Clinical trial results:
A Double-blind Randomized Controlled Trial to Assess the Lot-to-lot Consistency of Sci-B-Vac™ in Adults (CONSTANT)

Summary

EudraCT number	2017-001820-22
Trial protocol	GB DE FI BE
Global end of trial date	01 October 2019

Results information

Result version number	v1 (current)
This version publication date	14 January 2023
First version publication date	14 January 2023

Trial information

Trial identification

Sponsor protocol code	Sci-B-Vac–002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03408730
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VBI Vaccines
Sponsor organisation address	310 Hunt Club East, Nepean, Canada, K1V 1C1
Public contact	Bebi Yassin-Rajkumar, VBI Vaccines Inc., +1 613749-4200 151, byassin-rajkumar@vbivaccines.com
Scientific contact	Dr Francisco Diaz-Mitoma, VBI Vaccines Inc., +1 613749-4200 151, fdiazmitoma@vbivaccines.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	14 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2019
Global end of trial reached?	Yes
Global end of trial date	01 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the manufacturing equivalence, in terms of immunogenicity, of three independent consecutive lots of the Sci-B-Vac™ 4 weeks after the third vaccination on Study Day 196.

This objective will be met if the following condition is satisfied if the upper and lower bound of the two sided 95% confidence interval (CI) of the geometric mean concentration (GMC) of anti-HBs ratios 4 weeks after the third injection, for all three pairwise comparisons (GMC of anti-HBs in group A/GMC of anti-HBs in group B, GMC of anti-HBs in group A/ GMC of anti-HBs in group C, GMC of anti-HBs in group B/ GMC of anti-HBs in group C), are within [0.67, 1.5]

Protection of trial subjects:

An independent Data Monitoring Committee (DMC) was established to monitor subject safety. Subjects were provided with a 28-day diary card to record vaccine reactions. Subjects recorded solicited local and systemic AEs on the day of vaccination and for the next 6 days. A safety follow-up telephone call was made 7 days after each vaccination to inquire about local and systemic reactions. Subjects were followed a minimum of 48 weeks after receiving the first vaccination at Study Day 0, with at least a 24-week follow-up safety assessments after receiving the third vaccination.

Background therapy: -

Evidence for comparator:

Engerix-B is approved for active immunization against hepatitis B virus infection (HBV) caused by all known subtypes in non immune subjects.

Actual start date of recruitment	23 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 750
Country: Number of subjects enrolled	Canada: 121
Country: Number of subjects enrolled	European Union: 1965
Worldwide total number of subjects	2836
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2836
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited through radio and newspaper advertisements.

Pre-assignment

Screening details:

Screening was conducted within 28 days (4 weeks) prior to the first vaccination.

Period 1

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

Blinding implementation details:

This was a double-blind study. Both subjects and the study center staff performing outcome measurement were blinded. Randomization and administration of study vaccine was by unblinded qualified health personnel not involved in assessment of outcome measures, whose sole role was to prepare and administer the allocated study vaccine and to perform activities requiring vial handling.

Arms

Are arms mutually exclusive?	No
Arm title	Engerix-B®

Arm description:

Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168.
Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Arm type	Active comparator
Investigational medicinal product name	Engerix-B®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Engerix-B® Hepatitis B Vaccination, 20ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm title	Sci-B-Vac® Lot A

Arm description:

Sci-B-Vac Lot A Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm type	Experimental
Investigational medicinal product name	Sci-B-Vac® Lot A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm title	Sci-B-Vac® Lot B

Arm description:

Sci-B-Vac Lot B Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm type	Experimental
Investigational medicinal product name	Sci-B-Vac® Lot B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm title	Sci-B-Vac® Lot C

Arm description:

Sci-B-Vac Lot C Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm type	Experimental
Investigational medicinal product name	Sci-B-Vac® Lot C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Arm title	Pooled Sci-B-Vac

Arm description:

Pooled Sci-B-Vac® includes the Sci-B-Vac® Lot A, Sci-B-Vac® Lot B and Sci-B-Vac® Lot C

Arm type	Experimental
Investigational medicinal product name	Sci-B-Vac® Lot A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Investigational medicinal product name	Sci-B-Vac® Lot B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Investigational medicinal product name	Sci-B-Vac® Lot C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Number of subjects in period 1	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B
Started	712	711	708
Completed	643	636	637
Not completed	69	75	71
Moved from study area	5	3	1
Consent withdrawn by subject	12	15	13
Physician decision	-	-	1
Request of regulatory agency, sponsor or investiga	1	-	-
Other	1	-	-
Pregnancy	1	3	2
Non-serious adverse event	1	2	3
Serious adverse event	-	2	-
Lost to follow-up	48	49	51
Change in subject's medical condition	-	1	-
Protocol deviation	-	-	-

Number of subjects in period 1	Sci-B-Vac® Lot C	Pooled Sci-B-Vac
Started	705	2124
Completed	625	1898
Not completed	80	226
Moved from study area	3	7
Consent withdrawn by subject	17	45
Physician decision	-	1
Request of regulatory agency, sponsor or investiga	-	-
Other	-	-
Pregnancy	6	11
Non-serious adverse event	1	6
Serious adverse event	-	2
Lost to follow-up	51	151
Change in subject's medical condition	-	1
Protocol deviation	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Engerix-B®
Reporting group description:	
Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168. Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination	
Reporting group title	Sci-B-Vac® Lot A
Reporting group description:	
Sci-B-Vac Lot A Hepatitis B Vaccination Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.	

Reporting group title	Sci-B-Vac® Lot B
Reporting group description:	
Sci-B-Vac Lot B Hepatitis B Vaccination Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.	

Reporting group title	Sci-B-Vac® Lot C
Reporting group description:	
Sci-B-Vac Lot C Hepatitis B Vaccination Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.	
Reporting group title	Pooled Sci-B-Vac
Reporting group description:	
Pooled Sci-B-Vac® includes the Sci-B-Vac® Lot A, Sci-B-Vac® Lot B and Sci-B-Vac® Lot C	

Reporting group values	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B
Number of subjects	712	711	708
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	33.4	33.8	32.9
standard deviation	± 8.1	± 7.96	± 8
Gender categorical Units: Subjects			
Female	421	408	395
Male	291	303	313

Reporting group values	Sci-B-Vac® Lot C	Pooled Sci-B-Vac	Total

Number of subjects	705	2124	2836
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	33.9	33.5	
standard deviation	± 7.91	± 7.97	-
Gender categorical Units: Subjects			
Female	414	1217	1638
Male	291	907	1198

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the All Enrolled Set who received at least 1 vaccination. Subjects were analyzed as vaccinated, ie, a subject was assigned according to the vaccine received. In case of vaccination error, subjects were analyzed as treated.

Subject analysis set title	Per Protocol Set (PPS) 1
Subject analysis set type	Per protocol

Subject analysis set description:

Per-Protocol Set 1 (PPS1): All subjects in the Full Analysis Set who received all 3 vaccinations, had evaluable serum immunogenicity samples at baseline and at the timepoint of interest, were seronegative at baseline, and had no major protocol deviations leading to exclusion as identified prior to unblinding.

Subject analysis set title	Per Protocol Set (PPS) 2
Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol Set 2 included all subjects in Per Protocol Set 1 excluding subjects who attended visits outside of windows including Visit 3/Day 168 (±28 days) and Visit 44/Day 196 (-7/+14 days)

Reporting group values	Safety Set	Per Protocol Set (PPS) 1	Per Protocol Set (PPS) 2
Number of subjects	2836	2511	2381
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	33.5	33.5	33.6
standard deviation	± 8	± 7.95	± 7.93
Gender categorical Units: Subjects			
Female	1638	1458	1385
Male	1198	1053	996

End points

End points reporting groups

Reporting group title	Engerix-B®

Reporting group description:

Engerix-B® (hepatitis B vaccine) Hepatitis B Vaccination, Solution, 20ug, IM injection at Days 0, 28, and 168.
Hepatitis B Vaccination: Prophylactic Hepatitis B Vaccination

Reporting group title	Sci-B-Vac® Lot A

Reporting group description:

Sci-B-Vac Lot A Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Reporting group title	Sci-B-Vac® Lot B

Reporting group description:

Sci-B-Vac Lot B Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Reporting group title	Sci-B-Vac® Lot C

Reporting group description:

Sci-B-Vac Lot C Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B Vaccination, 10ug, intramuscular (IM) injection at Days 0, 28, and 168.

