7)		
IL-6r	26000 (21000 to 32000)	24000 (21000 to 29000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.3 (3.4 to 6.6)	4.2 (3.6 to 5.4)		
IP-10	239 (189 to 348)	220.5 (186 to 281)		
MCP-1	84.5 (65 to 110)	86.5 (73 to 109)		
MCP-2	18.5 (14 to 22)	20 (15 to 25)		

MCP-4	1150 (989 to 1270)	1060 (911 to 1360)		
MIG	429.5 (349 to 542)	403.5 (300 to 635)		
MIP-1 alpha	18 (18 to 23)	18 (18 to 19)		
MIP-1 beta	165 (117 to 196)	141 (106 to 181)		
MIP-3 alpha	20.5 (18 to 27)	21 (18 to 26)		
MPIF-1	1350 (1200 to 1700)	1300 (1100 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations during Step 1

End point title	Cytokines and chemokines concentrations during Step 1[11]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-placebo at Day -23

Notes:

[11] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5500 (4000 to 8300)	6150 (4700 to 7900)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.3)	3.3 (3.3 to 3.5)		
IL-18	184 (150 to 247)	176.5 (122 to 208)		
IL-2	5.9 (5.9 to 7)	5.9 (5.9 to 7)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		

IL-6r	27000 (17000 to 310000)	23500 (19000 to 28000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.5 (3.9 to 6.8)	5 (3.5 to 5.8)		
IP-10	241 (190 to 366)	223 (186 to 285)		
MCP-1	88 (55 to 143)	72 (66 to 96)		
MCP-2	15 (14 to 25)	19 (16 to 23)		
MCP-4	1390 (1000 to 1480)	1145 (1000 to 1350)		
MIG	391 (337 to 524)	375.5 (286 to 625)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 19)		
MIP-1 beta	165 (128 to 199)	138.5 (113 to 158)		
MIP-3 alpha	21 (13 to 28)	16 (10 to 21)		
MPIF-1	1600 (1200 to 1800)	1350 (1000 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines - study Step 1

End point title	Concentrations of cytokines and chemokines - study Step 1[12]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Pre-dose1 at Day 0

Notes:

[12] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6100 (4200 to 9000)	6150 (5000 to 8600)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.5)	3.3 (3.3 to 3.9)		

IL-18	169 (151 to 237)	171 (119 to 207)		
IL-2	5.9 (5.9 to 6.5)	5.9 (5.9 to 6.5)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	27000 (20000 to 32000)	24500 (22000 to 29000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.9 (4.2 to 6.2)	5 (4.2 to 7.4)		
IP-10	243 (199 to 294)	225 (178 to 334)		
MCP-1	94 (75 to 121)	92.5 (80 to 125)		
MCP-2	18 (14 to 22)	19 (16 to 28)		
MCP-4	1310 (1110 to 1570)	1260 (1030 to 1520)		
MIG	496 (328 to 705)	462.5 (303 to 701)		
MIP-1 alpha	18 (18 to 23)	18 (18 to 19)		
MIP-1 beta	164 (121 to 198)	153 (124 to 196)		
MIP-3 alpha	20 (11 to 27)	19.5 (14 to 24)		
MPIF-1	1500 (1300 to 1700)	1300 (1000 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines in Step 1 of study

End point title	Concentrations of cytokines and chemokines in Step 1 of

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 0 plus 1.5 Hours

Notes:

[13] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5500 (4000 to 8400)	5900 (4800 to 8100)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.8)	3.3 (3.3 to 3.9)		
IL-18	168 (144 to 220)	168 (126 to 208)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 7.4)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	26000 (21000 to 32000)	25000 (19000 to 29000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.9 (3.6 to 5.5)	4.2 (3.3 to 5.1)		
IP-10	224 (198 to 318)	226 (186 to 265)		
MCP-1	74 (56 to 97)	75 (56 to 108)		
MCP-2	18 (14 to 23)	20 (16 to 22)		
MCP-4	1240 (943 to 1520)	1240 (951 to 1340)		
MIG	423 (385 to 535)	378 (308 to 522)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 19)		
MIP-1 beta	164 (132 to 194)	137 (114 to 167)		
MIP-3 alpha	18 (15 to 26)	20 (14 to 24)		
MPIF-1	1500 (1300 to 1800)	1200 (970 to 1400)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines during Step 1 of study

End point title	Concentrations of cytokines and chemokines during Step 1 of study[14]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 0 plus 6 Hours

Notes:

[14] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5400 (4100 to 7600)	5900 (4300 to 7600)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.3)	3.3 (3.3 to 3.3)		
IL-18	170 (130 to 225)	169 (110 to 220)		
IL-2	5.9 (5.9 to 6)	5.9 (5.9 to 6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	3.4 (2.4 to 6)	1.6 (1.6 to 1.7)		
IL-6r	26000 (20000 to 33000)	25000 (22000 to 30000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.6 (3.9 to 5.5)	4.6 (3.9 to 7.2)		
IP-10	207 (179 to 270)	204 (180 to 282)		
MCP-1	94 (75 to 123)	85 (66 to 112)		
MCP-2	18 (15 to 20)	18.5 (16 to 23)		
MCP-4	1130 (912 to 1390)	1130 (989 to 1310)		
MIG	459 (332 to 567)	372.5 (302 to 557)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 19)		
MIP-1 beta	165 (129 to 181)	141 (111 to 174)		
MIP-3 alpha	19 (15 to 28)	18.5 (12 to 23)		
MPIF-1	1400 (1200 to 1600)	1300 (1000 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations - study Step 1

End point title	Cytokines and chemokines concentrations - study Step 1[15]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 0 plus 12 Hours

Notes:

[15] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5900 (4400 to 8800)	6400 (5000 to 8000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.9 (3.3 to 5.5)	3.3 (3.3 to 3.3)		
IL-18	171 (155 to 235)	181.5 (128 to 205)		
IL-2	5.9 (5.9 to 6.5)	5.9 (5.9 to 6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	6.3 (3.9 to 8.2)	1.6 (1.6 to 1.6)		
IL-6r	26000 (21000 to 32000)	24000 (22000 to 33000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.2 (3.5 to 5.1)	4.8 (4 to 5.6)		
IP-10	236 (197 to 281)	194 (167 to 282)		
MCP-1	111 (87 to 137)	111.5 (84 to 129)		
MCP-2	19 (15 to 27)	19.5 (15 to 25)		
MCP-4	1260 (1000 to 1530)	1265 (1030 to 1520)		
MIG	478 (361 to 614)	410 (296 to 588)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 19)		
MIP-1 beta	183 (142 to 212)	132 (102 to 171)		
MIP-3 alpha	20 (17 to 28)	19.5 (14 to 27)		
MPIF-1	1600 (1200 to 1700)	1300 (1000 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations in Step 1 of study

End point title	Cytokines and chemokines concentrations in Step 1 of study[16]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 0 plus 18 Hours

Notes:

[16] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	11		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5750 (3400 to 8000)	4700 (3500 to 5900)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.8 (1.6 to 2.4)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.8)	3.3 (3.3 to 3.3)		
IL-18	180 (155 to 217)	126 (93 to 168)		
IL-2	5.9 (5.9 to 6)	5.9 (5.9 to 6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	4.5 (3.1 to 6.9)	1.6 (1.6 to 1.6)		
IL-6r	22500 (17000 to 26000)	22000 (19000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.9 (4.5 to 6.4)	5.1 (4.2 to 6)		
IP-10	319 (268 to 477)	228 (184 to 258)		
MCP-1	111 (91 to 130)	115 (98 to 130)		
MCP-2	29.5 (19 to 34)	20 (17 to 22)		

MCP-4	1400 (1310 to 1650)	1400 (1220 to 1560)		
MIG	571 (443 to 684)	473 (367 to 722)		
MIP-1 alpha	18 (18 to 20)	18 (18 to 18)		
MIP-1 beta	258 (200 to 303)	134 (117 to 206)		
MIP-3 alpha	35.5 (24 to 45)	20 (17 to 30)		
MPIF-1	1850 (1500 to 2100)	1400 (1100 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations during Step 1 of study

End point title	Cytokines and chemokines concentrations during Step 1 of study[17]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 1

Notes:

[17] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5950 (4200 to 9500)	6000 (4900 to 8900)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	5.2 (3.6 to 6.8)	3.3 (3.3 to 3.6)		
IL-18	198.5 (167 to 267)	181 (123 to 200)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	3 (1.6 to 4.1)	1.6 (1.6 to 1.6)		

IL-6r	26500 (22000 to 35000)	24500 (21500 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.1 (4.1 to 6.3)	4.4 (3.8 to 5.6)		
IP-10	295 (251 to 414)	219 (179 to 326)		
MCP-1	85.5 (67 to 101)	92 (73 to 112)		
MCP-2	21 (16 to 26)	20 (17 to 25)		
MCP-4	1360 (1120 to 1600)	1270 (1100 to 1630)		
MIG	526 (441 to 678)	425 (299 to 606)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 20)		
MIP-1 beta	282.5 (234 to 408)	145 (130 to 207)		
MIP-3 alpha	17 (14 to 28)	16 (12 to 23)		
MPIF-1	2300 (2000 to 2600)	1400 (1200 to 1800)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines/chemokines concentrations - study Step 1

End point title	Cytokines/chemokines concentrations - study Step 1[18]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 2

Notes:

[18] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5800 (4300 to 9300)	6300 (5000 to 7400)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		

IL-10	3.6 (3.3 to 4.3)	3.3 (3.3 to 3.7)		
IL-18	219 (165 to 252)	167 (130 to 219)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	25000 (18000 to 33000)	24000 (20000 to 30000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.8 (3.8 to 6.4)	5 (4.2 to 5.6)		
IP-10	455 (291 to 569)	214 (174 to 303)		
MCP-1	83 (55 to 95)	79 (58 to 101)		
MCP-2	22 (17 to 25)	20 (15 to 25)		
MCP-4	1300 (1010 to 1600)	1230 (1010 to 1390)		
MIG	546 (435 to 593)	364 (255 to 620)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 21)		
MIP-1 beta	200 (160 to 265)	149 (126 to 189)		
MIP-3 alpha	19 (14 to 25)	21 (16 to 28)		
MPIF-1	1600 (1300 to 2000)	1300 (890 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines/chemokines concentrations in Step 1 of study

End point title	Cytokines/chemokines concentrations in Step 1 of study[19]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 7

Notes:

[19] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6600 (4100 to 8600)	6700 (4800 to 8500)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.6 (3.3 to 4.9)	3.3 (3.3 to 3.9)		
IL-18	202 (168 to 265)	191 (126 to 231)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	27000 (21000 to 35000)	25000 (21000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5 (4.2 to 6.9)	5.1 (4.2 to 6.7)		
IP-10	235 (178 to 350)	220.5 (185 to 279)		
MCP-1	94 (73 to 119)	88.5 (71 to 125)		
MCP-2	20 (16 to 24)	22.5 (18 to 30)		
MCP-4	1250 (1040 to 1390)	1240 (1010 to 1420)		
MIG	475 (384 to 582)	436.5 (304 to 687)		
MIP-1 alpha	18 (18 to 26)	18 (18 to 22)		
MIP-1 beta	171 (142 to 243)	173.5 (146 to 213)		
MIP-3 alpha	18 (14 to 26)	22 (16 to 34)		
MPIF-1	1600 (1300 to 2100)	1300 (1100 to 1500)		
TNF-alpha	13 (13 to 17)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines/chemokines concentrations during Step 1 of study

End point title	Cytokines/chemokines concentrations during Step 1 of study[20]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose1 at Day 30

Notes:

[20] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6200 (4300 to 9000)	6500 (5200 to 8000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.4)	3.3 (3.3 to 3.4)		
IL-18	202 (151 to 248)	183 (136 to 234)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 2.3)	1.6 (1.6 to 1.6)		
IL-6r	27000 (20000 to 32000)	26000 (21000 to 30000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.8 (3.9 to 6)	4.3 (3.4 to 5.8)		
IP-10	245 (211 to 349)	235 (183 to 264)		
MCP-1	99 (72 to 136)	86 (72 to 111)		
MCP-2	16 (14 to 23)	20 (14 to 24)		
MCP-4	1180 (937 to 1340)	1010 (937 to 1210)		
MIG	475 (393 to 768)	452 (281 to 691)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 18)		
MIP-1 beta	175 (141 to 240)	147 (126 to 181)		
MIP-3 alpha	20 (15 to 30)	20 (16 to 27)		
MPIF-1	1500 (1300 to 1800)	1300 (940 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines - Step 1

End point title	Plasma concentrations of cytokines and chemokines - Step 1[21]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 1.5 Hours

Notes:

[21] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6300 (3900 to 7600)	5700 (4900 to 6800)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.5)	3.3 (3.3 to 4.3)		
IL-18	171 (143 to 223)	176 (127 to 207)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	24000 (18000 to 30000)	25000 (20000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	3.2 (3 to 5.6)	4.3 (2.7 to 5)		
IP-10	223 (189 to 336)	215 (173 to 247)		
MCP-1	85 (58 to 112)	87 (66 to 104)		
MCP-2	15 (12 to 23)	18 (15 to 22)		
MCP-4	1250 (1030 to 1400)	1090 (1020 to 1330)		
MIG	421 (361 to 856)	367 (269 to 575)		
MIP-1 alpha	18 (18 to 22)	18 (18 to 20)		
MIP-1 beta	164 (132 to 196)	136 (115 to 170)		
MIP-3 alpha	17 (10 to 22)	14 (11 to 19)		
MPIF-1	1400 (1200 to 1500)	1200 (930 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines - study Step 1

End point title	Plasma concentrations of cytokines and chemokines - study Step 1[22]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 3 Hours

Notes:

[22] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	24		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6550 (4000 to 8200)	5700 (4450 to 6850)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 4.5)	3.3 (3.3 to 3.4)		
IL-18	171.5 (146 to 204)	158 (104 to 206.5)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 2.5)	1.6 (1.6 to 1.6)		
IL-6r	26000 (18000 to 31000)	23000 (19000 to 28500)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.7 (3.9 to 6)	4.5 (3.8 to 5)		
IP-10	208 (182 to 275)	205.5 (176 to 243.5)		
MCP-1	75 (62 to 95)	75 (51 to 85)		
MCP-2	15.5 (12 to 27)	18 (14.5 to 22.5)		

MCP-4	1095 (979 to 1410)	1085 (824.5 to 1250)		
MIG	378.5 (313 to 513)	358 (237 to 650.5)		
MIP-1 alpha	18 (18 to 20)	18 (18 to 18.5)		
MIP-1 beta	153 (135 to 220)	138 (123.5 to 157.5)		
MIP-3 alpha	15 (10 to 22)	14 (10 to 15.5)		
MPIF-1	1500 (1200 to 1600)	1200 (980 to 1450)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines in Step 1 of study

End point title	Plasma concentrations of cytokines and chemokines in Step 1 of study[23]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 6 hours

Notes:

[23] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	26		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6000 (4200 to 8100)	5850 (4550 to 7000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.7)	3.3 (3.3 to 3.3)		
IL-18	173.5 (151 to 227)	183 (127.5 to 211.5)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	4.4 (2.8 to 6.7)	1.6 (1.6 to 1.6)		

IL-6r	23000 (18000 to 29000)	24500 (20500 to 30500)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.2 (3.5 to 6.7)	4.5 (3.5 to 5.2)		
IP-10	210.5 (182 to 248)	196.5 (160 to 248.5)		
MCP-1	116.5 (98 to 132)	95 (79 to 121)		
MCP-2	17 (12 to 24)	18.5 (15 to 24)		
MCP-4	1245 (954 to 1590)	1065 (936 to 1350)		
MIG	375 (320 to 505)	387.5 (239 to 671)		
MIP-1 alpha	18 (18 to 19)	18 (18 to 18)		
MIP-1 beta	177.5 (128 to 225)	139.5 (127.5 to 163.5)		
MIP-3 alpha	16 (10 to 24)	16 (12 to 22)		
MPIF-1	1400 (1200 to 1600)	1300 (1015 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines during Step 1 of study

End point title	Plasma concentrations of cytokines and chemokines during Step 1 of study[24]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 9 Hours

Notes:

[24] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	24		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6200 (4100 to 7400)	5500 (4350 to 6850)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		

IL-10	3.3 (3.3 to 5.2)	3.3 (3.3 to 3.4)		
IL-18	177 (139 to 240)	165 (115 to 229.5)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 6.6)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	4.8 (3.2 to 6.7)	1.6 (1.6 to 1.6)		
IL-6r	23000 (17000 to 30000)	24500 (18500 to 30500)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.1 (3.2 to 5.5)	4 (3.2 to 5.4)		
IP-10	217 (180 to 326)	204 (168 to 234)		
MCP-1	103 (88 to 119)	80 (55 to 106)		
MCP-2	18 (14 to 24)	18.5 (14.5 to 20.5)		
MCP-4	1190 (999 to 1470)	1075 (820 to 1295)		
MIG	424 (384 to 621)	350 (300 to 620)		
MIP-1 alpha	18 (18 to 19)	18 (18 to 18)		
MIP-1 beta	167 (120 to 220)	123.5 (108.5 to 146.5)		
MIP-3 alpha	16 (14 to 23)	15.5 (11 to 19)		
MPIF-1	1400 (1100 to 1600)	1200 (950 to 1400)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines/chemokines during Step 1 of study

End point title	Plasma concentrations of cytokines/chemokines during Step 1 of study[25]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 12 Hours

Notes:

[25] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5800 (4000 to 7800)	5800 (4500 to 7000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	2.3 (1.6 to 3.1)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.8)	3.3 (3.3 to 3.3)		
IL-18	166 (146 to 212)	174 (124 to 220)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	6.4 (5 to 9)	1.6 (1.6 to 1.7)		
IL-6r	23000 (21000 to 31000)	24000 (21000 to 32000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.9 (4.1 to 6)	5.2 (3.2 to 6)		
IP-10	240 (228 to 335)	200 (166 to 240)		
MCP-1	117 (96 to 150)	95 (71 to 121)		
MCP-2	20 (14 to 26)	18 (15 to 22)		
MCP-4	1100 (916 to 1330)	1040 (852 to 1170)		
MIG	499 (398 to 872)	377 (290 to 689)		
MIP-1 alpha	18 (18 to 20)	18 (18 to 18)		
MIP-1 beta	191 (162 to 238)	134 (118 to 162)		
MIP-3 alpha	20 (15 to 26)	14 (11 to 20)		
MPIF-1	1500 (1100 to 1700)	1300 (1100 to 1500)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines/chemokines - Step 1 of study

End point title	Plasma concentrations of cytokines/chemokines - Step 1 of study[26]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 30 plus 18 Hours

Notes:

[26] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	11		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	5400 (3400 to 8000)	4500 (2900 to 5800)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	5.2 (1.6 to 7.4)	1.6 (1.6 to 1.6)		
IL-10	4.5 (3.3 to 6)	3.3 (3.3 to 3.4)		
IL-18	164.5 (151 to 241)	168 (128 to 197)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	6.3 (4.2 to 8.3)	1.6 (1.6 to 1.6)		
IL-6r	19500 (13000 to 24000)	24000 (17000 to 32000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	4.8 (4.1 to 5.4)	5 (3.5 to 5.9)		
IP-10	589.5 (296 to 715)	216 (196 to 430)		
MCP-1	104.5 (76 to 116)	96 (91 to 106)		
MCP-2	33 (19 to 54)	22 (16 to 23)		
MCP-4	1220 (1090 to 1290)	1260 (1000 to 1340)		
MIG	565.5 (373 to 791)	442 (300 to 633)		
MIP-1 alpha	18 (18 to 23)	18 (18 to 23)		
MIP-1 beta	283.5 (228 to 327)	144 (111 to 176)		
MIP-3 alpha	24 (19 to 31)	17 (11 to 20)		
MPIF-1	1600 (1300 to 2300)	1400 (1100 to 1700)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines/chemokines in Step 1 of study

End point title	Plasma concentrations of cytokines/chemokines in Step 1 of study[27]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 31

Notes:

[27] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6800 (4300 to 8200)	5800 (5200 to 7100)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	4.8 (1.7 to 8.6)	1.6 (1.6 to 1.6)		
IL-10	4.8 (3.3 to 6.3)	3.3 (3.3 to 3.3)		
IL-18	185 (151 to 258)	166 (137 to 217)		
IL-2	8.5 (5.9 to 8.5)	5.9 (5.9 to 8.5)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	3.6 (1.7 to 7.2)	1.6 (1.6 to 1.6)		
IL-6r	26000 (17000 to 33000)	24000 (22000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.6 (4.8 to 7)	4.8 (3.9 to 5.9)		
IP-10	763 (405 to 1130)	212 (197 to 270)		
MCP-1	101 (79 to 137)	71 (60 to 93)		
MCP-2	35 (19 to 67)	17 (14 to 19)		
MCP-4	1250 (1090 to 1400)	1090 (912 to 1330)		
MIG	763 (604 to 1260)	427 (308 to 597)		
MIP-1 alpha	18 (18 to 21)	18 (18 to 18)		
MIP-1 beta	383 (301 to 540)	142 (120 to 176)		
MIP-3 alpha	22 (17 to 25)	19 (12 to 28)		
MPIF-1	2000 (1500 to 2300)	1100 (950 to 1600)		
TNF-alpha	15 (13 to 21)	13 (13 to 13)		

TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of plasma cytokines and chemokines - Step 1

End point title	Concentrations of plasma cytokines and chemokines - Step

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 32

Notes:

[28] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	7000 (4400 to 9100)	6000 (4900 to 8000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.5 (3.3 to 5.3)	3.3 (3.3 to 3.5)		
IL-18	238 (195 to 269)	190 (135 to 238)		
IL-2	5.9 (5.9 to 7)	5.9 (5.9 to 7)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 2.5)	1.6 (1.6 to 1.6)		
IL-6r	27000 (21000 to 32000)	24000 (21000 to 31000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.5 (4.3 to 6.5)	5.1 (4 to 6.5)		
IP-10	760 (492 to 993)	226 (192 to 276)		
MCP-1	75 (55 to 94)	77 (65 to 121)		
MCP-2	24 (17 to 31)	21 (17 to 25)		

MCP-4	1350 (1080 to 1580)	1260 (1010 to 1560)		
MIG	850 (667 to 1070)	410 (320 to 581)		
MIP-1 alpha	18 (18 to 19)	18 (18 to 23)		
MIP-1 beta	268 (222 to 307)	142 (124 to 171)		
MIP-3 alpha	23 (16 to 30)	19 (13 to 28)		
MPIF-1	1800 (1400 to 2300)	1200 (990 to 1700)		
TNF-alpha	13 (13 to 14)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of plasma cytokines and chemokines in Step 1

End point title	Concentrations of plasma cytokines and chemokines in Step

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 33

Notes:

[29] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6400 (4400 to 8700)	6300 (5100 to 8000)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10	3.3 (3.3 to 3.6)	3.3 (3.3 to 3.6)		
IL-18	256 (195 to 351)	181 (142 to 231)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		

IL-6r	26000 (21000 to 33000)	25000 (21000 to 28000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.5 (4.3 to 7.4)	5.5 (4.3 to 6.2)		
IP-10	366 (288 to 524)	249 (220 to 319)		
MCP-1	85 (65 to 101)	93 (77 to 131)		
MCP-2	20 (16 to 28)	20 (17 to 26)		
MCP-4	1390 (1190 to 1600)	1280 (1090 to 1600)		
MIG	796 (586 to 908)	537 (456 to 722)		
MIP-1 alpha	22 (18 to 24)	19 (18 to 22)		
MIP-1 beta	241 (175 to 279)	163 (135 to 201)		
MIP-3 alpha	25 (21 to 40)	25 (21 to 32)		
MPIF-1	1800 (1400 to 2200)	1300 (1100 to 1600)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of plasma cytokines and chemokines during Step 1

End point title	Concentrations of plasma cytokines and chemokines during Step 1[30]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 37

Notes:

[30] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin	6200 (4000 to 8200)	6000 (5000 to 7700)		
GM-CSF	14 (14 to 14)	14 (14 to 14)		
IFN-γ	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		

IL-10	3.3 (3.3 to 3.3)	3.3 (3.3 to 3.3)		
IL-18	194 (156 to 256)	166 (123 to 196)		
IL-2	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r	28000 (16000 to 35000)	25000 (20000 to 27000)		
IL-7	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8	5.3 (3.9 to 6.6)	5.5 (4.6 to 6)		
IP-10	259 (213 to 296)	223 (179 to 289)		
MCP-1	83 (66 to 109)	85 (63 to 99)		
MCP-2	17 (13 to 23)	20 (16 to 24)		
MCP-4	1220 (1110 to 1480)	1210 (1010 to 1340)		
MIG	447 (398 to 535)	364 (284 to 472)		
MIP-1 alpha	18 (18 to 23)	18 (18 to 19)		
MIP-1 beta	150 (119 to 190)	151 (126 to 175)		
MIP-3 alpha	18 (15 to 28)	18 (15 to 24)		
MPIF-1	1600 (1200 to 1800)	1300 (1000 to 1400)		
TNF-alpha	13 (13 to 13)	13 (13 to 13)		
TNF-beta	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines - Step 2

End point title	Concentrations of cytokines and chemokines - Step 2[31]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.

End point type	Primary

End point timeframe:

Pre-dose 1 at Day 0

Notes:

[31] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=6, 9]	8100 (4200 to 8900)	5400 (4400 to 5500)		
GM-CSF [N=6, 9]	14 (14 to 14)	14 (14 to 14)		
IFN-γ [N=6, 9]	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-10 [N=6, 9]	3.3 (3.3 to 3.8)	3.3 (3.3 to 3.3)		
IL-18 [N=6, 9]	199.5 (175 to 377)	179 (152 to 182)		
IL-2 [N=6, 9]	5.9 (5.9 to 5.9)	5.9 (5.9 to 5.9)		
IL-3 [N=6, 9]	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-4 [N=6, 9]	9.4 (9.4 to 9.4)	9.4 (9.4 to 9.4)		
IL-5 [N=6, 9]	2.7 (2.7 to 2.7)	2.7 (2.7 to 2.7)		
IL-6 [N=6, 9]	1.6 (1.6 to 1.6)	1.6 (1.6 to 1.6)		
IL-6r [N=6, 9]	32000 (29000 to 36000)	30000 (28000 to 36000)		
IL-7 [N=6, 9]	8.2 (8.2 to 8.2)	8.2 (8.2 to 8.2)		
IL-8 [N=6, 9]	5.3 (3.5 to 11)	4.4 (3.5 to 6.2)		
IP-10 [N=6, 9]	300.5 (275 to 370)	234 (166 to 278)		
MCP-1 [N=6, 9]	86.5 (77 to 132)	87 (67 to 96)		
MCP-2 [N=6, 9]	22.5 (17 to 27)	27 (19 to 30)		
MCP-4 [N=6, 9]	1805 (1300 to 2010)	2120 (1720 to 2260)		
MIG [N=0, 0]	0 (0 to 0)	0 (0 to 0)		
MIP-1 alpha [N=6, 9]	18 (18 to 18)	18 (18 to 18)		
MIP-1 beta [N=6, 9]	234 (186 to 255)	253 (200 to 300)		
MIP-3 alpha [N=6, 9]	28.5 (23 to 64)	29 (17 to 42)		
MPIF-1 [N=6, 9]	1095 (820 to 1200)	1100 (930 to 1200)		
TNF-alpha [N=6, 9]	13 (13 to 13)	13 (13 to 13)		
TNF-beta [N=6, 9]	3 (3 to 3)	3 (3 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Cytokines and chemokines concentrations - Step 2

End point title	Cytokines and chemokines concentrations - Step 2[32]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the HBsAg/AS_2 Group.

End point type	Primary

End point timeframe:

Post-dose 1 at Day 1

Notes:

[32] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=7]	7900 (4300 to 9100)			
GM-CSF [N=7]	14 (14 to 14)			
IFN-γ [N=7]	1.6 (1.6 to 1.6)			
IL-10 [N=7]	3.8 (3.3 to 4.7)			
IL-18 [N=7]	206 (182 to 260)			
IL-2 [N=7]	5.9 (5.9 to 5.9)			
IL-3 [N=7]	1.6 (1.6 to 1.6)			
IL-4 [N=7]	9.4 (9.4 to 9.4)			
IL-5 [N=7]	2.7 (2.7 to 2.7)			
IL-6 [N=7]	1.7 (1.6 to 2.6)			
IL-6r [N=7]	24000 (22000 to 33000)			
IL-7 [N=7]	8.2 (8.2 to 8.2)			
IL-8 [N=7]	3.9 (2.6 to 7.1)			
IP-10 [N=7]	294 (199 to 390)			
MCP-1 [N=7]	35 (27 to 114)			
MCP-2 [N=7]	26 (20 to 29)			
MCP-4 [N=7]	1240 (1130 to 1640)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=7]	18 (18 to 32)			
MIP-1 beta [N=7]	318 (241 to 391)			
MIP-3 alpha [N=7]	32 (17 to 46)			
MPIF-1 [N=7]	1400 (1200 to 1500)			
TNF-alpha [N=7]	13 (13 to 13)			
TNF-beta [N=7]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines during Step 2

End point title	Concentrations of cytokines and chemokines during Step 2[33]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the HBsAg/AS_2 Group.

End point type	Primary

End point timeframe:

Post-dose 1 at Day 30

Notes:

[33] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=8]	6200 (3600 to 8450)			
GM-CSF [N=8]	14 (14 to 14)			
IFN-γ [N=8]	1.6 (1.6 to 1.6)			
IL-10 [N=8]	3.3 (3.3 to 3.6)			
IL-18 [N=8]	166.5 (132.5 to 271.5)			
IL-2 [N=8]	5.9 (5.9 to 5.9)			
IL-3 [N=8]	1.6 (1.6 to 1.6)			
IL-4 [N=8]	9.4 (9.4 to 11.2)			
IL-5 [N=8]	2.7 (2.7 to 2.7)			
IL-6 [N=8]	1.6 (1.6 to 1.7)			
IL-6r [N=8]	29000 (24500 to 33500)			
IL-7 [N=8]	8.2 (8.2 to 10.1)			
IL-8 [N=8]	4.3 (3.1 to 8.4)			
IP-10 [N=8]	231.5 (160.5 to 318.5)			
MCP-1 [N=8]	46 (35 to 115.5)			
MCP-2 [N=8]	19.5 (17 to 20.5)			
MCP-4 [N=8]	1340 (1115 to 1450)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=8]	18 (18 to 18)			
MIP-1 beta [N=8]	172 (158.5 to 196.5)			
MIP-3 alpha [N=8]	25 (15 to 30.5)			
MPIF-1 [N=8]	1200 (855 to 1400)			
TNF-alpha [N=8]	13 (13 to 13)			
TNF-beta [N=8]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines and chemokines in Step 2

End point title	Concentrations of cytokines and chemokines in Step 2[34]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the HBsAg/AS_2 Group.

End point type	Primary

End point timeframe:

Post-dose2 at Day 30 plus 6 Hours

Notes:

[34] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=7]	5400 (3400 to 8300)			
GM-CSF [N=7]	14 (14 to 14)			
IFN-γ [N=7]	1.6 (1.6 to 1.6)			
IL-10 [N=7]	3.3 (3.3 to 3.3)			
IL-18 [N=7]	172 (150 to 247)			
IL-2 [N=7]	5.9 (5.9 to 5.9)			
IL-3 [N=7]	1.6 (1.6 to 1.6)			
IL-4 [N=7]	9.4 (9.4 to 10)			
IL-5 [N=7]	2.7 (2.7 to 2.7)			
IL-6 [N=7]	3.7 (1.6 to 4.7)			
IL-6r [N=7]	34000 (27000 to 43000)			
IL-7 [N=7]	12 (8.2 to 21)			
IL-8 [N=7]	6.1 (3.6 to 9.1)			
IP-10 [N=7]	163 (128 to 205)			
MCP-1 [N=7]	59 (27 to 86)			
MCP-2 [N=7]	22 (18 to 25)			

MCP-4 [N=7]	1330 (979 to 1540)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=7]	18 (18 to 18)			
MIP-1 beta [N=7]	182 (154 to 266)			
MIP-3 alpha [N=7]	21 (13 to 28)			
MPIF-1 [N=7]	1300 (980 to 1700)			
TNF-alpha [N=7]	13 (13 to 13)			
TNF-beta [N=7]	3 (3 to 6.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines - Step 2

End point title	Concentrations of cytokines/chemokines - Step 2[35]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the HBsAg/AS_2 Group.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 31

Notes:

[35] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=8]	7450 (4600 to 10500)			
GM-CSF [N=8]	14 (14 to 14)			
IFN-γ [N=8]	6.2 (3.4 to 17.6)			
IL-10 [N=8]	3.3 (3.3 to 4.4)			
IL-18 [N=8]	234 (181 to 339.5)			
IL-2 [N=8]	5.9 (5.9 to 5.9)			
IL-3 [N=8]	1.6 (1.6 to 1.6)			
IL-4 [N=8]	9.7 (9.4 to 10)			
IL-5 [N=8]	2.7 (2.7 to 2.7)			
IL-6 [N=8]	4 (2.2 to 5.7)			

IL-6r [N=8]	30500 (27000 to 41500)			
IL-7 [N=8]	10.1 (8.2 to 23.5)			
IL-8 [N=8]	7.9 (7.3 to 10.9)			
IP-10 [N=8]	737.5 (510 to 1270)			
MCP-1 [N=8]	142.5 (104 to 153)			
MCP-2 [N=8]	40.5 (32 to 72.5)			
MCP-4 [N=8]	1330 (974 to 1780)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=8]	18 (18 to 18)			
MIP-1 beta [N=8]	580 (359.5 to 780.5)			
MIP-3 alpha [N=8]	28 (19 to 39.5)			
MPIF-1 [N=8]	1750 (1500 to 1850)			
TNF-alpha [N=8]	13 (13 to 13)			
TNF-beta [N=8]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines in Step 2

End point title	Concentrations of cytokines/chemokines in Step 2[36]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the HBsAg/AS_2 Group.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 37

Notes:

[36] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	hbsag/as_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=8]	6550 (3250 to 8450)			

GM-CSF [N=8]	14 (14 to 14)			
IFN-γ [N=8]	1.6 (1.6 to 1.6)			
IL-10 [N=8]	3.3 (3.3 to 3.8)			
IL-18 [N=8]	232 (145.5 to 322)			
IL-2 [N=8]	5.9 (5.9 to 5.9)			
IL-3 [N=8]	1.6 (1.6 to 1.6)			
IL-4 [N=8]	9.7 (9.4 to 14)			
IL-5 [N=8]	2.7 (2.7 to 2.7)			
IL-6 [N=8]	1.6 (1.6 to 1.7)			
IL-6r [N=8]	28000 (26500 to 34500)			
IL-7 [N=8]	8.2 (8.2 to 8.2)			
IL-8 [N=8]	8.5 (6.7 to 9.7)			
IP-10 [N=8]	170 (143 to 210)			
MCP-1 [N=8]	72.5 (27 to 104)			
MCP-2 [N=8]	18.5 (15 to 23)			
MCP-4 [N=8]	1275 (881.5 to 1635)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=8]	18 (18 to 18)			
MIP-1 beta [N=8]	174 (152.5 to 187.5)			
MIP-3 alpha [N=8]	17 (11.5 to 94)			
MPIF-1 [N=8]	1100 (995 to 1450)			
TNF-alpha [N=8]	13 (13 to 13)			
TNF-beta [N=8]	3 (3 to 11.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of cytokines/chemokines during Step 2

End point title	Concentrations of cytokines/chemokines during Step 2[37]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the Engerix-B_2 Group.

End point type	Primary

End point timeframe:

Post-dose 2 at Day 180

Notes:

[37] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	engerix-b_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=9]	4900 (4300 to 5800)			
GM-CSF [N=9]	14 (14 to 14)			
IFN-γ [N=9]	1.6 (1.6 to 1.6)			
IL-10 [N=9]	3.3 (3.3 to 3.3)			
IL-18 [N=9]	159 (144 to 190)			
IL-2 [N=9]	5.9 (5.9 to 5.9)			
IL-3 [N=9]	1.6 (1.6 to 1.6)			
IL-4 [N=9]	9.4 (9.4 to 9.4)			
IL-5 [N=9]	2.7 (2.7 to 2.7)			
IL-6 [N=9]	1.6 (1.6 to 1.6)			
IL-6r [N=9]	24000 (24000 to 32000)			
IL-7 [N=9]	8.2 (8.2 to 8.2)			
IL-8 [N=9]	4.4 (3.5 to 5.3)			
IP-10 [N=9]	156 (121 to 260)			
MCP-1 [N=9]	77 (57 to 77)			
MCP-2 [N=9]	20 (14 to 27)			
MCP-4 [N=9]	1640 (1540 to 1810)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=9]	18 (18 to 18)			
MIP-1 beta [N=9]	189 (177 to 257)			
MIP-3 alpha [N=9]	25 (13 to 32)			
MPIF-1 [N=9]	920 (830 to 970)			
TNF-alpha [N=9]	13 (13 to 13)			
TNF-beta [N=9]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines - study Step 2

End point title	Plasma concentrations of cytokines and chemokines - study Step 2[38]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma.The analysis was performed only on theEngerix-B_2 Group.

End point type	Primary

End point timeframe:

Post-dose2 at Day 30 plus 6 Hours

Notes:

[38] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	engerix-b_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=9]	4600 (4100 to 5800)			
GM-CSF [N=9]	14 (14 to 14)			
IFN-γ [N=9]	1.6 (1.6 to 1.6)			
IL-10 [N=9]	3.3 (3.3 to 3.3)			
IL-18 [N=9]	144 (133 to 152)			
IL-2 [N=9]	5.9 (5.9 to 5.9)			
IL-3 [N=9]	1.6 (1.6 to 1.6)			
IL-4 [N=9]	9.4 (9.4 to 9.4)			
IL-5 [N=9]	2.7 (2.7 to 2.7)			
IL-6 [N=9]	1.6 (1.6 to 1.6)			
IL-6r [N=9]	25000 (24000 to 30000)			
IL-7 [N=9]	8.2 (8.2 to 8.2)			
IL-8 [N=9]	3.5 (2.6 to 4.4)			
IP-10 [N=9]	145 (105 to 214)			
MCP-1 [N=9]	46 (35 to 67)			
MCP-2 [N=9]	22 (15 to 26)			
MCP-4 [N=9]	1640 (1350 to 1720)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=9]	18 (18 to 18)			
MIP-1 beta [N=9]	193 (175 to 211)			
MIP-3 alpha [N=9]	21 (15 to 25)			
MPIF-1 [N=9]	890 (840 to 1100)			
TNF-alpha [N=9]	13 (13 to 13)			
TNF-beta [N=9]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines in Step 2 of study

End point title	Plasma concentrations of cytokines and chemokines in Step 2 of study[39]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the Engerix-B_2 Group.

End point type	Primary

End point timeframe:

Post-dose 3 at Day 180 plus 6 Hours

Notes:

[39] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	engerix-b_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=8]	4900 (4300 to 5900)			
GM-CSF [N=8]	14 (14 to 14)			
IFN-γ [N=8]	1.6 (1.6 to 1.6)			
IL-10 [N=8]	3.3 (3.3 to 3.8)			
IL-18 [N=8]	152 (140.5 to 192)			
IL-2 [N=8]	5.9 (5.9 to 5.9)			
IL-3 [N=8]	1.6 (1.6 to 1.6)			
IL-4 [N=8]	9.4 (9.4 to 11.2)			
IL-5 [N=8]	2.7 (2.7 to 2.7)			
IL-6 [N=8]	1.6 (1.6 to 1.6)			
IL-6r [N=8]	24500 (22500 to 31500)			
IL-7 [N=8]	8.2 (8.2 to 8.2)			
IL-8 [N=8]	3.5 (2.6 to 3.5)			
IP-10 [N=8]	152 (119.5 to 211.5)			
MCP-1 [N=8]	67 (35 to 86.5)			
MCP-2 [N=8]	19.5 (13 to 25.5)			
MCP-4 [N=8]	1720 (1390 to 1790)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=8]	18 (18 to 18)			
MIP-1 beta [N=8]	173.5 (166.5 to 213)			
MIP-3 alpha [N=8]	17 (15 to 21)			
MPIF-1 [N=8]	875 (745 to 1100)			
TNF-alpha [N=8]	13 (13 to 13)			
TNF-beta [N=8]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentrations of cytokines and chemokines during Step 2 of study

End point title	Plasma concentrations of cytokines and chemokines during Step 2 of study[40]

End point description:

Cytokines and chemokines analysed were E-selectin, granulocyte macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ), interleukin-10 (IL-10), IL-18, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6r, IL-7, IL-8, IFN-γ-inducible protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), MCP-2, MCP-4, monokine induced by IFN-γ (MIG), macrophage inflammatory protein-1 alpha (MIP-1 alpha), MIP-1 beta, MIP3-alpha, MPIF-1, tumor necrosis factor-alpha (TNF-alpha) and TNF-beta. Concentrations are presented as median, expressed in picogram/milliliter (pg/mL), as measured by Multiplex in plasma. The analysis was performed only on the Engerix-B_2 Group.

End point type	Primary

End point timeframe:

Post-dose 3 at Day 187

Notes:

[40] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	engerix-b_2 group			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: pg/mL				
median (inter-quartile range (Q1-Q3))				
E-selectin [N=5]	4600 (4200 to 5500)			
GM-CSF [N=5]	14 (14 to 14)			
IFN-γ [N=5]	1.6 (1.6 to 1.6)			
IL-10 [N=5]	3.3 (3.3 to 3.3)			
IL-18 [N=5]	163 (137 to 167)			
IL-2 [N=5]	5.9 (5.9 to 5.9)			
IL-3 [N=5]	1.6 (1.6 to 1.6)			
IL-4 [N=5]	9.4 (9.4 to 9.4)			
IL-5 [N=5]	2.7 (2.7 to 2.7)			
IL-6 [N=5]	1.6 (1.6 to 1.6)			
IL-6r [N=5]	30000 (26000 to 35000)			
IL-7 [N=5]	8.2 (8.2 to 8.2)			
IL-8 [N=5]	3.5 (3.5 to 4.4)			
IP-10 [N=5]	201 (107 to 201)			
MCP-1 [N=5]	35 (35 to 35)			
MCP-2 [N=5]	22 (17 to 25)			

MCP-4 [N=5]	1810 (1720 to 2120)			
MIG [N=0]	0 (0 to 0)			
MIP-1 alpha [N=5]	18 (18 to 18)			
MIP-1 beta [N=5]	175 (175 to 193)			
MIP-3 alpha [N=5]	17 (17 to 25)			
MPIF-1 [N=5]	820 (750 to 970)			
TNF-alpha [N=5]	13 (13 to 13)			
TNF-beta [N=5]	3 (3 to 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 1

End point title	Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 1

End point description:

Anti-HBs antibody concentrations in serum were measured by Chemi Luminiscence Immuno Assay (CLIA). Concentrations were presented as geometric mean concentrations, in milli-International Units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

At Day 0 (PRE) and Day 60 (D60) post-vaccination

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	25		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE (D0)	3.1 (3.1 to 3.1)	3.1 (3.1 to 3.1)		
Anti-HBs, PII (D60)	3322.4 (2332.2 to 4733)	35.8 (11.6 to 111.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms - Step 1

End point title	Number of subjects with any and grade 3 solicited local symptoms - Step 1

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-placebo (PP) and post-vaccination period following each vaccine dose (D1 and D2) and across doses

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Any pain, PP [N=30, 30]	2	3		
Grade 3 pain, PP [N=30, 30]	0	1		
Any redness, PP [N=30, 30]	0	0		
Grade 3 redness, PP [N=30, 30]	0	0		
Any swelling, PP [N=30, 30]	0	0		
Grade 3 swelling, PP [N=30, 30]	0	0		
Any pain, D1 [N=28, 28]	18	7		
Grade 3 pain, D1 [N=28, 28]	0	0		
Any redness, D1 [N=28, 28]	6	1		
Grade 3 redness, D1 [N=28, 28]	0	0		
Any swelling, D1 [N=28, 28]	4	0		
Grade 3 swelling, D1 [N=28, 28]	0	0		
Any pain, D2 [N=27, 28]	15	6		
Grade 3 pain, D2 [N=27, 28]	0	1		
Any redness, D2 [N=27, 28]	5	0		
Grade 3 redness, D2 [N=27, 28]	1	0		
Any swelling, D2 [N=27, 28]	1	0		
Grade 3 swelling, D2 [N=27, 28]	0	0		
Any pain, Across Doses [N=28, 28]	21	8		
Grade 3 pain, Across Doses [N=28, 28]	0	1		
Any redness, Across Doses [N=28, 28]	8	1		
Grade 3 redness, Across Doses [N=28, 28]	1	0		
Any swelling, Across Doses [N=28, 28]	4	0		
Grade 3 swelling, Across Doses [N=28, 28]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms - Step 1

End point title	Number of subjects with any, grade 3 and related solicited general symptoms - Step 1

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms [nausea, vomiting, diarrhoea and /or abdominal pain], headache, malaise, myalgia, shivering and temperature [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-placebo (PP) and post-vaccination period following each vaccine dose (D1 and D2) and across doses

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Any fatigue, PP [N=30, 30]	8	12		
Grade 3 fatigue, PP [N=30, 30]	0	1		
Related fatigue, PP [N=30, 30]	2	2		
Any gastrointestinal symptoms, PP [N=30, 30]	8	8		
Grade 3 gastrointestinal symptoms, PP [N=30, 30]	0	2		
Related gastrointestinal symptoms, PP [N=30, 30]	1	0		
Any headache, PP [N=30, 30]	11	13		
Grade 3 headache, PP [N=30, 30]	0	1		
Related headache, PP [N=30, 30]	2	2		
Any malaise, PP [N=30, 30]	3	4		
Grade 3 malaise, PP [N=30, 30]	0	0		
Related malaise, PP [N=30, 30]	0	1		
Any myalgia, PP [N=30, 30]	2	5		
Grade 3 myalgia, PP [N=30, 30]	0	1		
Related myalgia, PP [N=30, 30]	1	0		
Any shivering, PP [N=30, 30]	4	3		
Grade 3 shivering, PP [N=30, 30]	0	1		
Related shivering, PP [N=30, 30]	0	0		
Any temperature, PP [N=30, 30]	1	2		
Grade 3 temperature, PP [N=30, 30]	0	0		
Related temperature, PP [N=30, 30]	0	0		
Any Fatigue, D1 [N=28, 28]	3	6		
Grade 3 fatigue, D1 [N=28, 28]	1	0		
Related fatigue, D1 [N=28, 28]	2	6		
Any gastrointestinal symptoms, D1 [N=28, 28]	4	6		
Grade 3 gastrointestinal symptoms, D1 [N=28, 28]	0	1		
Related gastrointestinal symptoms, D1 [N=28, 28]	4	3		
Any headache, D1 [N=28, 28]	14	5		
Grade 3 headache, D1 [N=28, 28]	0	1		
Related headache, D1 [N=28, 28]	11	4		
Any malaise, D1 [N=28, 28]	4	2		

Grade 3 malaise, D1 [N=28, 28]	0	0		
Related malaise, D1 [N=28, 28]	4	2		
Any myalgia, D1 [N=28, 28]	10	1		
Grade 3 myalgia, D1 [N=28, 28]	0	0		
Related myalgia, D1 [N=28, 28]	9	1		
Any shivering, D1 [N=28, 28]	2	0		
Grade 3 shivering, D1 [N=28, 28]	0	0		
Related shivering, D1 [N=28, 28]	2	0		
Any temperature (≥37.5 °C), D1 [N=28, 28]	2	1		
Grade 3 temperature (> 39.5 °C), D1 [N=28, 28]	0	0		
Related temperature, D1 [N=28, 28]	1	0		
Any Fatigue, D2 [N=27, 28]	10	8		
Grade 3 fatigue, D2 [N=27, 28]	1	0		
Related fatigue, D2 [N=27, 28]	10	7		
Any gastrointestinal symptoms, D2 [N=27, 28]	4	5		
Grade 3 gastrointestinal symptoms, D2 [N=27, 28]	0	3		
Related gastrointestinal symptoms, D2 [N=27, 28]	4	5		
Any headache, D2 [N=27, 28]	14	5		
Grade 3 headache, D2 [N=27, 28]	0	1		
Related headache, D2 [N=27, 28]	14	5		
Any malaise, D2 [N=27, 28]	7	6		
Grade 3 malaise, D2 [N=27, 28]	2	1		
Related malaise, D2 [N=27, 28]	7	6		
Any myalgia, D2 [N=27, 28]	10	2		
Grade 3 myalgia, D2 [N=27, 28]	0	0		
Related myalgia, D2 [N=27, 28]	10	1		
Any shivering, D2 [N=27, 28]	9	2		
Grade 3 shivering, D2 [N=27, 28]	0	0		
Related shivering, D2 [N=27, 28]	9	2		
Any temperature (≥37.5 °C), D2 [N=27, 28]	5	1		
Grade 3 temperature (> 39.5 °C), D2 [N=27, 28]	0	0		
Related temperature, D2 [N=27, 28]	4	0		
Any Fatigue, Across Doses [N=28, 28]	10	9		
Grade 3 fatigue, Across Doses [N=28, 28]	2	0		
Related fatigue, Across Doses [N=28, 28]	10	9		
Any Gastro. sympt., Across Doses [N=28, 28]	8	8		
Grade 3 Gastro. sympt., Across Doses [N=28, 28]	0	4		
Related Gastro. sympt., Across Doses [N=28, 28]	8	7		
Any headache, Across Doses [N=28, 28]	17	6		
Grade 3 headache, Across Doses [N=28, 28]	0	1		
Related headache, Across Doses [N=28, 28]	15	6		
Any malaise, Across Doses [N=28, 28]	8	7		

Grade 3 malaise, Across Doses [N=28, 28]	2	1		
Related malaise, Across Doses [N=28, 28]	8	7		
Any myalgia, Across Doses [N=28, 28]	14	2		
Grade 3 myalgia, Across Doses [N=28, 28]	0	0		
Related myalgia, Across Doses [N=28, 28]	13	2		
Any shivering, Across Doses [N=28, 28]	10	2		
Grade 3 shivering, Across Doses [N=28, 28]	0	0		
Related shivering, Across Doses [N=28, 28]	10	2		
Any temperature, Across Doses [N=28, 28]	6	2		
Grade 3 temperature, Across Doses [N=28, 28]	0	0		
Related temperature, Across Doses [N=28, 28]	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited symptoms, as assessed by the investigator/study nurse

End point title	Number of subjects with solicited symptoms, as assessed by the investigator/study nurse

End point description:

Assessed solicited symptoms were fever [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)], pain, redness [spreading beyond 20 millimeters (mm) of injection site], induration [spreading beyond 20 millimeters (mm) of injection site], swelling [spreading beyond 20 millimeters (mm) of injection site] and muscle stiffness.

End point type	Secondary

End point timeframe:

Up to 4 days post-placebo/vaccine administration.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Fever (≥37.5), placebo [N=30, 30]	0	0		
Fever (≥37.5), D1 [N=28, 30]	2	2		
Fever (≥37.5), D2 [N=27, 28]	8	0		
Pain, placebo [N=30, 30]	1	4		
Pain, D1 [N=28, 30]	19	9		
Pain, D2 [N=27, 28]	19	8		
Redness, placebo [N=30, 30]	0	0		
Redness, D1 [N=28, 30]	8	1		

Redness, D2 [N=27, 28]	7	0		
Induration, placebo [N=30, 30]	0	0		
Induration, D1 [N=28, 30]	0	0		
Induration, D2 [N=27, 28]	1	0		
Swelling, placebo [N=30, 30]	0	0		
Swelling, D1 [N=28, 30]	3	1		
Swelling, D2 [N=27, 28]	4	1		
Muscle stiffness, placebo [N=30, 30]	0	2		
Muscle stiffness, D1 [N=28, 30]	14	5		
Muscle stiffness, D2 [N=27, 28]	15	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) - Step 1

End point title	Number of subjects with any unsolicited adverse events (AEs) - Step 1

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset out-side the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Within the 28-day (Days 0-27) post-placebo (PP) and post-product administration period.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Any AEs, post-placebo [N=30, 30]	12	16		
Any AEs, post-product administration [N=28, 29]	14	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) - Step 1

End point title	Number of subjects with serious adverse events (SAEs) - Step 1

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life

threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

From Day 0 up to Day 60.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential immune-mediated disorders (pIMDs) - Step 1

End point title	Number of subjects with any potential immune-mediated disorders (pIMDs) - Step 1

End point description:

PIMD(s) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

End point type	Secondary

End point timeframe:

From Day 0 up to Day 60.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any new medical conditions requiring medical attention (MAEs) - Step 1

End point title	Number of subjects with any new medical conditions requiring medical attention (MAEs) - Step 1

End point description:

MAEs were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any MAE(s) = Occurrence of any MAE(s) regardless of intensity grade or relation to vaccination. Analysis of intensity and relationship to vaccination of MAEs was not performed.

End point type	Secondary

End point timeframe:

From Day 0 up to Day 60.

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Alanine aminotransferase (ALT) in blood samples - Step 1

End point title	Levels of Alanine aminotransferase (ALT) in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included ALT levels. ALT concentrations were expressed in units per liter (U/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
ALT, D1, Day 0 [N=28, 29]	27.5 (22.5 to 32.5)	27 (23 to 31)		
ALT, D1 (Day 0 H6) [N=28, 29]	26.5 (22 to 33)	26 (22 to 34)		
ALT, D1 (Day 0 H12) [N=28, 29]	27 (23.5 to 31.5)	26 (24 to 33)		
ALT, D1 (Day 0 H18) [N=15, 14]	28 (25 to 35)	24 (16 to 48)		
ALT, D1, Day 1 [N=28, 29]	25.5 (20 to 33)	27 (20 to 35)		
ALT, D1, Day 7 [N=28, 29]	26.5 (22 to 32.5)	28 (19 to 34)		
ALT, D2, Day 30 [N=27, 27]	27 (22 to 36)	30 (24 to 33)		
ALT, D2 (Day 30 H6) [N=27, 28]	27 (23 to 34)	28 (25 to 32)		

ALT, D2 (Day 30 H12) [N=27, 28]	27 (24 to 34)	28 (23 to 33.5)		
ALT, D2 (Day 30 H18) [N=14, 14]	32 (25 to 37)	26 (24 to 46)		
ALT, D2, Day 31 [N=27, 28]	27 (22 to 33)	27 (23 to 34)		
ALT, D2, Day 37 [N=27, 28]	27 (22 to 30)	26 (23.5 to 33)		
ALT, D2, Day 60 [N=27, 28]	28 (23 to 32)	28 (22.5 to 36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Aspartate aminotransferase (AST) in blood samples - Step 1

End point title	Levels of Aspartate aminotransferase (AST) in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included AST levels. AST concentrations were expressed in units per liter (U/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
AST, D1, Day 0 [N=28, 29]	21 (18 to 26)	23 (18 to 25)		
AST, D1 (Day 0 H6) [N=28, 29]	20.5 (18.5 to 24)	21 (17 to 25)		
AST, D1 (Day 0 H12) [N=28, 29]	20 (18.5 to 22.5)	20 (17 to 25)		
AST, D1 (Day 0 H18) [N=15, 14]	19 (15 to 24)	18 (17 to 28)		
AST, D1, Day 1 [N=28, 29]	19 (16 to 22.5)	20 (18 to 23)		
AST, D1, Day 7 [N=28, 29]	21 (18.5 to 25.5)	21 (18 to 29)		
AST, D2, Day 30 [N=27, 27]	21 (19 to 26)	23 (19 to 25)		
AST, D2 (Day 30 H6) [N=27, 29]	21 (19 to 24)	22 (20 to 25.5)		
AST, D2 (Day 30 H12) [N=27, 29]	20 (18 to 25)	21 (20 to 24.5)		
AST, D2 (Day 30 H18) [N=14, 14]	20 (19 to 22)	19.5 (16 to 30)		
AST, D2, Day 31 [N=27, 28]	19 (17 to 23)	21 (18 to 25.5)		
AST, D2, Day 37 [N=27, 28]	22 (19 to 25)	23 (18 to 29.5)		
AST, D2, Day 60 [N=27, 28]	21 (18 to 26)	21.5 (18 to 28.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Basophils in blood samples - Step 1

End point title	Levels of Basophils in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included basophil levels. Basophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Basophils, D1, Day 0 [N=28, 29]	0.03 (0.02 to 0.04)	0.02 (0.02 to 0.03)		
Basophils, D1 (Day 0 H6) [N=28, 29]	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.03)		
Basophils, D1 (Day 0 H12) [N=28, 29]	0.03 (0.02 to 0.05)	0.02 (0.02 to 0.03)		
Basophils, D1 (Day 0 H18) [N=15, 14]	0.03 (0.01 to 0.03)	0.02 (0.01 to 0.03)		
Basophils, D1, Day 1 [N=28, 29]	0.03 (0.01 to 0.04)	0.02 (0.02 to 0.03)		
Basophils, D1, Day 7 [N=28, 29]	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.04)		
Basophils, D2, Day 30 [N=27, 27]	0.03 (0.02 to 0.04)	0.02 (0.02 to 0.04)		
Basophils, D2 (Day 30 H6) [N=27, 28]	0.03 (0.02 to 0.04)	0.02 (0.02 to 0.03)		
Basophils, D2 (Day 30 H12) [N=27, 28]	0.02 (0.01 to 0.03)	0.02 (0.02 to 0.04)		
Basophils, D2 (Day 30 H18) [N=14, 14]	0.03 (0.01 to 0.03)	0.02 (0.01 to 0.03)		
Basophils, D2, Day 31 [N=27, 28]	0.02 (0.01 to 0.03)	0.03 (0.02 to 0.04)		
Basophils, D2, Day 37 [N=27, 28]	0.03 (0.02 to 0.06)	0.03 (0.02 to 0.03)		
Basophils, D2, Day 60 [N=27, 28]	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of total Bilirubin in blood samples - Step 1

End point title	Levels of total Bilirubin in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included total bilirubin levels. Bilirubin concentrations were expressed in milligrams per deciliter (mG/dL).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Total bilirubin, D1, Day 0 [N=28, 29]	0.5 (0.4 to 0.7)	0.5 (0.3 to 0.7)		
Total bilirubin, D1 (Day 0 H6) [N=28, 29]	0.4 (0.25 to 0.5)	0.4 (0.3 to 0.5)		
Total bilirubin, D1 (Day 0 H12) [N=28, 29]	0.4 (0.3 to 0.6)	0.3 (0.3 to 0.5)		
Total bilirubin, D1 (Day 0 H18) [N=15, 14]	0.6 (0.4 to 0.8)	0.5 (0.3 to 0.6)		
Total bilirubin, D1, Day 1 [N=28, 29]	0.7 (0.6 to 0.9)	0.5 (0.3 to 0.8)		
Total bilirubin, D1, Day 7 [N=28, 29]	0.5 (0.4 to 0.7)	0.5 (0.3 to 0.6)		
Total bilirubin, D2, Day 30 [N=27, 27]	0.6 (0.4 to 0.7)	0.5 (0.4 to 0.7)		
Total bilirubin, D2 (Day 30 H6) [N=27, 28]	0.4 (0.3 to 0.5)	0.4 (0.3 to 0.5)		
Total bilirubin, D2 (Day 30 H12) [N=27, 28]	0.5 (0.4 to 0.6)	0.4 (0.3 to 0.5)		
Total bilirubin, D2 (Day 30 H18) [N=14, 14]	0.6 (0.4 to 0.7)	0.45 (0.3 to 0.5)		
Total bilirubin, D2, Day 31 [N=27, 28]	0.7 (0.5 to 1)	0.5 (0.45 to 0.7)		
Total bilirubin, D2, Day 37 [N=27, 28]	0.5 (0.3 to 0.8)	0.5 (0.4 to 0.65)		
Total bilirubin, D2, Day 60 [N=27, 28]	0.5 (0.4 to 0.6)	0.5 (0.4 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of serum Creatinine in blood samples - Step 1

End point title	Levels of serum Creatinine in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included creatinine levels. Creatinine concentrations were expressed in milligrams per deciliter (mg/dL).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Creatinine, D1, Day 0 [N=28, 29]	0.8 (0.75 to 0.93)	0.79 (0.72 to 0.85)		
Creatinine, D1 (Day 0 H6) [N=28, 29]	0.75 (0.66 to 0.85)	0.72 (0.69 to 0.82)		
Creatinine, D1 (Day 0 H12) [N=28, 29]	0.78 (0.66 to 0.83)	0.73 (0.68 to 0.83)		
Creatinine, D1 (Day 0 H18) [N=15, 14]	0.7 (0.61 to 0.77)	0.71 (0.63 to 0.84)		
Creatinine, D1, Day 1 [N=28, 29]	0.74 (0.68 to 0.91)	0.77 (0.71 to 0.85)		
Creatinine, D1, Day 7 [N=28, 29]	0.81 (0.71 to 0.93)	0.76 (0.69 to 0.87)		
Creatinine, D2, Day 30 [N=27, 27]	0.82 (0.74 to 0.96)	0.79 (0.72 to 0.83)		
Creatinine, D2 (Day 30 H6) [N=27, 28]	0.75 (0.68 to 0.85)	0.73 (0.67 to 0.83)		
Creatinine, D2 (Day 30 H12) [N=27, 28]	0.76 (0.68 to 0.85)	0.72 (0.69 to 0.82)		
Creatinine, D2 (Day 30 H18) [N=14, 14]	0.74 (0.68 to 0.81)	0.73 (0.65 to 0.82)		
Creatinine, D2, Day 31 [N=27, 28]	0.79 (0.69 to 0.93)	0.76 (0.7 to 0.87)		
Creatinine, D2, Day 37 [N=27, 28]	0.81 (0.73 to 0.93)	0.73 (0.7 to 0.9)		
Creatinine, D2, Day 60 [N=27, 28]	0.84 (0.69 to 0.97)	0.78 (0.72 to 0.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Creatinine phosphokinase (CPK) in blood samples - Step 1

End point title	Levels of Creatinine phosphokinase (CPK) in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included CPK levels. CPK concentrations were expressed in milligrams per deciliter (mg/dL).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
CPK, D1, Day 0 [N=28, 29]	75 (56.5 to 108)	80 (62 to 148)		
CPK, D1 (Day 0 H6 [N=28, 29]	69.5 (53 to 106)	75 (60 to 120)		
CPK, D1 (Day 0 H12) [N=28, 29]	64.5 (51 to 94.5)	77 (57 to 110)		
CPK, D1 (Day 0 H18) [N=15, 14]	59 (49 to 90)	61 (44 to 103)		
CPK, D1, Day 1 [N=28, 29]	54 (42.5 to 79.5)	69 (46 to 96)		
CPK, D1, Day 7 [N=28, 29]	66 (55.5 to 95)	80 (57 to 117)		
CPK, D2, Day 30 [N=27, 27]	83 (48 to 122)	87 (55 to 145)		
CPK, D2 (Day 30 H6) [N=27, 28]	81 (45 to 108)	86 (53.5 to 140.5)		
CPK, D2 (Day 30 H12) [N=27, 28]	72 (50 to 98)	80.5 (54 to 134)		
CPK, D2 (Day 30 H18) [N=14, 14]	68.5 (53 to 103)	70 (37 to 120)		
CPK, D2, Day 31 [N=27, 28]	67 (44 to 87)	75 (50 to 119)		
CPK, D2, Day 37 [N=27, 28]	83 (59 to 119)	93.5 (54 to 115.5)		
CPK, D2, Day 60 [N=27, 28]	82 (55 to 118)	82.5 (62 to 122)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of c-reactive protein (CRP) in blood samples - Step 1

End point title	Levels of c-reactive protein (CRP) in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included CRP levels. CRP concentrations were expressed in milligrams per liter (mg/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: mg/L				
median (inter-quartile range (Q1-Q3))				
CRP, D1, Day 0 [N=28, 29]	1.15 (0.5 to 3)	1.7 (0.5 to 2.5)		
CRP, D1 (Day 0 H6) [N=28, 29]	0.8 (0.5 to 2.9)	1.6 (0.5 to 2.4)		

CRP, D1 (Day 0 H12) [N=28, 29]	1.5 (0.5 to 3.35)	1.4 (0.5 to 2.1)		
CRP, D1 (Day 0 H18) [N=15, 14]	2.9 (1.5 to 4.4)	1.25 (0.5 to 1.8)		
CRP, D1, Day 1 [N=28, 29]	5.8 (3.1 to 11.1)	1.2 (0.5 to 1.8)		
CRP, D1, Day 7 [N=28, 29]	1.9 (0.5 to 4.25)	1.3 (0.5 to 2.6)		
CRP, D2, Day 30 [N=27, 27]	1.3 (0.5 to 4.3)	1.4 (0.5 to 3.1)		
CRP, D2 (Day 30 H6) [N=27, 28]	1.2 (0.5 to 2.3)	1.5 (0.5 to 3.05)		
CRP, D2 (Day 30 H12) [N=27, 28]	1.8 (0.5 to 2.8)	1.55 (0.5 to 3.1)		
CRP, D2 (Day 30 H18) [N=14, 14]	3.15 (2.1 to 5.3)	0.75 (0.5 to 2.8)		
CRP, D2, Day 31 [N=27, 28]	5.8 (2.6 to 14.5)	1.2 (0.5 to 2.65)		
CRP, D2, Day 37 [N=27, 28]	2.1 (1.1 to 5.8)	1.3 (0.5 to 2.95)		
CRP, D2, Day 60 [N=27, 28]	1.4 (0.5 to 3.9)	1.05 (0.5 to 3.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Eosinophils in blood samples - Step 1

End point title	Levels of Eosinophils in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included eosinophil levels. Eosinophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Eosinophils, D1, Day 0 [N=28, 29]	0.2 (0.11 to 0.25)	0.13 (0.1 to 0.21)		
Eosinophils, D1 (Day 0 H6) [N=28, 29]	0.19 (0.13 to 0.27)	0.13 (0.09 to 0.21)		
Eosinophils, D1 (Day 0 H12) [N=28, 29]	0.21 (0.15 to 0.27)	0.17 (0.12 to 0.21)		
Eosinophils, D1 (Day 0 H18) [N=15, 14]	0.16 (0.12 to 0.3)	0.2 (0.16 to 0.31)		
Eosinophils, D1, Day 1 [N=28, 29]	0.15 (0.08 to 0.25)	0.1 (0.07 to 0.2)		

Eosinophils, D1, Day 7 [N=28, 29]	0.14 (0.08 to 0.2)	0.11 (0.09 to 0.17)		
Eosinophils, D2, Day 30 [N=27, 27]	0.18 (0.11 to 0.25)	0.14 (0.09 to 0.26)		
Eosinophils, D2 (Day 30 H6) [N=27, 28]	0.18 (0.1 to 0.29)	0.13 (0.09 to 0.22)		
Eosinophils, D2 (Day 30 H12) [N=27, 28]	0.19 (0.12 to 0.31)	0.14 (0.09 to 0.24)		
Eosinophils, D2 (Day 30 H18) [N=14, 14]	0.14 (0.05 to 0.21)	0.19 (0.12 to 0.32)		
Eosinophils, D2, Day 31 [N=27, 28]	0.14 (0.05 to 0.2)	0.13 (0.09 to 0.22)		
Eosinophils, D2, Day 37 [N=27, 28]	0.19 (0.11 to 0.24)	0.15 (0.09 to 0.23)		
Eosinophils, D2, Day 60 [N=27, 28]	0.19 (0.1 to 0.28)	0.14 (0.11 to 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Haemoglobin in blood samples - Step 1

End point title	Levels of Haemoglobin in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included haemoglobin levels, expressed in gram per deciliter (d/dL).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: g/dL				
median (inter-quartile range (Q1-Q3))				
Haemoglobin, D1, Day 0 [N=28, 29]	13.35 (12.7 to 14.5)	13.8 (12.5 to 14.8)		
Haemoglobin, D1 (Day 0 H6) [N=28, 29]	13.45 (12.3 to 14.05)	13.6 (12.5 to 14.6)		
Haemoglobin, D1 (Day 0 H12) [N=28, 29]	13.25 (12.3 to 14.3)	13.2 (12.6 to 14.5)		
Haemoglobin, D1 (Day 0 H18) [N=15, 14]	12.6 (12 to 13.9)	13.15 (12.5 to 14.5)		
Haemoglobin, D1, Day 1 [N=28, 29]	13.5 (12.6 to 14.45)	13.8 (12.9 to 14.7)		
Haemoglobin, D1, Day 7 [N=28, 29]	13.35 (12.55 to 14.35)	13.8 (12.8 to 14.6)		
Haemoglobin, D2, Day 30 [N=27, 27]	13.7 (12.7 to 14.3)	13.4 (12.6 to 14.3)		
Haemoglobin, D2 (Day 30 H6) [N=27, 28]	13.4 (12.5 to 14)	13.55 (12.45 to 14.15)		

Haemoglobin, D2 (Day 30 H12) [N=27, 28]	13.2 (12.6 to 14.1)	13.1 (12.4 to 14.15)		
Haemoglobin, D2 (Day 30 H18) [N=14, 14]	13.15 (11.7 to 13.9)	13.05 (12.3 to 14.1)		
Haemoglobin, D2, Day 31 [N=27, 28]	13.5 (12.5 to 14.4)	13.75 (12.65 to 14.6)		
Haemoglobin, D2, Day 37 [N=27, 28]	13.6 (12.6 to 14.5)	13.65 (12.35 to 14.5)		
Haemoglobin, D2, Day 60 [N=27, 28]	13.5 (12.4 to 14.5)	13.8 (12.2 to 14.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Lactate dehydrogenase (LDH) in blood samples - Step 1

End point title	Levels of Lactate dehydrogenase (LDH) in blood samples - Step 1
End point description:	
Biochemical laboratory parameters assessed included LDH levels, expressed in units per liter (U/L).	
End point type	Secondary
End point timeframe:	
At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60	

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
LDH, D1, Day 0 [N=28, 29]	401.5 (377 to 473.5)	382 (346 to 438)		
LDH, D1 (Day 0 H6) [N=28, 29]	414 (388.5 to 449.5)	389 (353 to 423)		
LDH, D1 (Day 0 H12) [N=28, 29]	412 (392 to 457.5)	378 (339 to 426)		
LDH, D1 (Day 0 H18) [N=15, 14]	422 (341 to 461)	369.5 (302 to 410)		
LDH, D1, Day 1 [N=28, 29]	389 (352 to 466)	367 (342 to 411)		
LDH, D1, Day 7 [N=28, 29]	417.5 (382.5 to 479.5)	392 (371 to 436)		
LDH, D2, Day 30 [N=27, 27]	391 (360 to 456)	395 (348 to 426)		
LDH, D2 (Day 30 H6) [N=27, 28]	437 (397 to 470)	396.5 (350.5 to 428)		
LDH, D2 (Day 30 H12) [N=27, 28]	425 (403 to 470)	382.5 (338.5 to 424)		
LDH, D2 (Day 30 H18) [N=14, 14]	403 (365 to 450)	334.5 (297 to 390)		
LDH, D2, Day 31 [N=27, 28]	408 (373 to 453)	372 (354 to 403)		

LDH, D2, Day 37 [N=27, 28]	442 (412 to 464)	403 (368.5 to 446)		
LDH, D2, Day 60 [N=27, 28]	422 (397 to 478)	404 (374 to 431.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Lymphocytes in blood samples - Step 1

End point title	Levels of Lymphocytes in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included lymphocyte levels. Lymphocyte levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Lymphocytes, D1, Day 0 [N=28, 29]	1.84 (1.45 to 1.98)	1.99 (1.61 to 2.26)		
Lymphocytes, D1 (Day 0 H6) [N=28, 29]	1.89 (1.48 to 2.35)	2.07 (1.52 to 2.46)		
Lymphocytes, D1 (Day 0 H12) [N=28, 29]	1.97 (1.72 to 2.33)	2.39 (2 to 2.97)		
Lymphocytes, D1 (Day 0 H18) [N=15, 14]	1.73 (1.41 to 2.48)	3.08 (2.45 to 3.53)		
Lymphocytes, D1, Day 1 [N=28, 29]	1.58 (1.25 to 1.83)	1.94 (1.66 to 2.26)		
Lymphocytes, D1, Day 7 [N=28, 29]	1.69 (1.37 to 1.91)	1.97 (1.56 to 2.17)		
Lymphocytes, D2, Day 30 [N=27, 27]	1.67 (1.36 to 2.03)	1.97 (1.64 to 2.5)		
Lymphocytes, D2 (Day 30 H6 [N=27, 28]	1.81 (1.56 to 2.16)	2.11 (1.78 to 2.59)		
Lymphocytes, D2 (Day 30 H12) [N=27, 28]	1.9 (1.36 to 2.39)	2.35 (2.1 to 2.82)		
Lymphocytes, D2 (Day 30 H18) [N=14, 14]	1.46 (1.06 to 1.83)	2.99 (2.45 to 3.53)		
Lymphocytes, D2, Day 31 [N=27, 28]	1.19 (0.89 to 1.43)	2.01 (1.75 to 2.5)		
Lymphocytes, D2, Day 37 [N=27, 28]	1.74 (1.41 to 2.21)	2.01 (1.64 to 2.36)		
Lymphocytes, D2, Day 60 [N=27, 28]	1.76 (1.4 to 2.29)	2.09 (1.73 to 2.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Monocytes in blood samples - Step 1

End point title	Levels of Monocytes in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included monocyte levels. Monocyte levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Monocytes, D1, Day 0 [N=28, 29]	0.55 (0.45 to 0.66)	0.55 (0.4 to 0.62)		
Monocytes, D1 (Day 0 H6) [N=28, 29]	0.67 (0.59 to 0.76)	0.52 (0.4 to 0.55)		
Monocytes, D1 (Day 0 H12) [N=28, 29]	0.79 (0.62 to 0.9)	0.53 (0.41 to 0.6)		
Monocytes, D1 (Day 0 H18) [N=15, 14]	0.79 (0.66 to 0.92)	0.59 (0.5 to 0.61)		
Monocytes, D1, Day 1 [N=28, 29]	0.72 (0.6 to 0.84)	0.45 (0.4 to 0.54)		
Monocytes, D1, Day 7 [N=28, 29]	0.54 (0.43 to 0.63)	0.44 (0.37 to 0.58)		
Monocytes, D2, Day 30 [N=27, 27]	0.55 (0.47 to 0.65)	0.5 (0.43 to 0.63)		
Monocytes, D2 (Day 30 H6) [N=27, 28]	0.67 (0.54 to 0.78)	0.48 (0.4 to 0.56)		
Monocytes, D2 (Day 30 H12) [N=27, 28]	0.66 (0.57 to 0.87)	0.51 (0.39 to 0.61)		
Monocytes, D2 (Day 30 H18) [N=14, 14]	0.8 (0.62 to 0.94)	0.49 (0.43 to 0.59)		
Monocytes, D2, Day 31 [N=27, 28]	0.67 (0.53 to 0.81)	0.51 (0.44 to 0.67)		
Monocytes, D2, Day 37 [N=27, 28]	0.51 (0.39 to 0.64)	0.51 (0.44 to 0.59)		
Monocytes, D2, Day 60 [N=27, 28]	0.51 (0.39 to 0.68)	0.52 (0.44 to 0.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Neutrophils in blood samples - Step 1

End point title	Levels of Neutrophils in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included neutrophil levels. Neutrophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Neutrophils, D1, Day 0 [N=28, 29]	3.7 (3 to 5.49)	3.36 (2.77 to 4.21)		
Neutrophils, D1 (Day 0 H6) [N=28, 29]	6.48 (5.02 to 7.84)	4.12 (2.96 to 4.41)		
Neutrophils, D1 (Day 0 H12) [N=28, 29]	7.61 (6.87 to 9.01)	3.39 (3 to 4.53)		
Neutrophils, D1 (Day 0 H18) [N=15, 14]	6.07 (5.56 to 8.31)	3.61 (3.31 to 4.12)		
Neutrophils, D1, Day 1 [N=28, 29]	6.13 (4.26 to 6.76)	3.76 (3.12 to 4.23)		
Neutrophils, D1, Day 7 [N=28, 29]	4.17 (3.05 to 5.17)	3.46 (2.73 to 4.19)		
Neutrophils, D2, Day 30 [N=27, 27]	3.66 (3.08 to 4.49)	2.91 (2.43 to 3.91)		
Neutrophils, D2 (Day 30 H6) [N=27, 28]	5.9 (5.28 to 7.75)	3.39 (2.93 to 4.07)		
Neutrophils, D2 (Day 30 H12) [N=27, 28]	7.07 (6.47 to 8.58)	3.36 (2.59 to 4.12)		
Neutrophils, D2 (Day 30 H18) [N=14, 14]	7.42 (6.84 to 9.35)	3.02 (2.39 to 3.74)		
Neutrophils, D2, Day 31 [N=27, 28]	6.32 (4.78 to 7.41)	3.2 (2.77 to 4.9)		
Neutrophils, D2, Day 37 [N=27, 28]	3.64 (2.73 to 5.48)	3.13 (2.68 to 4.47)		
Neutrophils, D2, Day 60 [N=27, 28]	3.96 (3.16 to 4.96)	2.95 (2.5 to 3.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count in blood samples - Step 1

End point title	Platelet count in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included platelet count levels. Platelet count levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Platelets, D1, Day 0 [N=28, 29]	228 (191.5 to 261.5)	225 (207 to 266)		
Platelets, D1 (Day 0 H6) [N=28, 29]	229 (204 to 259.5)	231 (212 to 263)		
Platelets, D1 (Day 0 H12) [N=28, 29]	235 (193 to 259)	230 (217 to 263)		
Platelets, D1 (Day 0 H18) [N=15, 14]	222 (186 to 260)	233 (215 to 274)		
Platelets, D1, Day 1 [N=28, 29]	220.5 (187.5 to 258)	227 (206 to 269)		
Platelets, D1, Day 7 [N=28, 29]	263.5 (215.5 to 291)	247 (217 to 268)		
Platelets, D2, Day 30 [N=27, 27]	224 (185 to 267)	228 (204 to 260)		
Platelets, D2 (Day 30 H6) [N=27, 28]	238 (195 to 270)	232 (212 to 261.5)		
Platelets, D2 (Day 30 H12) [N=27, 28]	226 (194 to 260)	234 (213.5 to 258)		
Platelets, D2 (Day 30 H18) [N=14, 14]	230.5 (179 to 276)	229 (199 to 275)		
Platelets, D2, Day 31 [N=27, 28]	218 (170 to 238)	217.5 (204.5 to 256.5)		
Platelets, D2, Day 37 [N=27, 28]	253 (205 to 301)	243 (208.5 to 282)		
Platelets, D2, Day 60 [N=27, 28]	240 (195 to 283)	241.5 (208 to 276.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Red Blood Cell (RBC) in blood samples - Step 1

End point title	Levels of Red Blood Cell (RBC) in blood samples - Step 1

End point description:

Haematological laboratory parameters assessed included red blood cells levels, expressed in trillion cells per liter (trillion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: trillion cells/L				
median (inter-quartile range (Q1-Q3))				
RBC, D1, Day 0 [N=28, 29]	4.51 (4.33 to 4.83)	4.56 (4.27 to 4.96)		
RBC, D1 (Day 0 H6) [N=28, 29]	4.45 (4.18 to 4.82)	4.58 (4.24 to 4.78)		
RBC, D1 (Day 0 H12) [N=28, 29]	4.42 (4.12 to 4.68)	4.51 (4.27 to 4.78)		
RBC, D1 (Day 0 H18) [N=15, 14]	4.19 (4.02 to 4.79)	4.36 (4.19 to 4.72)		
RBC, D1, Day 1 [N=28, 29]	4.48 (4.25 to 4.85)	4.62 (4.36 to 4.78)		
RBC, D1, Day 7 [N=28, 29]	4.54 (4.24 to 4.75)	4.54 (4.38 to 4.92)		
RBC, D2, Day 30 [N=27, 27]	4.48 (4.27 to 4.7)	4.53 (4.25 to 4.79)		
RBC, D2 (Day 30 H6) [N=27, 28]	4.43 (4.14 to 4.6)	4.49 (4.26 to 4.8)		
RBC, D2 (Day 30 H12) [N=27, 28]	4.33 (4.21 to 4.62)	4.46 (4.25 to 4.71)		
RBC, D2 (Day 30 H18) [N=14, 14]	4.22 (3.86 to 4.66)	4.34 (4.09 to 4.62)		
RBC, D2, Day 31 [N=27, 28]	4.42 (4.12 to 4.85)	4.58 (4.38 to 4.9)		
RBC, D2, Day 37 [N=27, 28]	4.5 (4.13 to 4.84)	4.52 (4.2 to 4.88)		
RBC, D2, Day 60 [N=27, 28]	4.5 (4.14 to 4.94)	4.61 (4.41 to 4.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of urea in blood samples - Step 1

End point title	Levels of urea in blood samples - Step 1

End point description:

Biochemical laboratory parameters assessed included urea levels, expressed in miligrams per deciliter (mg/dL).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Urea Nitrogen, D1, Day 0 [N=28, 29]	27.5 (23 to 35.5)	30 (26 to 35)		
Urea Nitrogen, D1 (Day 0 H6) [N=28, 29]	27 (24 to 31.5)	30 (26 to 34)		
Urea Nitrogen, D1 (Day 0 H12) [N=28, 29]	27 (24 to 31.5)	29 (27 to 32)		
Urea Nitrogen, D1 (Day 0 H18) [N=15, 14]	23 (21 to 32)	27 (24 to 30)		
Urea Nitrogen, D1, Day 1 [N=28, 29]	23.5 (18.5 to 29)	25 (23 to 30)		
Urea Nitrogen, D1, Day 7 [N=28, 29]	27.5 (24.5 to 35)	27 (23 to 31)		
Urea Nitrogen, D2, Day 30 [N=27, 27]	28 (25 to 37)	26 (22 to 33)		
Urea Nitrogen, D2 (Day 30 H6) [N=27, 28]	29 (24 to 34)	26 (23 to 32.5)		
Urea Nitrogen, D2 (Day 30 H12) [N=27, 28]	28 (24 to 34)	27 (23.5 to 32)		
Urea Nitrogen, D2 (Day 30 H18) [N=14, 14]	25.5 (21 to 31)	24.5 (22 to 28)		
Urea Nitrogen, D2, Day 31 [N=27, 28]	23 (19 to 30)	26 (21 to 28.5)		
Urea Nitrogen, D2, Day 37 [N=27, 28]	26 (22 to 36)	25.5 (23 to 31)		
Urea Nitrogen, D2, Day 60 [N=27, 28]	29 (22 to 33)	27 (23.5 to 30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of White Blood Cells (WBC) - Step 1

End point title	Levels of White Blood Cells (WBC) - Step 1

End point description:

Haematological laboratory parameters assessed included WBC levels. WBC levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 1, Day 7, Day 30, Day 31, Day 37 and Day 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	29		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
WBC, D1, Day 0 [N=28, 29]	6.25 (5.53 to 8.49)	6.33 (5.46 to 7.03)		
WBC, D1 (Day 0 H6) [N=28, 29]	9.73 (7.7 to 11.3)	6.49 (5.78 to 7.37)		
WBC, D1 (Day 0 H12) [N=28, 29]	10.45 (9.75 to 12.4)	6.84 (6 to 7.4)		
WBC, D1 (Day 0 H18) [N=15, 14]	8.72 (7.63 to 12.2)	7.43 (7.15 to 8.02)		
WBC, D1, Day 1 [N=28, 29]	8.7 (6.37 to 9.7)	6.25 (5.85 to 6.83)		
WBC, D1, Day 7 [N=28, 29]	6.67 (5.49 to 8.17)	6.14 (5.27 to 7.32)		
WBC, D2, Day 30 [N=27, 27]	6.04 (5.48 to 8.07)	5.77 (4.96 to 7.21)		
WBC, D2 (Day 30 H6) [N=27, 28]	9.28 (7.91 to 10.4)	6.07 (5.76 to 6.96)		
WBC, D2 (Day 30 H12) [N=27, 28]	9.88 (9.29 to 11.4)	6.28 (5.8 to 7.37)		
WBC, D2 (Day 30 H18) [N=14, 14]	9.57 (8.24 to 12.2)	6.8 (6.49 to 7.21)		
WBC, D2, Day 31 [N=27, 28]	8.21 (6.78 to 9.36)	6.34 (5.67 to 7.16)		
WBC, D2, Day 37 [N=27, 28]	5.7 (5.13 to 8.46)	6.25 (5.46 to 7.31)		
WBC, D2, Day 60 [N=27, 28]	6.48 (5.45 to 8.24)	6.07 (5.04 to 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Diastolic Blood Pressure - Step 1

End point title	Levels of Diastolic Blood Pressure - Step 1

End point description:

Diastolic pressure was part of the list of vital signs followed at specific protocol-defined timepoints during this study, measured in millimeter of mercury (mmHg).

End point type	Secondary

End point timeframe:

At Day -30, -29, - 28, - 27, -23, 0, 1, 2, 7, 30, 31, 32, 33, 37 and 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: mmHg				
median (inter-quartile range (Q1-Q3))				
Diastolic, placebo (D-30) [N=30, 30]	81 (74 to 86)	76.5 (67 to 83)		
Diastolic, placebo (D-30 H1.5) [N=30, 30]	75 (69 to 83)	72 (65 to 79)		
Diastolic, placebo (D-30 H3) [N=30, 30]	75.5 (68 to 83)	71.5 (65 to 80)		
Diastolic, placebo (D-30 H6) [N=30, 30]	73.5 (67 to 83)	71.5 (67 to 82)		
Diastolic, placebo (D-30 H9) [N=30, 30]	76 (71 to 86)	75 (67 to 84)		
Diastolic, placebo (D-30 H12) [N=30, 30]	78 (69 to 84)	72.5 (66 to 80)		
Diastolic, placebo (D-30 H18) [N=15, 15]	75 (67 to 80)	68 (64 to 84)		
Diastolic, placebo (D-29) [N=30, 30]	77 (70 to 83)	73.5 (64 to 81)		
Diastolic, placebo (D-28) [N=29, 30]	75 (70 to 83)	74.5 (69 to 78)		
Diastolic, placebo (D-27) [N=29, 30]	78 (72 to 82)	75 (71 to 81)		
Diastolic, placebo (D-23) [N=29, 30]	76 (71 to 81)	75.5 (66 to 80)		
Diastolic, Dose 1 (D0) [N=28, 29]	76 (70.5 to 83)	76 (68 to 85)		
Diastolic, Dose 1 (D0 H1.5) [N=28, 29]	74 (70 to 81)	73 (67 to 78)		
Diastolic, Dose 1 (D0 H6) [N=28, 29]	73.5 (67.5 to 80)	72 (65 to 78)		
Diastolic, Dose 1 (D0 H12) [N=28, 29]	72 (69 to 79.5)	72 (66 to 79)		
Diastolic, Dose 1 (D0 H18) [N=15, 14]	73 (61 to 78)	66.5 (60 to 78)		
Diastolic, Dose 1 (D1) [N=28, 29]	72 (69 to 79)	76 (66 to 80)		
Diastolic, Dose 1 (D2) [N=28, 29]	74 (70 to 81.5)	73 (67 to 79)		
Diastolic, Dose 1 (D7) [N=28, 29]	75 (71 to 79.5)	73 (70 to 82)		
Diastolic, Dose 2 (D30) [N=27, 28]	76 (69 to 80)	77.5 (68.5 to 83)		
Diastolic, Dose 2 (D30 H1.5) [N=27, 28]	72 (67 to 78)	70 (66 to 76.5)		
Diastolic, Dose 2 (D30 H3) [N=27, 28]	72 (68 to 79)	72 (63 to 78)		
Diastolic, Dose 2 (D30 H6) [N=27, 28]	72 (69 to 75)	70.5 (65.5 to 75.5)		
Diastolic, Dose 2 (D30 H9) [N=27, 28]	75 (71 to 79)	75 (65.5 to 81.5)		
Diastolic, Dose 2 (D30 H12) [N=27, 28]	73 (68 to 78)	72.5 (66.5 to 79.5)		
Diastolic, Dose 2 (D30 H18) [N=14, 14]	70 (64 to 74)	71.5 (66 to 79)		
Diastolic, Dose 2 (D31) [N=27, 28]	71 (67 to 77)	71 (65.5 to 80)		
Diastolic, Dose 2 (D32) [N=27, 28]	77 (71 to 81)	74 (67 to 79)		
Diastolic, Dose 2 (D33) [N=27, 28]	77 (71 to 81)	73 (70.5 to 79.5)		

Diastolic, Dose 2 (D37) [N=27, 28]	76 (68 to 86)	74 (68.5 to 79.5)		
Diastolic, Dose 2 (D60) [N=27, 28]	78 (72 to 84)	73 (67 to 81.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Heart Rate - Step 1

End point title	Levels of Heart Rate - Step 1

End point description:

Heart rate was part of the list of vital signs followed at specific protocol-defined timepoints during this study. It was expressed in beats per minute.

End point type	Secondary

End point timeframe:

At Day -30, -29, - 28, - 27, -23, 0, 1, 2, 7, 30, 31, 32, 33, 37 and 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: beats/minute				
median (inter-quartile range (Q1-Q3))				
Heart rate, placebo (D-30) [N=30, 30]	75.5 (62 to 86)	70 (64 to 79)		
Heart rate, placebo (D-30 H1.5) [N=30, 30]	75 (62 to 82)	73 (62 to 77)		
Heart rate, placebo (D-30 H3) [N=30, 30]	69.5 (56 to 76)	63.5 (58 to 71)		
Heart rate, placebo (D-30 H6) [N=30, 30]	69 (61 to 78)	69 (60 to 80)		
Heart rate, placebo (D-30 H9) [N=30, 30]	66.5 (56 to 82)	65 (55 to 70)		
Heart rate, placebo (D-30 H12) [N=30, 30]	71.5 (64 to 80)	72.5 (60 to 81)		
Heart rate, placebo (D-30 H18) [N=15, 15]	66 (55 to 75)	70 (66 to 77)		
Heart rate, placebo (D-29) [N=30, 30]	74.5 (63 to 82)	65.5 (62 to 70)		
Heart rate, placebo (D-28) [N=29, 30]	70 (66 to 82)	73.5 (65 to 81)		
Heart rate, placebo (D-27) [N=29, 30]	72 (66 to 80)	70 (65 to 81)		
Heart rate, placebo (D-23) [N=29, 30]	72 (66 to 80)	66 (58 to 75)		
Heart rate, Dose 1 (D0) [N=28, 29]	69.5 (62 to 80.5)	72 (62 to 79)		
Heart rate, Dose 1 (D0 H1.5) [N=28, 29]	67.5 (62 to 76)	68 (62 to 77)		
Heart rate, Dose 1 (D0 H6) [N=28, 29]	66 (60.5 to 80.5)	68 (65 to 79)		
Heart rate, Dose 1 (D0 H12) [N=28, 29]	76 (66.5 to 83)	69 (61 to 79)		
Heart rate, Dose 1 (D0 H18) [N=15, 14]	76 (60 to 83)	67 (60 to 77)		
Heart rate, Dose 1 (D1) [N=28, 29]	72 (65 to 82)	67 (64 to 75)		
Heart rate, Dose 1 (D2) [N=28, 29]	71.5 (60 to 80)	69 (65 to 79)		

Heart rate, Dose 1 (D7) [N=28, 29]	74 (63 to 80.5)	71 (62 to 82)		
Heart rate, Dose 2 (D30) [N=27, 28]	65 (59 to 77)	66.5 (58 to 76.5)		
Heart rate, Dose 2 (D30 H1.5) [N=27, 28]	69 (60 to 78)	68.5 (57.5 to 79)		
Heart rate, Dose 2 (D30 H3) [N=27, 28]	66 (55 to 74)	65 (60.5 to 76)		
Heart rate, Dose 2 (D30 H6) [N=27, 28]	73 (64 to 80)	71.5 (62.5 to 81)		
Heart rate, Dose 2 (D30 H9) [N=27, 28]	72 (57 to 81)	65.5 (59 to 79)		
Heart rate, Dose 2 (D30 H12) [N=27, 28]	79 (66 to 85)	69.5 (63 to 81)		
Heart rate, Dose 2 (D30 H18) [N=14, 14]	84.5 (79 to 90)	74.5 (66 to 80)		
Heart rate, Dose 2 (D31) [N=27, 28]	81 (65 to 89)	66.5 (58 to 77.5)		
Heart rate, Dose 2 (D32) [N=27, 28]	70 (63 to 83)	70.5 (62 to 77.5)		
Heart rate, Dose 2 (D33) [N=27, 28]	69 (63 to 81)	70.5 (64.5 to 79)		
Heart rate, Dose 2 (D37) [N=27, 28]	67 (59 to 79)	72.5 (61.5 to 79.5)		
Heart rate, Dose 2 (D60) [N=27, 28]	72 (67 to 80)	71 (63.5 to 79.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Respiratory Rate - Step 1

End point title	Levels of Respiratory Rate - Step 1

End point description:

Respiratory Rate was part of the list of vital signs followed at specific protocol-defined timepoints during this study. It was expressed as breaths per minute (breaths/min).

End point type	Secondary

End point timeframe:

At Day -30, -29, - 28, - 27, -23, 0, 1, 2, 7, 30, 31, 32, 33, 37 and 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: breaths/min				
median (inter-quartile range (Q1-Q3))				
Respiratory Rate, placebo (D-30) [N=30, 30]	14 (12 to 16)	13 (12 to 16)		
Respiratory Rate, placebo (D-30 H1.5) [N=30, 30]	13 (12 to 15)	14.5 (13 to 16)		
Respiratory Rate, placebo (D-30 H3) [N=30, 30]	13 (12 to 15)	14 (12 to 15)		
Respiratory Rate, placebo (D-30 H6) [N=30, 30]	12.5 (12 to 16)	14 (13 to 16)		

Respiratory Rate, placebo (D-30 H9) [N=30, 30]	13 (12 to 15)	15 (13 to 16)		
Respiratory Rate, placebo (D-30 H12) [N=30, 30]	14 (12 to 15)	14.5 (13 to 15)		
Respiratory Rate, placebo (D-30 H18) [N=15, 15]	13 (12 to 14)	12 (11 to 14)		
Respiratory Rate, placebo (D-29) [N=30, 30]	13.5 (12 to 16)	14 (13 to 15)		
Respiratory Rate, placebo (D-28) [N=29, 30]	14 (12 to 16)	14 (13 to 16)		
Respiratory Rate, placebo (D-27) [N=29, 30]	14 (12 to 14)	14 (13 to 14)		
Respiratory Rate, placebo (D-23) [N=29, 30]	14 (12 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 1 (D0) [N=28, 29]	14 (12.5 to 15.5)	14 (12 to 15)		
Respiratory Rate, Dose 1 (D0 H1.5) [N=28, 29]	14 (12 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 1 (D0 H6) [N=28, 29]	14 (13 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 1 (D0 H12) [N=28, 29]	13.5 (12 to 14)	14 (13 to 14)		
Respiratory Rate, Dose 1 (D0 H18) [N=15, 14]	13 (12 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 1 (D1) [N=28, 29]	14 (12 to 15)	14 (13 to 14)		
Respiratory Rate, Dose 1 (D2) [N=28, 29]	14 (13 to 14.5)	14 (12 to 15)		
Respiratory Rate, Dose 1 (D7) [N=28, 29]	13.5 (13 to 14.5)	13 (13 to 14)		
Respiratory Rate, Dose 2 (D30) [N=27, 28]	14 (12 to 15)	14 (12 to 16)		
Respiratory Rate, Dose 2 (D30 H1.5) [N=27, 28]	14 (13 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 2 (D30 H3) [N=27, 28]	14 (12 to 15)	14 (12 to 15)		
Respiratory Rate, Dose 2 (D30 H6) [N=27, 28]	13 (12 to 15)	14 (12 to 15)		
Respiratory Rate, Dose 2 (D30 H9) [N=27, 28]	14 (12 to 15)	13.5 (12.5 to 14)		
Respiratory Rate, Dose 2 (D30 H12) [N=27, 28]	14 (12 to 15)	14 (13 to 15)		
Respiratory Rate, Dose 2 (D30 H18) [N=14, 14]	14 (12 to 15)	14 (14 to 15)		
Respiratory Rate, Dose 2 (D31) [N=27, 28]	13 (12 to 15)	14 (12 to 15)		
Respiratory Rate, Dose 2 (D32) [N=27, 28]	14 (12 to 14)	14 (13 to 15)		
Respiratory Rate, Dose 2 (D33) [N=27, 28]	13 (12 to 14)	14 (13 to 15)		
Respiratory Rate, Dose 2 (D37) [N=27, 28]	14 (12 to 16)	14 (12.5 to 15)		
Respiratory Rate, Dose 2 (D60) [N=25, 26]	14 (12 to 15)	14 (13 to 16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Systolic pressure - Step 1

End point title	Levels of Systolic pressure - Step 1

End point description:

Systolic pressure was part of the list of vital signs followed at specific protocol-defined timepoints during this study, measured in millimeter of mercury (mmHg).

End point type	Secondary

End point timeframe:

At Day -30, -29, - 28, - 27, -23, 0, 1, 2, 7, 30, 31, 32, 33, 37 and 60

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: mmHg				
median (inter-quartile range (Q1-Q3))				
Systolic, placebo (D-30) [N=30, 30]	123.5 (112 to 130)	116 (106 to 125)		
Systolic, placebo (D-30 H1.5) [N=30, 30]	117 (111 to 124)	114 (103 to 124)		
Systolic, placebo (D-30 H3) [N=30, 30]	117.5 (112 to 126)	114 (105 to 118)		
Systolic, placebo (D-30 H6) [N=30, 30]	118 (113 to 124)	112 (105 to 124)		
Systolic, placebo (D-30 H9) [N=30, 30]	120.5 (112 to 131)	114.5 (106 to 123)		
Systolic, placebo (D-30 H12) [N=30, 30]	121.5 (112 to 129)	112 (105 to 125)		
Systolic, placebo (D-30 H18) [N=15, 15]	111 (106 to 122)	106 (96 to 118)		
Systolic, placebo (D-29) [N=30, 30]	116.5 (111 to 124)	112 (104 to 122)		
Systolic, placebo (D-28) [N=29, 30]	121 (110 to 124)	114 (103 to 121)		
Systolic, placebo (D-27) [N=29, 30]	119 (112 to 124)	115.5 (109 to 121)		
Systolic, placebo (D-23) [N=29, 30]	118 (110 to 123)	115 (104 to 122)		
Systolic, Dose 1 (D0) [N=28, 29]	118 (112 to 122.5)	114 (108 to 124)		
Systolic, Dose 1 (D0 H1.5) [N=28, 29]	116 (110.5 to 121.5)	109 (102 to 119)		
Systolic, Dose 1 (D0 H6) [N=28, 29]	117 (111 to 121.5)	112 (103 to 117)		
Systolic, Dose 1 (D0 H12) [N=28, 29]	115 (110 to 126)	114 (107 to 120)		
Systolic, Dose 1 (D0 H18) [N=15, 14]	112 (104 to 121)	105 (99 to 122)		
Systolic, Dose 1 (D1) [N=28, 29]	114 (108.5 to 119)	114 (104 to 123)		
Systolic, Dose 1 (D2) [N=28, 29]	115 (110 to 124)	111 (103 to 118)		
Systolic, Dose 1 (D7) [N=28, 29]	116 (111 to 120.5)	113 (107 to 123)		

Systolic, Dose 2 (D30) [N=27, 28]	115 (112 to 121)	112.5 (106.5 to 122.5)		
Systolic, Dose 2 (D30 H1.5) [N=27, 28]	115 (108 to 124)	109.5 (102 to 117.5)		
Systolic, Dose 2 (D30 H3) [N=27, 28]	116 (111 to 124)	113 (103 to 120.5)		
Systolic, Dose 2 (D30 H6) [N=27, 28]	117 (107 to 122)	112 (103.5 to 118)		
Systolic, Dose 2 (D30 H9) [N=27, 28]	117 (108 to 121)	116 (108.5 to 124)		
Systolic, Dose 2 (D30 H12) [N=27, 28]	116 (109 to 125)	116.5 (105 to 122)		
Systolic, Dose 2 (D30 H18) [N=14, 14]	109.5 (102 to 115)	107 (100 to 122)		
Systolic, Dose 2 (D31) [N=27, 28]	114 (108 to 123)	109.5 (104 to 119)		
Systolic, Dose 2 (D32) [N=27, 28]	116 (113 to 120)	110.5 (103 to 115.5)		
Systolic, Dose 2 (D33) [N=27, 28]	116 (112 to 122)	111.5 (106 to 119.5)		
Systolic, Dose 2 (D37) [N=27, 28]	120 (108 to 126)	112 (106 to 124.5)		
Systolic, Dose 2 (D60) [N=27, 28]	120 (109 to 125)	115 (106.5 to 122.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 2 immuno

End point title	Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 2 immuno

End point description:

Anti-HBs antibody concentrations in serum were measured by CLIA Assay. Concentrations were presented as geometric mean concentrations, in milli-International Units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

At Day 0 (PRE) and post-vaccination (Day 44 for HBsAg/AS_2 Group and Day 194 for Engerix-B_2 Group)

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE [N=10, 8]	3.1 (3.1 to 3.1)	3.1 (3.1 to 3.1)		
Anti-HBs, D44 [N=10, 0]	8447.1 (4040.7 to 17658.9)	0 (0 to 0)		

Anti-HBs, D194 [N=0, 8]	0 (0 to 0)	1996.3 (143.8 to 27707.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 2 persistence

End point title	Anti-Hepatitis B surface (anti-HBs) antibody concentrations in serum - Step 2 persistence

End point description:

Anti-HBs antibody concentrations in serum were measured by CLIA Assay. Concentrations were presented as geometric mean concentrations, in milli-International Units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

At Day 0 (PRE) and post-vaccination (Day 44 for HBsAg/AS_2 Group and Day 194 for Engerix-B_2 Group)

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE [N=10, 10]	3.1 (3.1 to 3.1)	3.1 (3.1 to 3.1)		
Anti-HBs, D44 [N=10, 0]	8447.1 (4040.7 to 17658.9)	0 (0 to 0)		
Anti-HBs, D194 [N=0, 10]	0 (0 to 0)	2454.9 (311.4 to 19354.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms - Step 2

End point title	Number of subjects with any and grade 3 solicited local symptoms - Step 2

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each vaccine dose and across doses

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Any Pain, Dose 1 [N=10, 11]	10	3		
Grade 3 Pain, Dose 1 [N=10, 11]	0	0		
Any Redness, Dose 1 [N=10, 11]	3	0		
Grade 3 Redness, Dose 1 [N=10, 11]	0	0		
Any Swelling, Dose 1 [N=10, 11]	2	0		
Grade 3 Swelling, Dose 1 [N=10, 11]	0	0		
Any Pain, Dose 2 [N=10, 10]	10	1		
Grade 3 Pain, Dose 2 [N=10, 10]	2	0		
Any Redness, Dose 2 [N=10, 10]	2	0		
Grade 3 Redness, Dose 2 [N=10, 10]	0	0		
Any Swelling, Dose 2 [N=10, 10]	3	0		
Grade 3 Swelling, Dose 2 [N=10, 10]	0	0		
Any Pain, Dose 3 [N=0, 10]	0	1		
Grade 3 Pain, Dose 3 [N=0, 10]	0	0		
Any Redness, Dose 3 [N=0, 10]	0	0		
Grade 3 Redness, Dose 3 [N=0, 10]	0	0		
Any Swelling, Dose 3 [N=0, 10]	0	0		
Grade 3 Swelling, Dose 3 [N=0, 10]	0	0		
Any Pain, Across doses [N=10, 11]	10	4		
Grade 3 Pain, Across doses [N=10, 11]	2	0		
Any Redness, Across doses [N=10, 11]	4	0		
Grade 3 Redness, Across doses [N=10, 11]	0	0		
Any Swelling, Across doses [N=10, 11]	3	0		
Grade 3 Swelling, Across doses [N=10, 11]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms - Pooling Step

End point title	Number of subjects with any and grade 3 solicited local symptoms - Pooling Step

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each vaccine dose and across doses

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: Participants				
Any Pain, Dose 1 [N=38, 39]	28	10		
Grade 3 Pain, Dose 1 [N=38, 39]	0	0		
Any Redness, Dose 1 [N=38, 39]	9	1		
Grade 3 Redness, Dose 1 [N=38, 39]	0	0		
Any Swelling, Dose 1 [N=38, 39]	6	0		
Grade 3 Swelling, Dose 1 [N=38, 39]	0	0		
Any Pain, Dose 2 [N=37, 38]	25	7		
Grade 3 Pain, Dose 2 [N=37, 38]	2	1		
Any Redness, Dose 2 [N=37, 38]	7	0		
Grade 3 Redness, Dose 2 [N=37, 38]	1	0		
Any Swelling, Dose 2 [N=37, 38]	4	0		
Grade 3 Swelling, Dose 2 [N=37, 38]	0	0		
Any Pain, Dose 3 [N=0, 10]	0	1		
Grade 3 Pain, Dose 3 [N=0, 10]	0	0		
Any Redness, Dose 3 [N=0, 10]	0	0		
Grade 3 Redness, Dose 3 [N=0, 10]	0	0		
Any Swelling, Dose 3 [N=0, 10]	0	0		
Grade 3 Swelling, Dose 3 [N=0, 10]	0	0		
Any Pain, Across doses [N=38, 39]	31	12		
Grade 3 Pain, Across doses [N=38, 39]	2	1		
Any Redness, Across doses [N=38, 39]	12	1		
Grade 3 Redness, Across doses [N=38, 39]	1	0		
Any Swelling, Across doses [N=38, 39]	7	0		
Grade 3 Swelling, Across doses [N=38, 39]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms - Step 2

End point title	Number of subjects with any, grade 3 and related solicited general symptoms - Step 2

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms [nausea, vomiting, diarrhoea and/or abdominal pain], headache, malaise, myalgia, shivering and temperature [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination.

At Day 0 of dose 2, two temperatures were collected: one at Hour 0 (H0) and a second one at Hour 18 (H18). The highest temperature between H0 et H18 was taken.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each vaccine dose and across doses

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Any Fatigue, Dose 1 [N=10, 11]	8	3		
Grade 3 Fatigue, Dose 1 [N=10, 11]	1	0		
Related Fatigue, Dose 1 [N=10, 11]	7	2		
Any Gastr. Sympt., Dose 1 [N=10, 11]	5	3		
Grade 3 Gastr. Sympt., Dose 1 [N=10, 11]	1	0		
Related Gastr. Sympt., Dose 1 [N=10, 11]	5	3		
Any Headache, Dose 1 [N=10, 11]	7	4		
Grade 3 Headache, Dose 1 [N=10, 11]	1	0		
Related Headache, Dose 1 [N=10, 11]	7	3		
Any Malaise, Dose 1 [N=10, 11]	5	0		
Grade 3 Malaise, Dose 1 [N=10, 11]	1	0		
Related Malaise, Dose 1 [N=10, 11]	5	0		
Any Myalgia, Dose 1 [N=10, 11]	7	1		
Grade 3 Myalgia, Dose 1 [N=10, 11]	0	0		
Related Myalgia, Dose 1 [N=10, 11]	7	1		
Any Shivering, Dose 1 [N=10, 11]	2	1		
Grade 3 Shivering, Dose 1 [N=10, 11]	1	0		
Related Shivering, Dose 1 [N=10, 11]	2	1		
Any Temperature, Dose 1 [N=10, 11]	3	1		
Grade 3 Temperature, Dose 1 [N=10, 11]	0	0		
Related Temperature, Dose 1 [N=10, 11]	3	0		
Any Fatigue, Dose 2 [N=10, 10]	7	1		
Grade 3 Fatigue, Dose 2 [N=10, 10]	1	0		
Related Fatigue, Dose 2 [N=10, 10]	7	1		
Any Gastr. Sympt., Dose 2 [N=10, 10]	3	0		
Grade 3 Gastr. Sympt., Dose 2 [N=10, 10]	1	0		
Related Gastr. Sympt., Dose 2 [N=10, 10]	3	0		
Any Headache, Dose 2 [N=10, 10]	6	0		
Grade 3 Headache, Dose 2 [N=10, 10]	3	0		
Related Headache, Dose 2 [N=10, 10]	6	0		
Any Malaise, Dose 2 [N=10, 10]	7	0		
Grade 3 Malaise, Dose 2 [N=10, 10]	1	0		
Related Malaise, Dose 2 [N=10, 10]	7	0		
Any Myalgia, Dose 2 [N=10, 10]	9	0		

Grade 3 Myalgia, Dose 2 [N=10, 10]	0	0		
Related Myalgia, Dose 2 [N=10, 10]	9	0		
Any Shivering, Dose 2 [N=10, 10]	5	0		
Grade 3 Shivering, Dose 2 [N=10, 10]	0	0		
Related Shivering, Dose 2 [N=10, 10]	5	0		
Any Temperature, Dose 2 [N=10, 10]	4	2		
Grade 3 Temperature, Dose 2 [N=10, 10]	0	0		
Related Temperature, Dose 2 [N=10, 10]	1	0		
Any Fatigue, Dose 3 [N=0, 10]	0	1		
Grade 3 Fatigue, Dose 3 [N=0, 10]	0	0		
Related Fatigue, Dose 3 [N=0, 10]	0	1		
Any Gastr. Sympt., Dose 3 [N=0, 10]	0	1		
Grade 3 Gastr. Sympt., Dose 3 [N=0, 10]	0	0		
Related Gastr. Sympt., Dose 3 [N=0, 10]	0	1		
Any Headache, Dose 3 [N=0, 10]	0	2		
Grade 3 Headache, Dose 3 [N=0, 10]	0	0		
Related Headache, Dose 3 [N=0, 10]	0	2		
Any Malaise, Dose 3 [N=0, 10]	0	0		
Grade 3 Malaise, Dose 3 [N=0, 10]	0	0		
Related Malaise, Dose 3 [N=0, 10]	0	0		
Any Myalgia, Dose 3 [N=0, 10]	0	0		
Grade 3 Myalgia, Dose 3 [N=0, 10]	0	0		
Related Myalgia, Dose 3 [N=0, 10]	0	0		
Any Shivering, Dose 3 [N=0, 10]	0	0		
Grade 3 Shivering, Dose 3 [N=0, 10]	0	0		
Related Shivering, Dose 3 [N=0, 10]	0	0		
Any Temperature, Dose 3 [N=0, 10]	0	0		
Grade 3 Temperature, Dose 3 [N=0, 10]	0	0		
Related Temperature, Dose 3 [N=0, 10]	0	0		
Any Fatigue, Across doses [N=10, 11]	8	3		
Grade 3 Fatigue, Across doses [N=10, 11]	2	0		
Related Fatigue, Across doses [N=10, 11]	8	2		
Any Gastr. Sympt., Across doses [N=10, 11]	6	4		
Grade 3 Gastr. Sympt., Across doses [N=10, 11]	2	0		
Related Gastr. Sympt., Across doses [N=10, 11]	6	4		
Any Headache, Across doses [N=10, 11]	9	5		
Grade 3 Headache, Across doses [N=10, 11]	4	0		
Related Headache, Across doses [N=10, 11]	9	4		
Any Malaise, Across doses [N=10, 11]	7	0		
Grade 3 Malaise, Across doses [N=10, 11]	2	0		
Related Malaise, Across doses [N=10, 11]	7	0		
Any Myalgia, Across doses [N=10, 11]	9	1		

Grade 3 Myalgia, Across doses [N=10, 11]	0	0		
Related Myalgia, Across doses [N=10, 11]	9	1		
Any Shivering, Across doses [N=10, 11]	6	1		
Grade 3 Shivering, Across doses [N=10, 11]	1	0		
Related Shivering, Across doses [N=10, 11]	6	1		
Any Temperature, Across doses [N=10, 11]	6	3		
Grade 3 Temperature, Across doses [N=10, 11]	0	0		
Related Temperature, Across doses [N=10, 11]	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms - Pooling Step

End point title	Number of subjects with any, grade 3 and related solicited general symptoms - Pooling Step

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms [nausea, vomiting, diarrhoea and/or abdominal pain], headache, malaise, myalgia, shivering and temperature [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination. There was no pooling for temperature symptom between Step 1 and Step 2 due to difference in recording approach for the 18 hour data (nurse or self-assessment).

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each vaccine dose and across doses

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: Participants				
Any Fatigue, Dose 1 [N=38, 39]	11	9		
Grade 3 Fatigue, Dose 1 [N=38, 39]	2	0		
Related Fatigue, Dose 1 [N=38, 39]	9	8		
Any Gastro. Sympt., Dose 1 [N=38, 39]	9	9		
Grade 3 Gastro. Sympt., Dose 1 [N=38, 39]	1	1		
Related Gastro. Sympt., Dose 1 [N=38, 39]	9	6		
Any Headache, Dose 1 [N=38, 39]	21	9		
Grade 3 Headache, Dose 1 [N=38, 39]	1	1		
Related Headache, Dose 1 [N=38, 39]	18	7		

Any Malaise, Dose 1 [N=38, 39]	9	2		
Grade 3 Malaise, Dose 1 [N=38, 39]	1	0		
Related Malaise, Dose 1 [N=38, 39]	9	2		
Any Myalgia, Dose 1 [N=38, 39]	17	2		
Grade 3 Myalgia, Dose 1 [N=38, 39]	0	0		
Related Myalgia, Dose 1 [N=38, 39]	16	2		
Any Shivering, Dose 1 [N=38, 39]	4	1		
Grade 3 Shivering, Dose 1 [N=38, 39]	1	0		
Related Shivering, Dose 1 [N=38, 39]	4	1		
Any Fatigue, Dose 2 [N=37, 38]	17	9		
Grade 3 Fatigue, Dose 2 [N=37, 38]	2	0		
Related Fatigue, Dose 2 [N=37, 38]	17	8		
Any Gastro. Sympt., Dose 2 [N=37, 38]	7	5		
Grade 3 Gastro. Sympt., Dose 2 [N=37, 38]	1	3		
Related Gastro. Sympt., Dose 2 [N=37, 38]	7	5		
Any Headache, Dose 2 [N=37, 38]	20	5		
Grade 3 Headache, Dose 2 [N=37, 38]	3	1		
Related Headache, Dose 2 [N=37, 38]	20	5		
Any Malaise, Dose 2 [N=37, 38]	14	6		
Grade 3 Malaise, Dose 2 [N=37, 38]	3	1		
Related Malaise, Dose 2 [N=37, 38]	14	6		
Any Myalgia, Dose 2 [N=37, 38]	19	3		
Grade 3 Myalgia, Dose 2 [N=37, 38]	0	0		
Related Myalgia, Dose 2 [N=37, 38]	19	1		
Any Shivering, Dose 2 [N=37, 38]	14	2		
Grade 3 Shivering, Dose 2 [N=37, 38]	0	0		
Related Shivering, Dose 2 [N=37, 38]	14	2		
Any Fatigue, Dose 3 [N=0, 10]	0	1		
Grade 3 Fatigue, Dose 3 [N=0, 10]	0	0		
Related Fatigue, Dose 3 [N=0, 10]	0	1		
Any Gastro. Sympt., Dose 3 [N=0, 10]	0	1		
Grade 3 Gastro. Sympt., Dose 3 [N=0, 10]	0	0		
Related Gastro. Sympt., Dose 3 [N=0, 10]	0	1		
Any Headache, Dose 3 [N=0, 10]	0	2		
Grade 3 Headache, Dose 3 [N=0, 10]	0	0		
Related Headache, Dose 3 [N=0, 10]	0	2		
Any Malaise, Dose 3 [N=0, 10]	0	0		
Grade 3 Malaise, Dose 3 [N=0, 10]	0	0		
Related Malaise, Dose 3 [N=0, 10]	0	0		
Any Myalgia, Dose 3 [N=0, 10]	0	0		
Grade 3 Myalgia, Dose 3 [N=0, 10]	0	0		
Related Myalgia, Dose 3 [N=0, 10]	0	0		
Any Shivering, Dose 3 [N=0, 10]	0	0		
Grade 3 Shivering, Dose 3 [N=0, 10]	0	0		
Related Shivering, Dose 3 [N=0, 10]	0	0		
Any Fatigue, Across doses [N=38, 39]	18	12		
Grade 3 Fatigue, Across doses [N=38, 39]	4	0		
Related Fatigue, Across doses [N=38, 39]	18	11		

Any Gastro. Sympt., Across doses [N=38, 39]	14	12		
Grade 3 Gastro. Sympt., Across doses [N=38, 39]	2	4		
Related Gastro. Sympt., Across doses [N=38, 39]	14	11		
Any Headache, Across doses [N=38, 39]	26	11		
Grade 3 Headache, Across doses [N=38, 39]	4	1		
Related Headache, Across doses [N=38, 39]	24	10		
Any Malaise, Across doses [N=38, 39]	15	7		
Grade 3 Malaise, Across doses [N=38, 39]	4	1		
Related Malaise, Across doses [N=38, 39]	15	7		
Any Myalgia, Across doses [N=38, 39]	23	4		
Grade 3 Myalgia, Across doses [N=38, 39]	0	0		
Related Myalgia, Across doses [N=38, 39]	22	3		
Any Shivering, Across doses [N=38, 39]	16	3		
Grade 3 Shivering, Across doses [N=38, 39]	1	0		
Related Shivering, Across doses [N=38, 39]	16	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) - Step 2

End point title	Number of subjects with any unsolicited adverse events (AEs) - Step 2

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset out-side the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Within the 28-day (Days 0-27) and post-vaccination period

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Participants	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) - Pooling Step

End point title	Number of subjects with any unsolicited adverse events (AEs) - Pooling Step

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset out-side the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Within the 28-day (Days 0-27) post-vaccination period.

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: Participants				
Participants	20	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) - Step 2

End point title	Number of subjects with serious adverse events (SAEs) - Step 2

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_2 Group and up to Day 330 for the Engerix-B_2 Group

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential immune-mediated disorders (pIMDs) - Step 2

End point title	Number of subjects with any potential immune-mediated disorders (pIMDs) - Step 2

End point description:

PIMD(s) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_2 Group and up to Day 330 for the Engerix-B_2 Group

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) - Pooling Step

End point title	Number of subjects with serious adverse events (SAEs) - Pooling Step

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_1+2 Group and up to Day 330 for the Engerix-B_1+2 Group

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: Participants				
Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential immune-mediated disorders (pIMDs) - Pooling Step

End point title	Number of subjects with any potential immune-mediated disorders (pIMDs) - Pooling Step

End point description:

PIMD(s) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_1+2 Group and up to Day 330 for the Engerix-B_1+2 Group

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any new medical conditions requiring medical attention (MAEs) - Step 2

End point title	Number of subjects with any new medical conditions requiring medical attention (MAEs) - Step 2

End point description:

MAEs were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any MAE(s) = Occurrence of any MAE(s) regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_2 Group and up to Day 330 for the Engerix-B_2 Group

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: Participants				
Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any new medical conditions requiring medical attention (MAEs) - Pooling Step

End point title	Number of subjects with any new medical conditions requiring medical attention (MAEs) - Pooling Step

End point description:

MAEs were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any MAE(s) = Occurrence of any MAE(s) regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

Up to Day 180 for the HBsAg/AS_1+2 Group and up to Day 330 for the Engerix-B_1+2 Group

End point values	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: Participants				
Participants	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Alanine aminotransferase (ALT) in blood samples - Step 2

End point title	Levels of Alanine aminotransferase (ALT) in blood samples - Step 2

End point description:

Biochemical laboratory parameters assessed included ALT levels. ALT concentrations were expressed in units per liter (U/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
ALT, PRE [N=10, 11]	27.5 (23 to 33)	31 (28 to 38)		
ALT, D30 [N=10, 0]	25.5 (25 to 31)	0 (0 to 0)		
ALT, D32 [N=10, 0]	27 (20 to 36)	0 (0 to 0)		
ALT, D37 [N=10, 0]	23 (18 to 31)	0 (0 to 0)		
ALT, D60 [N=10, 0]	30 (23 to 33)	0 (0 to 0)		
ALT, D180 [N=0, 10]	0 (0 to 0)	34.5 (27 to 45)		
ALT, D182 [N=0, 9]	0 (0 to 0)	31 (25 to 42)		
ALT, D187 [N=0, 9]	0 (0 to 0)	34 (29 to 40)		
ALT, D210 [N=0, 10]	0 (0 to 0)	29.5 (22 to 48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Aspartate aminotransferase (AST) in blood samples - Step 2

End point title	Levels of Aspartate aminotransferase (AST) in blood samples - Step 2

End point description:

Biochemical laboratory parameters assessed included AST levels. AST concentrations were expressed in units per liter (U/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: U/L				
median (inter-quartile range (Q1-Q3))				
AST, PRE [N=10, 11]	22.5 (21 to 24)	28 (23 to 38)		
AST, D30 [N=10, 0]	22.5 (20 to 26)	0 (0 to 0)		
AST, D32 [N=10, 0]	24 (22 to 26)	0 (0 to 0)		
AST, D37 [N=10, 0]	20.5 (18 to 24)	0 (0 to 0)		
AST, D60 [N=10, 0]	21.5 (18 to 31)	0 (0 to 0)		
AST, D180 [N=0, 10]	0 (0 to 0)	25 (18 to 43)		

AST, D182 [N=0, 9]	0 (0 to 0)	29 (23 to 39)		
AST, D187 [N=0, 9]	0 (0 to 0)	25 (20 to 36)		
AST, D210 [N=0, 10]	0 (0 to 0)	22.5 (20 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Basophils in blood samples - Step 2

End point title	Levels of Basophils in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included basophil levels. Basophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Basophils, PRE [N=10, 11]	0.04 (0.02 to 0.05)	0.03 (0.02 to 0.04)		
Basophils, D30 [N=10, 0]	0.02 (0.01 to 0.07)	0 (0 to 0)		
Basophils, D32 [N=10, 0]	0.04 (0.02 to 0.05)	0 (0 to 0)		
Basophils, D37 [N=10, 0]	0.03 (0.01 to 0.06)	0 (0 to 0)		
Basophils, D60 [N=10, 0]	0.05 (0.02 to 0.06)	0 (0 to 0)		
Basophils, D180 [N=0, 10]	0 (0 to 0)	0.02 (0.01 to 0.04)		
Basophils, D182 [N=0, 9]	0 (0 to 0)	0.02 (0.01 to 0.04)		
Basophils, D187 [N=0, 9]	0 (0 to 0)	0.03 (0.02 to 0.05)		
Basophils, D210 [N=0, 10]	0 (0 to 0)	0.03 (0.01 to 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of serum C Reactive Protein (CRP) in blood samples - Step 2

End point title	Levels of serum C Reactive Protein (CRP) in blood samples - Step 2

End point description:

Biochemical laboratory parameters assessed included CRP levels. CRP concentrations were expressed in milligrams per liter (mg/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 2, Day 30, Day 31, Day 32, Day 37, Day 60, Day 180, Day 181, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: mg/L				
median (inter-quartile range (Q1-Q3))				
CRP, PRE [N=10, 11]	5.55 (5 to 6.8)	5.8 (5 to 9.5)		
CRP, D2 [N=10, 11]	24.2 (16.6 to 32.7)	5 (5 to 8.8)		
CRP, D30 [N=10, 0]	6.8 (5.1 to 8.2)	0 (0 to 0)		
CRP, D31 [N=10, 0]	20.45 (10.4 to 21.9)	0 (0 to 0)		
CRP, D32 [N=10, 0]	33.75 (12.7 to 44.6)	0 (0 to 0)		
CRP, D37 [N=10, 0]	6.7 (5.5 to 10)	0 (0 to 0)		
CRP, D60 [N=10, 0]	5 (5 to 6.2)	0 (0 to 0)		
CRP, D180 [N=0, 10]	0 (0 to 0)	5.25 (5 to 6.8)		
CRP, D181 [N=0, 9]	0 (0 to 0)	5 (5 to 6)		
CRP, D182 [N=0, 9]	0 (0 to 0)	5 (5 to 7.3)		
CRP, D187 [N=0, 9]	0 (0 to 0)	5 (5 to 6.7)		
CRP, D210 [N=0, 10]	0 (0 to 0)	5 (5 to 7.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Eosinophils in blood samples - Step 2

End point title	Levels of Eosinophils in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included eosinophil levels. Eosinophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Eosinophils, PRE [N=10, 11]	0.16 (0.09 to 0.23)	0.18 (0.1 to 0.29)		
Eosinophils, D30 [N=10, 0]	0.17 (0.12 to 0.23)	0 (0 to 0)		
Eosinophils, D32 [N=10, 0]	0.25 (0.17 to 0.33)	0 (0 to 0)		
Eosinophils, D37 [N=10, 0]	0.19 (0.11 to 0.26)	0 (0 to 0)		
Eosinophils, D60 [N=10, 0]	0.2 (0.09 to 0.26)	0 (0 to 0)		
Eosinophils, D180 [N=0, 10]	0 (0 to 0)	0.14 (0.1 to 0.2)		
Eosinophils, D182 [N=0, 9]	0 (0 to 0)	0.17 (0.11 to 0.19)		
Eosinophils, D187 [N=0, 9]	0 (0 to 0)	0.18 (0.16 to 0.27)		
Eosinophils, D210 [N=0, 10]	0 (0 to 0)	0.16 (0.09 to 0.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of White Blood Cell (WBC) in blood samples - Step 2

End point title	Levels of White Blood Cell (WBC) in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included white blood cells levels. WBC levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
WBC, PRE [N=10, 11]	6.93 (5.51 to 9.67)	5.67 (5.13 to 7.46)		
WBC, D30 [N=10, 0]	6.41 (5.7 to 6.6)	0 (0 to 0)		
WBC, D32 [N=10, 0]	6.29 (5.24 to 8.09)	0 (0 to 0)		
WBC, D37 [N=10, 0]	6.37 (5.42 to 7.06)	0 (0 to 0)		

WBC, D60 [N=10, 0]	7.03 (5.65 to 8.5)	0 (0 to 0)		
WBC, D180 [N=0, 10]	0 (0 to 0)	6.02 (5.25 to 8.3)		
WBC, D182 [N=0, 9]	0 (0 to 0)	6.15 (5.6 to 8.1)		
WBC, D187 [N=0, 9]	0 (0 to 0)	7.35 (5.46 to 7.61)		
WBC, D210 [N=0, 10]	0 (0 to 0)	5.91 (4.48 to 8.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Lymphocytes in blood samples - Step 2

End point title	Levels of Lymphocytes in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included lymphocyte levels. Lymphocyte levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Lymphocytes, D0 [N=10, 11]	2.13 (1.83 to 2.55)	1.96 (1.69 to 2.37)		
Lymphocytes, D30 [N=10, 0]	2.14 (1.8 to 2.47)	0 (0 to 0)		
Lymphocytes, D32 [N=10, 0]	1.7 (1.47 to 1.82)	0 (0 to 0)		
Lymphocytes, D37 [N=10, 0]	2.12 (1.98 to 2.32)	0 (0 to 0)		
Lymphocytes, D60 [N=10, 0]	2.12 (1.72 to 2.34)	0 (0 to 0)		
Lymphocytes, D180 [N=0, 10]	0 (0 to 0)	1.93 (1.84 to 2.45)		
Lymphocytes, D182 [N=0, 9]	0 (0 to 0)	2.04 (1.75 to 2.44)		
Lymphocytes, D187 [N=0, 9]	0 (0 to 0)	2.07 (1.76 to 2.27)		
Lymphocytes, D210 [N=0, 10]	0 (0 to 0)	1.91 (1.46 to 2.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Monocytes in blood samples - Step 2

End point title	Levels of Monocytes in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included monocyte levels. Monocyte levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0, Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Monocytes, D0 [N=10, 11]	0.64 (0.47 to 0.74)	0.5 (0.28 to 0.69)		
Monocytes, D30 [N=10, 0]	0.54 (0.38 to 0.62)	0 (0 to 0)		
Monocytes, D32 [N=10, 0]	0.87 (0.8 to 1.07)	0 (0 to 0)		
Monocytes, D37 [N=10, 0]	0.47 (0.43 to 0.58)	0 (0 to 0)		
Monocytes, D60 [N=10, 0]	0.58 (0.49 to 0.68)	0 (0 to 0)		
Monocytes, D180 [N=0, 10]	0 (0 to 0)	0.46 (0.39 to 0.57)		
Monocytes, D182 [N=0, 9]	0 (0 to 0)	0.43 (0.42 to 0.66)		
Monocytes, D187 [N=0, 9]	0 (0 to 0)	0.44 (0.37 to 0.55)		
Monocytes, D210 [N=0, 10]	0 (0 to 0)	0.52 (0.34 to 0.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Neutrophils in blood samples - Step 2

End point title	Levels of Neutrophils in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included neutrophil levels. Neutrophil levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Neutrophils, D0 [N=10, 11]	4.02 (3.12 to 6.22)	3.11 (2.3 to 4.56)		
Neutrophils, D30 [N=10, 0]	3.41 (2.87 to 3.93)	0 (0 to 0)		
Neutrophils, D32 [N=10, 0]	3.42 (2.78 to 5.01)	0 (0 to 0)		
Neutrophils, D37 [N=10, 0]	3.22 (2.76 to 3.9)	0 (0 to 0)		
Neutrophils, D60 [N=10, 0]	4.18 (2.96 to 5.34)	0 (0 to 0)		
Neutrophils, D180 [N=0, 10]	0 (0 to 0)	3.29 (2.99 to 4.67)		
Neutrophils, D182 [N=0, 9]	0 (0 to 0)	3.16 (2.89 to 4.88)		
Neutrophils, D187 [N=0, 9]	0 (0 to 0)	3.9 (3.18 to 4.29)		
Neutrophils, D210 [N=0, 10]	0 (0 to 0)	3.28 (2.29 to 4.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count in blood samples - Step 2

End point title	Platelet count in blood samples - Step 2

End point description:

Haematological laboratory parameters assessed included platelet count levels. Platelet count levels were expressed in billion cells per liter (billion cells/L).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 30, Day 32, Day 37, Day 60, Day 180, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: billion cells/L				
median (inter-quartile range (Q1-Q3))				
Platelets, D0 [N=10, 11]	269 (255 to 312)	272 (215 to 322)		

Platelets, D30 [N=10, 0]	272.5 (215 to 330)	0 (0 to 0)		
Platelets, D32 [N=10, 0]	257 (204 to 303)	0 (0 to 0)		
Platelets, D37 [N=10, 0]	315.5 (286 to 330)	0 (0 to 0)		
Platelets, D60 [N=10, 0]	282 (257 to 323)	0 (0 to 0)		
Platelets, D180 [N=0, 10]	0 (0 to 0)	247 (237 to 276)		
Platelets, D182 [N=0, 9]	0 (0 to 0)	263 (248 to 274)		
Platelets, D187 [N=0, 9]	0 (0 to 0)	272 (260 to 280)		
Platelets, D210 [N=0, 10]	0 (0 to 0)	264.5 (214 to 314)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of total Bilirubin in blood samples - Step 2

End point title	Levels of total Bilirubin in blood samples - Step 2

End point description:

Biochemical laboratory parameters assessed included total bilirubin levels. Bilirubin concentrations were expressed in milligrams per deciliter (mG/dL).

End point type	Secondary

End point timeframe:

At Day 0 (PRE), Day 2, Day 30, Day 31, Day 32, Day 37, Day 60, Day 180, Day 181, Day 182, Day 187 and Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Total Bilirubin, PRE [N=10, 11]	0.4 (0.4 to 0.8)	0.5 (0.3 to 0.7)		
Total Bilirubin, D2 [N=10, 11]	0.45 (0.4 to 0.6)	0.5 (0.3 to 1.5)		
Total Bilirubin, D30 [N=10, 0]	0.45 (0.3 to 0.8)	0 (0 to 0)		
Total Bilirubin, D31 [N=10, 0]	0.55 (0.4 to 1)	0 (0 to 0)		
Total Bilirubin, D32 [N=10, 0]	0.4 (0.2 to 0.6)	0 (0 to 0)		
Total Bilirubin, D37 [N=10, 0]	0.45 (0.3 to 0.6)	0 (0 to 0)		
Total Bilirubin, D60 [N=10, 0]	0.4 (0.3 to 0.6)	0 (0 to 0)		
Total Bilirubin, D180 [N=0, 10]	0 (0 to 0)	0.45 (0.4 to 0.6)		
Total Bilirubin, D181 [N=0, 9]	0 (0 to 0)	0.6 (0.4 to 0.7)		
Total Bilirubin, D182 [N=0, 9]	0 (0 to 0)	0.6 (0.5 to 0.7)		

Total Bilirubin, D187 [N=0, 9]	0 (0 to 0)	0.5 (0.5 to 0.7)		
Total Bilirubin, D210 [N=0, 10]	0 (0 to 0)	0.6 (0.5 to 0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Diastolic Blood Pressure - Step 2

End point title	Levels of Diastolic Blood Pressure - Step 2

End point description:

Diastolic pressure was part of the list of vital signs followed at specific protocol-defined timepoints during this study, measured in millimeter of mercury (mmHg).

End point type	Secondary

End point timeframe:

Pre-dose 1 at Day 0 (PRE), and at Day 30 at Hour 0 (D30H0); post-dose 2 at Day 30 at Hour 6 (D30H6), at Day 31, at Day 32, at Day 37, at Day 60 and at Day 180 at Hour 0; post-dose 3 at Day 181, at Day 182, at Day 187 and at Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: mmHg				
median (inter-quartile range (Q1-Q3))				
Diastolic, D0 [N=10, 11]	74 (69 to 75)	70 (67 to 72)		
Diastolic, D30 H0 [N=10, 0]	74.5 (73 to 78)	0 (0 to 0)		
Diastolic, D30 H6 [N=9, 0]	71 (69 to 75)	0 (0 to 0)		
Diastolic, D31 [N=10, 0]	71.5 (68 to 78)	0 (0 to 0)		
Diastolic, D32 [N=10, 0]	71.5 (66 to 82)	0 (0 to 0)		
Diastolic, D37 [N=10, 0]	70 (69 to 76)	0 (0 to 0)		
Diastolic, D60 [N=10, 0]	72 (68 to 77)	0 (0 to 0)		
Diastolic, D180 H0 [N=0, 10]	0 (0 to 0)	69 (63 to 71)		
Diastolic, D180 H6 [N=0, 10]	0 (0 to 0)	68.5 (65 to 71)		
Diastolic, D181 [N=0, 9]	0 (0 to 0)	72 (66 to 75)		
Diastolic, D182 [N=0, 9]	0 (0 to 0)	70 (69 to 72)		
Diastolic, D187 [N=0, 9]	0 (0 to 0)	72 (64 to 77)		
Diastolic, D210 [N=0, 10]	0 (0 to 0)	71.5 (65 to 74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Heart Rate - Step 2

End point title	Levels of Heart Rate - Step 2

End point description:

Heart rate was part of the list of vital signs followed at specific protocol-defined timepoints during this study. It was expressed in beats per minute.

End point type	Secondary

End point timeframe:

Pre-dose 1 at Day 0 (PRE), and at Day 30 at Hour 0 (D30H0); post-dose 2 at Day 30 at Hour 6 (D30H6), at Day 31, at Day 32, at Day 37, at Day 60 and at Day 180 at Hour 0; post-dose 3 at Day 181, at Day 182, at Day 187 and at Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: beats/minute				
median (inter-quartile range (Q1-Q3))				
Heart rate, PRE [N=10, 11]	72 (63 to 80)	70 (62 to 80)		
Heart rate, D30 H0 [N=10, 0]	70 (65 to 81)	0 (0 to 0)		
Heart rate, D30 H6 [N=9, 0]	68 (64 to 77)	0 (0 to 0)		
Heart rate, D31 [N=10, 0]	84 (70 to 90)	0 (0 to 0)		
Heart rate, D32 [N=10, 0]	73 (67 to 83)	0 (0 to 0)		
Heart rate, D37 [N=10, 0]	65 (56 to 73)	0 (0 to 0)		
Heart rate, D60 [N=10, 0]	65 (62 to 72)	0 (0 to 0)		
Heart rate, D180 H0 [N=0, 10]	0 (0 to 0)	71.5 (63 to 86)		
Heart rate, D180 H6 [N=0, 10]	0 (0 to 0)	70 (58 to 80)		
Heart rate, D181 [N=0, 9]	0 (0 to 0)	81 (73 to 91)		
Heart rate, D182 [N=0, 9]	0 (0 to 0)	72 (71 to 83)		
Heart rate, D187 [N=0, 9]	0 (0 to 0)	78 (67 to 84)		
Heart rate, D210 [N=0, 10]	0 (0 to 0)	76.5 (68 to 79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Respiratory Rate - Step 2

End point title	Levels of Respiratory Rate - Step 2

End point description:

Respiratory Rate was part of the list of vital signs followed at specific protocol-defined timepoints during this study. It was expressed as breaths per minute (breaths/min).

End point type	Secondary

End point timeframe:

Pre-dose 1 at Day 0 (PRE), and at Day 30 at Hour 0 (D30H0); post-dose 2 at Day 30 at Hour 6 (D30H6), at Day 31, at Day 32, at Day 37, at Day 60 and at Day 180 at Hour 0; post-dose 3 at Day 181, at Day 182, at Day 187 and at Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: breaths/min				
median (inter-quartile range (Q1-Q3))				
Respiratory rate, PRE [N=10, 11]	12 (12 to 14)	12 (12 to 14)		
Respiratory rate, D30 H0 [N=10, 0]	12.5 (11 to 13)	0 (0 to 0)		
Respiratory rate, D30 H6 [N=9, 0]	12 (12 to 14)	0 (0 to 0)		
Respiratory rate, D31 [N=10, 0]	13 (12 to 14)	0 (0 to 0)		
Respiratory rate, D32 [N=10, 0]	12 (12 to 13)	0 (0 to 0)		
Respiratory rate, D37 [N=10, 0]	13.5 (12 to 14)	0 (0 to 0)		
Respiratory rate, D60 [N=10, 0]	12 (12 to 13)	0 (0 to 0)		
Respiratory rate, D180 H0 [N=0, 10]	0 (0 to 0)	12.5 (12 to 15)		
Respiratory rate, D180 H6 [N=0, 10]	0 (0 to 0)	12.5 (12 to 14)		
Respiratory rate, D181 [N=0, 9]	0 (0 to 0)	12 (12 to 14)		
Respiratory rate, D182 [N=0, 9]	0 (0 to 0)	13 (12 to 14)		
Respiratory rate, D187 [N=0, 9]	0 (0 to 0)	13 (12 to 15)		
Respiratory rate, D210 [N=0, 10]	0 (0 to 0)	13.5 (12 to 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Levels of Systolic pressure - Step 2

End point title	Levels of Systolic pressure - Step 2

End point description:

Systolic pressure was part of the list of vital signs followed at specific protocol-defined timepoints during this study, measured in millimeter of mercury (mmHg).

End point type	Secondary

End point timeframe:

Pre-dose 1 at Day 0 (PRE), and at Day 30 at Hour 0 (D30H0); post-dose 2 at Day 30 at Hour 6 (D30H6), at Day 31, at Day 32, at Day 37, at Day 60 and at Day 180 at Hour 0; post-dose 3 at Day 181, at Day 182, at Day 187 and at Day 210

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: mmHg				
median (inter-quartile range (Q1-Q3))				
Systolic, PRE [N=10, 11]	114 (110 to 116)	112 (103 to 115)		
Systolic, D30 H0 [N=10, 0]	114 (109 to 118)	0 (0 to 0)		
Systolic, D30 H6 [N=9, 0]	116 (104 to 121)	0 (0 to 0)		
Systolic, D31 [N=10, 0]	112 (108 to 113)	0 (0 to 0)		

Systolic, D32 [N=10, 0]	111.5 (102 to 116)	0 (0 to 0)		
Systolic, D37 [N=10, 0]	108.5 (105 to 117)	0 (0 to 0)		
Systolic, D60 [N=10, 0]	113 (104 to 122)	0 (0 to 0)		
Systolic, D180 H0 [N=0, 10]	0 (0 to 0)	111.5 (105 to 119)		
Systolic, D180 H6 [N=0, 10]	0 (0 to 0)	111.5 (108 to 114)		
Systolic, D181 [N=0, 9]	0 (0 to 0)	115 (112 to 129)		
Systolic, D182 [N=0, 9]	0 (0 to 0)	117 (108 to 120)		
Systolic, D187 [N=0, 9]	0 (0 to 0)	112 (110 to 115)		
Systolic, D210 [N=0, 10]	0 (0 to 0)	112 (108 to 116)		

Statistical analyses

No statistical analyses for this end point

Secondary: -Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)4+ T-cells expressing at least 2 immune markers - Step 1

End point title	-Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)4+ T-cells expressing at least 2 immune markers - Step 1

End point description:

Markers expressed were Interleukin-2 (IL-2), Interferon gamma (IFN-γ), Tumor Necrosis Factor (TNF)-α and Cluster of differentiation 40-Ligand (CD40L), as measured by classical (qualified assay) Intracellular Cytokine Staining (ICS),using frozen Peripheral blood mononuclear cells (PBMCs).

End point type	Secondary

End point timeframe:

At Day 0 prior to vaccination (PRE) and Day 44 post-vaccination

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	25		
Units: T cells/million cells				
median (inter-quartile range (Q1-Q3))				
PRE [N=26, 25]	8 (1 to 52)	1 (1 to 18)		
Day 44 [N=26, 24]	4494 (2441 to 7494)	268 (76 to 509)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)4+ T-cells expressing at least 2 immune markers - Step 1

End point title	Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)4+ T-cells expressing at least 2 immune markers - Step 1

End point description:

Markers expressed were Interleukin-2 (IL-2), Interferon gamma (IFN-γ), Tumor Necrosis Factor (TNF)-α and Cluster of differentiation 40-Ligand (CD40L), as measured by classical (qualified assay) Intracellular Cytokine Staining (ICS),using frozen Peripheral blood mononuclear cells (PBMCs).

End point type	Secondary

End point timeframe:

At Day 0 prior to vaccination (PRE), Day 44 and Day 180 post-vaccination

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	24		
Units: T cells/ million cells				
median (inter-quartile range (Q1-Q3))				
PRE [N=26, 24]	8 (1 to 52)	1 (1 to 21)		
Day 44 [N=26, 23]	4494 (2441 to 7494)	260 (33 to 527)		
Day 180 [N=27, 22]	1119 (748 to 2181)	34 (1 to 155)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)8+ T-cells expressing at least 2 immune markers - Step 1

End point title	Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)8+ T-cells expressing at least 2 immune markers - Step 1

End point description:

Markers expressed were Interleukin-2 (IL-2), Interferon gamma (IFN-γ), Tumor Necrosis Factor (TNF)-α and Cluste of differentiation 40-Ligand (CD40L), as measured by classical (qualified assay) Intracellular Cytokine Staining (ICS),using frozen Peripheral blood mononuclear cells (PBMCs).

End point type	Secondary

End point timeframe:

At Day 0 prior to vaccination (PRE) and Day 44 post-vaccination

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	25		
Units: T cells/ million cells				
median (inter-quartile range (Q1-Q3))				
PRE [N=26, 25]	1 (1 to 24)	1 (1 to 1)		
Day 44 [N=26, 24]	38 (1 to 108)	1 (1 to 33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)8+ T-cells expressing at least 2 immune markers - Step 1

End point title	Frequency of Hepatitis B virus (HBs)-specific Cluster of Differentiation (CD)8+ T-cells expressing at least 2 immune markers - Step 1

End point description:

Markers expressed were Interleukin-2 (IL-2), Interferon gamma (IFN-γ), Tumor Necrosis Factor (TNF)-α and Cluster of differentiation 40-Ligand (CD40L), as measured by classical (qualified assay) Intracellular Cytokine Staining (ICS),using frozen Peripheral blood mononuclear cells (PBMCs).

End point type	Secondary

End point timeframe:

At Day 0 prior to vaccination (PRE), Day 44 and Day 180 post-vaccination

End point values	hbsag/as_1 group	engerix-b_1 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	24		
Units: T ceclls/ million cells				
median (inter-quartile range (Q1-Q3))				
PRE	1 (1 to 24)	1 (1 to 1)		
Day 44	38 (1 to 108)	1 (1 to 42)		
Day 180	1 (1 to 17)	1 (1 to 31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited symptoms, as assessed by the investigator/study nurse - Step 2

End point title	Number of subjects with solicited symptoms, as assessed by the investigator/study nurse - Step 2

End point description:

Assessed solicited symptoms were fever [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)], pain, redness [spreading beyond 20 millimeters (mm) of injection site],

induration [spreading beyond 20 millimeters (mm) of injection site], swelling [spreading beyond 20 millimeters (mm) of injection site] and muscle stiffness.

End point type	Secondary

End point timeframe:

Up to 3 days post-placebo/vaccine administration.

End point values	hbsag/as_2 group	engerix-b_2 group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Participants				
Pain, Dose 2 [N=10, 0]	8	0		
Pain, Dose 3 [N=0, 10]	0	1		
Redness, Dose 2 [N=10, 0]	5	0		
Redness, Dose 3 [N=0, 10]	0	0		
Swelling, Dose 2 [N=10, 0]	3	0		
Swelling, Dose 3 [N=0, 10]	0	0		
Induration, Dose 2 [N=7, 0]	1	0		
Induration, Dose 3 [N=1, 0]	0	0		
Fever, Dose 2 [N=10, 0]	0	0		
Fever, Dose 3 [N=0, 10]	0	0		
Muscle stiffness, Dose 2 [N=10, 0]	7	0		
Muscle stiffness, Dose 3 [N=0, 10]	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited symptoms, as assessed by the investigator/study nurse - Pooling Step

End point title	Number of subjects with solicited symptoms, as assessed by the investigator/study nurse - Pooling Step[41]

End point description:

Assessed solicited symptoms were fever [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)], pain, redness [spreading beyond 20 millimeters (mm) of injection site], induration [spreading beyond 20 millimeters (mm) of injection site], swelling [spreading beyond 20 millimeters (mm) of injection site] and muscle stiffness

End point type	Secondary

End point timeframe:

Up to 3 days post-placebo/vaccine administration.

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by vaccine groups in study steps. Hence for each related endpoint, they are presented for only the groups in the respective study step, while the results for multiple endpoints account for all vaccine groups in all study steps.

End point values	HBsAg/AS_1+2 Group			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Participants				
Pain [N=37]	26			
Redness [N=37]	12			
Swelling [N=37]	7			
Induration [N=25]	2			
Muscle stiffness [N=37]	22			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited symptoms during the 28 Day (Days 0-27) post vaccination; SAEs up to Day 180 for the HBsAg/AS_1+2 Group and up to Day 330 for the Engerix-B_1+2 Group

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	HBsAg/AS_1+2 Group

Reporting group description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30, followed by 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30; and during Step 2 of the study, 2 doses of HBsAg/AS vaccine, at Day 0 and Day 30. All vaccines were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Reporting group title	Engerix-B_1+2 Group

Reporting group description:

Subjects received, during Step 1 of the study, 1 dose of Placebo vaccine at Day -30 followed by 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180; and during Step 2 of the study, 3 doses of Engerix™-B vaccine at Day 0, Day 30 and Day 180. All vaccine were administered intramuscularly into the deltoid muscle of the non-dominant upper arm.

Serious adverse events	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	1 / 40 (2.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HBsAg/AS_1+2 Group	Engerix-B_1+2 Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 38 (42.11%)	13 / 40 (32.50%)	
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 38 (5.26%)	5 / 40 (12.50%)	
occurrences (all)	3	5	
Migraine			
subjects affected / exposed	0 / 38 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 38 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Influenza like illness			
subjects affected / exposed	2 / 38 (5.26%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 38 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 38 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	6 / 38 (15.79%)	1 / 40 (2.50%)	
occurrences (all)	7	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 38 (7.89%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Oral herpes			
subjects affected / exposed	2 / 38 (5.26%)	1 / 40 (2.50%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	5 / 38 (13.16%)	1 / 40 (2.50%)	
occurrences (all)	5	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2013	Amendment 1 was developed to: •update the method that will be used, as well as, the laboratory that will perform the testing for determination of anti-HBs IgG antibodies. •add a further contraindication to vaccination in case of any planned administration / administration of any medications/products and/or any medical condition that may interfere with the study endpoints of the innate/early immune response. •clarify the follow-up of subjects withdrawn from investigational vaccine after receiving only the placebo dose. •take the opportunity to clarify some other minor wordings.
10 December 2014	Amendment 2 was developed to: •define the exact timings of blood collection for Step 2 based on results of Step 1 analysis. •define informative readouts, blood volumes and additional endpoints for Step 2. •given the weak immunological response observed after the administration of two doses of the Alum-based formulation in Step 1, the immunological response induced by this formulation will be evaluated in Step 2 after the third vaccine dose administration at which time point the response is expected to be higher (versus after the second vaccine dose administration of the AS01B-based formulation). •modify the sequence of analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported