Clinical trial results:
An open, single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-028 (208127/021) in which healthy adults were vaccinated with Twinrix Adult following a three-dose schedule.

Summary

EudraCT number	2009-014275-53
Trial protocol	BE
Global end of trial date	25 July 2014

Results information

Result version number	v3 (current)
This version publication date	15 September 2018
First version publication date	07 August 2015
Version creation reason	• Correction of full data set Results update after CTRS vs CSR QC.

Trial information

Trial identification

Sponsor protocol code	112267

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01000324
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	18 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 July 2014
Global end of trial reached?	Yes
Global end of trial date	25 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate anti-HAV and anti-HBs antibody persistence at Years 16, 17, 18, 19 and 20 after a three-dose primary vaccination course with Twinrix Adult.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis following the administration of the vaccine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 November 2009
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who entered the study at Year 16, Year 17, 18 and Year 19 time points were subjects who completed the primary study and who returned for blood sampling at the considered time point.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Twinrix Group

Arm description:

Pooled group of subjects from groups who were vaccinated with either Lot 1, Lot 2 or Lot 3 of Twinrix in the primary study according to a 0, 1, 6-Month schedule

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

Dosage and administration details:

Engerix-B was administered to subjects who are not seroprotected against hepatitis B.

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	HAV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Havrix was administered to subjects who are seronegative for anti-HAV antibodies.

Number of subjects in period 1	Twinrix Group
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	Twinrix Group
Reporting group description:	
Pooled group of subjects from groups who were vaccinated with either Lot 1, Lot 2 or Lot 3 of Twinrix in the primary study according to a 0, 1, 6-Month schedule	

Reporting group values	Twinrix Group	Total	
Number of subjects	40	40	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	35.5		
standard deviation	± 2.87	-	
Gender categorical			
Units: Subjects			
Female	29	29	
Male	11	11	

End points

End points reporting groups

Reporting group title	Twinrix Group

Reporting group description:

Pooled group of subjects from groups who were vaccinated with either Lot 1, Lot 2 or Lot 3 of Twinrix in the primary study according to a 0, 1, 6-Month schedule

Primary: Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)

End point title	Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)[1]

End point description:

The analysis was performed on LT Total cohort that included all subjects who returned at each annual time point and who belonged to the Total Vaccinated cohort in the primary study

End point type	Primary

End point timeframe:

At Year 16

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Subjects				
Anti-HAV >=15 mIU/mL [at Year 16]	23			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)

End point title	Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)[2]

End point description:

The analysis was performed on LT Total cohort that included all subjects who returned at each annual time point and who belonged to the Total Vaccinated cohort in the primary study

End point type	Primary

End point timeframe:

At Year 17

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subjects				
Anti-HAV >=15 mIU/mL [at Year 17]	19			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)

End point title	Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)[3]

End point description:

The analysis was performed on LT Total cohort that included all subjects who returned at each annual time point and who belonged to the Total Vaccinated cohort in the primary study

End point type	Primary

End point timeframe:

At Year 18

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Subjects				
Anti-HAV >=15 mIU/mL [at Year 18]	10			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)

End point title	Number of subjects with anti-hepatitis A (anti-HAV) antibody concentration equal to or above 15 milli-international units per milliliter (mIU/mL)[4]

End point description:

The analysis was performed on LT Total cohort that included all subjects who returned at each annual time point and who belonged to the Total Vaccinated cohort in the primary study

End point type	Primary

End point timeframe:

At Year 19

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Subjects				
Anti-HAV >=15 mIU/mL [at Year 19]	17			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis A (anti-HAV) antibodies

End point title	Concentration of anti-hepatitis A (anti-HAV) antibodies[5]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 17

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: mIU/mL				
geometric mean (confidence interval 95%)	479.2 (298.2 to 769.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis A (anti-HAV) antibodies

End point title	Concentration of anti-hepatitis A (anti-HAV) antibodies[6]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 18

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: mIU/mL				
geometric mean (confidence interval 95%)	653.2 (333.2 to 1280.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis A (anti-HAV) antibodies

End point title	Concentration of anti-hepatitis A (anti-HAV) antibodies[7]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 19

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: mIU/mL				
geometric mean (confidence interval 95%)	728.7 (469.6 to 1130.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values[8]

End point description:

Anti-HBs antibody cut-off values assessed include 6.2 and 10 milli-international units per milliliter

(mIU/mL).

End point type	Primary

End point timeframe:

At Year 16

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Subjects				
≥ 6.2 mIU/mL	20			
≥ 10 mIU/mL	20			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values[9]

End point description:

Anti-HBs antibody cut-off values assessed include 6.2 and 10 milli-international units per milliliter (mIU/mL).

End point type	Primary

End point timeframe:

At Year 17

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subjects				
≥ 6.2 mIU/mL	17			
>=10 mIU/mL	17			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs)

antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values[10]

End point description:

Anti-HBs antibody cut-off values assessed include 6.2 and 10 milli-international units per milliliter (mIU/mL).

End point type	Primary

End point timeframe:

At Year 18

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Subjects				
≥ 6.2 mIU/mL	9			
>=10 mIU/mL	9			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations equal to or above the cut-off values[11]

End point description:

Anti-HBs antibody cut-off values assessed include 6.2 and 10 milli-international units per milliliter (mIU/mL).

End point type	Primary

End point timeframe:

At Year 19

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Subjects				
≥ 6.2 mIU/mL	17			
≥ 10 mIU/mL	17			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies

End point title	Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies[12]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 16

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: mIU/mL				
geometric mean (confidence interval 95%)	138.7 (61.3 to 313.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies

End point title	Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies[13]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 17

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: mIU/mL				
geometric mean (confidence interval 95%)	165.1 (64.8 to 420.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies

End point title	Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies[14]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 18

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: mIU/mL				
geometric mean (confidence interval 95%)	278.3 (70.3 to 1101.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies

End point title	Concentration of anti-hepatitis B surface antigen (anti-HBs) antibodies[15]

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Primary

End point timeframe:

At Year 19

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: mIU/mL				
geometric mean (confidence interval 95%)	198.4 (80.1 to 491.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects seropositive for anti-hepatitis A virus antibodies (anti-HAV) and anti-hepatitis B surface antigen (anti-HBs) antibodies and with anti-HBs antibody concentrations >= 10 milli-international units per milliliter (mIU/mL).

End point title	Number of subjects seropositive for anti-hepatitis A virus antibodies (anti-HAV) and anti-hepatitis B surface antigen (anti-HBs) antibodies and with anti-HBs antibody concentrations >= 10 milli-international units per milliliter (mIU/mL).[16]

End point description:

Seropositivity for anti-HAV antibodies is defined as antibody concentrations >= 15 milliinternational units per milliliter (mIU/mL). Seropositivity for anti-HBs antibodies is defined as antibody concentrations >= 6.2 mIU/mL..

End point type	Primary

End point timeframe:

At Year 20

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Subjects				
anti-HAV >= 15 mIU/mL [at Year 20] (N=18)	18			
anti-HBs >= 6.2 mIU/mL [at Year 20] (N=18)	17			
anti-HBs >= 10 mIU/mL [at Year 20] (N=18)	17			

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HAV and anti-HBs Geometric Mean Concentrations (GMCs)

End point title	Anti-HAV and anti-HBs Geometric Mean Concentrations

End point description:

Concentrations were expressed as GMCs in mIU/mL.

End point type	Primary

End point timeframe:

At Year 20

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 endpoint was descriptive, no statistical analyses were conducted.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
anti-HAV [at Year 20] (N=18)	511.9 (343.8 to 762)			
anti-HBs [at Year 20] (N=18)	195.8 (79.9 to 480.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of anti-hepatitis A (anti-HAV) antibodies

End point title	Concentration of anti-hepatitis A (anti-HAV) antibodies

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs).

End point type	Secondary

End point timeframe:

At Year 16

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: mIU/mL				
geometric mean (confidence interval 95%)	614.2 (404.1 to 933.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with immune response to the challenge vaccine

antigen	
End point title	Number of subjects with immune response to the challenge vaccine antigen

End point description:

None of the subjects received a challenge dose at Years 16, 17 and 18 while, one subject received the challenge dose at Year 19.

End point type	Secondary

End point timeframe:

Before, 14 days and one month after the challenge dose at Year 19.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Subjects with immune reponse to challenge dose	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B Virus (Anti-HBs) Antibody Concentration

End point title	Anti-hepatitis B Virus (Anti-HBs) Antibody Concentration

End point description:

Concentrations are given as Geometric Mean Concentrations (GMCs) expressed as mIU/mL.

End point type	Secondary

End point timeframe:

At Year 18, 14 days and 30 days post challenge dose (Year 19)

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	1[18]			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
[Subject 1; at year 18]	13.26 (13.26 to 13.26)			
[Subject 1; 14 days post challenge dose]	21926 (21926 to 21926)			
[Subject 1; 30 days post challenge dose]	12736 (12736 to 12736)			

Notes:

[18] - One subject received the challenge dose at Year 19.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)

End point description:

A SAE is any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

Up to Year 20.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Subjects				
Any SAE(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)

End point description:

A serious adverse event was any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 31-day (Day 0 to 30) period after administration of the challenge dose at Year 19.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Any SAE(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AE).

End point title	Number of subjects reporting unsolicited adverse events (AE).

End point description:

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

End point type	Secondary

End point timeframe:

During the 31-day (Day 0 to 30) period after administration of the challenge dose at Year 19.

End point values	Twinrix Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Any AE(s)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: During the 31-day (Days 0 to 30) follow-up period after the challenge dose and from the beginning of the long term follow-up to Year 20; Unsolicited symptoms: During the 31-day (Days 0 to 30) follow-up period after the challenge dose.

Adverse event reporting additional description:

As no challenge dose was administered during Years 16, 17, 18 and 20 time points, SAEs and other adverse events were not assessed. 1 subject received the challenge dose at Year 19 for whom the SAEs and other adverse events were assessed during the 31 day period post challenge dose. SAEs were also collected for the entire safety follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Twinrix Group

Reporting group description:

Pooled group of subjects from groups who were vaccinated with either Lot 1, Lot 2 or Lot 3 of Twinrix in the primary study according to a 0, 1, 6-Month schedule

Serious adverse events	Twinrix Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Twinrix Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)		
General disorders and administration site conditions			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed[1]	1 / 1 (100.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Musculoskeletal stiffness subjects affected / exposed[2] occurrences (all)	1 / 1 (100.00%) 1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only 1 subject received the challenge dose at Year 19 for whom the other adverse events were assessed during the 31 day period post challenge dose.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only 1 subject received the challenge dose at Year 19 for whom the other adverse events were assessed during the 31 day period post challenge dose.

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