Reporting group title	Pooled Sci-B-Vac

Reporting group description:

Pooled Sci-B-Vac® includes the Sci-B-Vac® Lot A, Sci-B-Vac® Lot B and Sci-B-Vac® Lot C

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the All Enrolled Set who received at least 1 vaccination. Subjects were analyzed as vaccinated, ie, a subject was assigned according to the vaccine received. In case of vaccination error, subjects were analyzed as treated.

Subject analysis set title	Per Protocol Set (PPS) 1
Subject analysis set type	Per protocol

Subject analysis set description:

Per-Protocol Set 1 (PPS1): All subjects in the Full Analysis Set who received all 3 vaccinations, had evaluable serum immunogenicity samples at baseline and at the timepoint of interest, were seronegative at baseline, and had no major protocol deviations leading to exclusion as identified prior to unblinding.

Subject analysis set title	Per Protocol Set (PPS) 2
Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol Set 2 included all subjects in Per Protocol Set 1 excluding subjects who attended visits outside of windows including Visit 3/Day 168 (±28 days) and Visit 44/Day 196 (-7/+14 days)

Primary: Geometric mean concentration (GMC) of anti-HBs at day 196 for lot-to-lot consistency (Per Protocol Set 1)

End point title	Geometric mean concentration (GMC) of anti-HBs at day 196 for lot-to-lot consistency (Per Protocol Set 1)[1]

End point description:

To demonstrate the manufacturing equivalence, in terms of immunogenicity, as measured by GMC of antibodies, of 3 independent consecutive lots of the Sci-B-Vac® 4 weeks after the third vaccination. Lot-to-lot manufacturing consistency of Sci-B-Vac® is demonstrated if the 95% CIs of the adjusted anti-HBs GMC ratios between lots are within the pre-specified range of [0.67, 1.5].

End point type	Primary

End point timeframe:

4 weeks after third vaccination (Study Day 196)

Notes:

[1] - 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 Engerix-B® arm and the Pooled Sci-B-Vac arm, which is a pool of data from the three Sci-B-Vac arms, are not included in this analysis as the intent is to demonstrate consistency among the three lots of Sci-B-Vac.

End point values	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	611	610	619	
Units: mIU/mL				
geometric mean (standard deviation)	5883.93 (± 5.423)	4824.06 (± 6.293)	5505.98 (± 5.975)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Lot A to Lot B Consistency of Sci-B-Vac

Comparison groups	Sci-B-Vac® Lot A v Sci-B-Vac® Lot B
Number of subjects included in analysis	1221
Analysis specification	Pre-specified
Analysis type	other[2]
Method	ANCOVA
Parameter estimate	Adjusted GMC Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1

Notes:

[2] - Superiority Criterion: The two-sided 95 % CI of the GMC ratio between all pairs of lots are within [0.67, 1.5]

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Lot A to Lot C Consistency of Sci-B-Vac

Comparison groups	Sci-B-Vac® Lot A v Sci-B-Vac® Lot C
Number of subjects included in analysis	1230
Analysis specification	Pre-specified
Analysis type	other[3]
Method	ANCOVA
Parameter estimate	Adjusted GMC Ratio
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.15

Notes:

[3] - Superiority Criterion: The two-sided 95 % CI of the GMC ratio between all pairs of lots are within [0.67, 1.5]

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Lot B to Lot C Consistency of Sci-B-Vac

Comparison groups	Sci-B-Vac® Lot C v Sci-B-Vac® Lot B
Number of subjects included in analysis	1229
Analysis specification	Pre-specified
Analysis type	other[4]
Method	ANCOVA
Parameter estimate	Adjusted GMC Ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.41

Notes:

[4] - Superiority Criterion: The two-sided 95 % CI of the GMC ratio between all pairs of lots are within [0.67, 1.5]

Secondary: Seroprotection rate (SPR) of anti-HBs at day 196 for Sci-B-Vac® compared to day 196 for Engerix-B® (Per Protocol Set 2)

End point title	Seroprotection rate (SPR) of anti-HBs at day 196 for Sci-B-Vac® compared to day 196 for Engerix-B® (Per Protocol Set 2)[5]

End point description:

The difference in proportions [SPR(Sci-B-Vac®)–SPR(Engerix-B®)] and two-sided 95% CIs were summarized. If the lower bound of the 95% CI was > 5%, Sci-B-Vac® was to be declared non-inferior to Engerix-B®

End point type	Secondary

End point timeframe:

4 weeks after third vaccination (Study Day 196)

Notes:

[5] - 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 arms for individual Sci-B-Vac lots are not included in this analysis as the intent is to compare results for the Engerix-B® arm with those of the Pooled Sci-B-Vac arm.

End point values	Engerix-B®	Pooled Sci-B-Vac		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	592	1753		
Units: Number of Subjects				
number (not applicable)	561	1753		

Statistical analyses

Statistical analysis title	Secondary1
Statistical analysis description:	
Seroprotection rate (SPR) at Study Day 196 in PPS2	
Comparison groups	Engerix-B® v Pooled Sci-B-Vac
Number of subjects included in analysis	2345
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen
Parameter estimate	Difference in proportions
Point estimate	4.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	6.63

Secondary: Number of subjects reporting solicited local adverse events day 1 through day 7 after any vaccination

End point title	Number of subjects reporting solicited local adverse events day 1 through day 7 after any vaccination[6]
End point description:	
Analysis of local solicited adverse events with an interval of onset of Day 1 to Day 7 after any vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥18 years old.	
End point type	Secondary
End point timeframe:	
Day of vaccine administration and six subsequent days	

Notes:

[6] - 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 Pooled Sci-B-Vac arm, which is a pool of data from the three Sci-B-Vac arms, is not included in this analysis as the intent is to demonstrate consistency among the three lots of Sci-B-Vac and Engerix-B®.

End point values	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	712	711	708	705
Units: Number of events	469	589	602	614

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited systemic adverse events day 1 through day 7 after any vaccination

End point title	Number of subjects reporting solicited systemic adverse events day 1 through day 7 after any vaccination[7]

End point description:

Analysis of systemic solicited adverse events with an interval of onset of Day 1 to Day 7 after any vaccination with either Sci-B-Vac® or Engerix-B®, in adults ≥18 years old

End point type	Secondary

End point timeframe:

Day of vaccine administration and six subsequent days

Notes:

[7] - 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 Pooled Sci-B-Vac arm, which is a pool of data from the three Sci-B-Vac arms, is not included in this analysis as the intent is to demonstrate safety among the three lots of Sci-B-Vac and Engerix-B®.

End point values	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	712	711	708	705
Units: Number of events	428	451	498	496

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events through end of study

End point title	Number of subjects reporting unsolicited adverse events through end of study[8]

End point description:

Summary of unsolicited treatment-emergent adverse events reported in ≥1% of subjects after vaccination with either Sci-B-Vac® Lots A, B or C or with Engerix-B®, in adults ≥18 years old.

End point type	Secondary

End point timeframe:

Through end of study (day 336)

Notes:

[8] - 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 Pooled Sci-B-Vac arm, which is a pool of data from the three Sci-B-Vac arms, is not included in this analysis as the intent is to demonstrate consistency among the three lots of Sci-B-Vac and Engerix-B®.

End point values	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	712	711	708	705
Units: Number of events	371	362	380	386

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events through end of study

End point title	Number of subjects reporting serious adverse events through end of study[9]

End point description:

Summary of unsolicited serious adverse events reported after vaccination with either Sci-B-Vac® Lots A, B and C or with Engerix-B®, in adults ≥18 years old.

End point type	Secondary

End point timeframe:

Through end of study (day 336)

Notes:

[9] - 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 Pooled Sci-B-Vac arm, which is a pool of data from the three Sci-B-Vac arms, is not included in this analysis as the intent is to demonstrate consistency among the three lots of Sci-B-Vac and Engerix-B®.

End point values	Engerix-B®	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	712	711	708	705
Units: Number of events	4	15	20	12

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Includes serious adverse events collected throughout the trial and non adverse events starting from Day 1 to Day 28 post any vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Sci-B-Vac® Lot A

Reporting group description:

Sci-B-Vac® Lot A Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B vaccination, 10 ug, intramuscular (IM) injection at Days 1, 28, and 168

Reporting group title	Sci-B-Vac® Lot B

Reporting group description:

Sci-B-Vac® Lot B Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B vaccination, 10 ug, intramuscular (IM) injection at Days 1, 28, and 168

Reporting group title	Sci-B-Vac® Lot C

Reporting group description:

Sci-B-Vac® Lot C Hepatitis B Vaccination
Sci-B-Vac® Hepatitis B vaccination, 10 ug, intramuscular (IM) injection at Days 1, 28, and 168

Reporting group title	Engerix-B®

Reporting group description:

Engerix-B® (hepatitis B vaccine) Hepatitis B vaccination, Solution, 20 ug, IM injection at Days 0, 28, and 168

Serious adverse events	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 711 (1.69%)	18 / 708 (2.54%)	12 / 705 (1.70%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			

subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Gastrointestinal arteriovenous malformation			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Stress cardiomyopathy			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo positional			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Alcoholic liver disease			

subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 711 (0.14%)	2 / 708 (0.28%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal osteoarthritis			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 711 (0.14%)	1 / 708 (0.14%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chlamydial infection			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
subjects affected / exposed	0 / 711 (0.00%)	0 / 708 (0.00%)	1 / 705 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 711 (0.00%)	1 / 708 (0.14%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	1 / 711 (0.14%)	0 / 708 (0.00%)	0 / 705 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Engerix-B®		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 712 (0.42%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 712 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			

subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Post procedural haemorrhage				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	1 / 712 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Gastrointestinal arteriovenous malformation				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Stress cardiomyopathy				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Migraine				

subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo positional			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 712 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 712 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chlamydial infection				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 712 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				

subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vestibular neuronitis			
subjects affected / exposed	0 / 712 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sci-B-Vac® Lot A	Sci-B-Vac® Lot B	Sci-B-Vac® Lot C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	618 / 711 (86.92%)	640 / 708 (90.40%)	636 / 705 (90.21%)
Nervous system disorders			
Headache	Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	273 / 711 (38.40%)	307 / 708 (43.36%)	303 / 705 (42.98%)
occurrences (all)	460	489	486
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	266 / 711 (37.41%)	296 / 708 (41.81%)	292 / 705 (41.42%)
occurrences (all)	449	481	485
Injection site pain	Additional description: Injection site pain events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	590 / 711 (82.98%)	598 / 708 (84.46%)	608 / 705 (86.24%)
occurrences (all)	1381	1400	1445
Injection site pruritus	Additional description: Injection site pruritus events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	84 / 711 (11.81%)	105 / 708 (14.83%)	92 / 705 (13.05%)
occurrences (all)	102	143	126
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	97 / 711 (13.64%)	90 / 708 (12.71%)	100 / 705 (14.18%)
occurrences (all)	118	114	129
Nausea	Additional description: Nausea events that occurred after 7 days post-vaccination were considered as unsolicited AE		

subjects affected / exposed	87 / 711 (12.24%)	88 / 708 (12.43%)	80 / 705 (11.35%)
occurrences (all)	103	114	101
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	28 / 711 (3.94%)	23 / 708 (3.25%)	40 / 705 (5.67%)
occurrences (all)	50	31	60
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	289 / 711 (40.65%)	317 / 708 (44.77%)	338 / 705 (47.94%)
occurrences (all)	474	524	575
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	61 / 711 (8.58%)	69 / 708 (9.75%)	66 / 705 (9.36%)
occurrences (all)	73	79	71
Nasopharyngitis			
subjects affected / exposed	30 / 711 (4.22%)	36 / 708 (5.08%)	38 / 705 (5.39%)
occurrences (all)	32	38	42

Non-serious adverse events	Engerix-B®		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	559 / 712 (78.51%)		
Nervous system disorders			
Headache	Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	289 / 712 (40.59%)		
occurrences (all)	485		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	284 / 712 (39.89%)		
occurrences (all)	466		
Injection site pain	Additional description: Injection site pain events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	461 / 712 (64.75%)		
occurrences (all)	897		
Injection site pruritus	Additional description: Injection site pruritus events that occurred after 7 days post-vaccination were considered as unsolicited AE		

subjects affected / exposed	88 / 712 (12.36%)		
occurrences (all)	120		
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	106 / 712 (14.89%)		
occurrences (all)	141		
Nausea	Additional description: Nausea events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	86 / 712 (12.08%)		
occurrences (all)	101		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	31 / 712 (4.35%)		
occurrences (all)	46		
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE		
subjects affected / exposed	235 / 712 (33.01%)		
occurrences (all)	348		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	63 / 712 (8.85%)		
occurrences (all)	78		
Nasopharyngitis			
subjects affected / exposed	45 / 712 (6.32%)		
occurrences (all)	50		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported