



Clinical trial results:

An open multicentre, multicountry study to evaluate long-term antibody persistence and immune memory between Years 11 and 15 after the primary study HAB-084 in which healthy adolescents were vaccinated with Twinrix Adult following a two-dose schedule or Twinrix Junior following a three-dose schedule

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2008-006083-11 |
| Trial protocol | BE CZ |
| Global end of trial date | 18 July 2014 |

Results information

| | |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number | v3 (current) |
| This version publication date | 06 April 2023 |
| First version publication date | 06 June 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Correction of full data set and alignment between registries. |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | 110699 to 110704 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00875485 |
| 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 July 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 July 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 July 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

For the long-term follow-up phase:

To evaluate anti-HAV and anti-HBs antibody persistence at Years 11, 12, 13, 14 and 15 after the first vaccine dose of a two-dose Twinrix Adult or a three-dose Twinrix Junior primary vaccination course.

For the Challenge dose phase:

To evaluate the immune memory 15 years after primary vaccination with a two-dose Twinrix Adult versus a three-dose Twinrix Junior vaccination course in subjects who became seronegative for anti-HAV antibodies (less than 15 mIU/ml) or whose anti-HBs antibody concentrations decreased below 10 mIU/ml during the long-term follow-up period.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment | 01 May 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: 72 |
| Country: Number of subjects enrolled | Czech Republic: 138 |
| Worldwide total number of subjects | 210 |
| EEA total number of subjects | 210 |

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) | 210 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In this study, a total of 210 subjects were enrolled who participated at Year 11 (Y11) and Y12. There were a total of 8 additional subjects at Y13 and Y14 who came back from the primary study but did not participate in Y11 and Y12 as allowed by the protocol. One subject from the 210 subjects who participated in Y11 and Y12 did not return at Y15.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Year 11 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Twinrix Adult Group |

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|------------------|----------------------|
| Arm title | Twinrix Junior Group |
|------------------|----------------------|

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

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

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| Number of subjects in period 1 | Twinrix Adult Group | Twinrix Junior Group |
|--------------------------------|---------------------|----------------------|
| Started | 99 | 111 |
| Completed | 99 | 111 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Year 12 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Twinrix Adult Group |

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|------------------|----------------------|
| Arm title | Twinrix Junior Group |
|------------------|----------------------|

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0,

1, 6 month schedule in the primary study.

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

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| Number of subjects in period 2 | Twinrix Adult Group | Twinrix Junior Group |
|--------------------------------|---------------------|----------------------|
| Started | 101 | 109 |
| Completed | 101 | 109 |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Year 13 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Twinrix Adult Group |

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------------------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 2 doses administered intramuscularly into the upper arm (deltoid muscle) region. | |
| Arm title | Twinrix Junior Group |

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

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

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| Number of subjects in period 3 | Twinrix Adult Group | Twinrix Junior Group |
|---------------------------------------|---------------------|----------------------|
| Started | 101 | 109 |
| Year 13, Started | 102 | 113 |
| Completed | 102 | 113 |

| | | |
|-------------------------------------------|---|---|
| Joined | 1 | 4 |
| Additional subjects who joined at Year 13 | 1 | 4 |

Period 4

| | |
|------------------------------|-------------------------|
| Period 4 title | Year 14 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------------------|
| Arm title | Twinrix Adult Group |
|------------------|---------------------|

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|------------------|----------------------|
| Arm title | Twinrix Junior Group |
|------------------|----------------------|

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

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

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| Number of subjects in period 4^[1] | Twinrix Adult Group | Twinrix Junior Group |
|-----------------------------------------------------|---------------------|----------------------|
| Started | 100 | 113 |
| Completed | 100 | 113 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: In this study, a total of 210 subjects were enrolled who participated at Year 11 (Y11) and Y12. There were a total of 8 additional subjects at Y13 and Y14 who came back from the primary study but did not participate in Y11 and Y12 as allowed by the protocol. One subject from the 210 subjects who participated in Y11 and Y12 did not return at Y15

Period 5

| | |
|------------------------------|-------------------------|
| Period 5 title | Year 15 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Twinrix Adult Group |

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|------------------|----------------------|
| Arm title | Twinrix Junior Group |
|------------------|----------------------|

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

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

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| Number of subjects in period 5^[2] | Twinrix Adult Group | Twinrix Junior Group |
|-----------------------------------------------------|---------------------|----------------------|
| Started | 98 | 111 |
| Completed | 98 | 111 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: In this study, a total of 210 subjects were enrolled who participated at Year 11 (Y11) and Y12. There were a total of 8 additional subjects at Y13 and Y14 who came back from the primary study but did not participate in Y11 and Y12 as allowed by the protocol. One subject from the 210 subjects who participated in Y11 and Y12 did not return at Y15.

Period 6

| | |
|------------------------------|-------------------------|
| Period 6 title | Challenge dose epoch |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Twinrix Adult Group |

Arm description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

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

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses administered intramuscularly into the upper arm (deltoid muscle) region.

| | |
|------------------|----------------------|
| Arm title | Twinrix Junior Group |
|------------------|----------------------|

Arm description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|----------------------------------------------------------------------------------|--------------------------|
| Investigational medicinal product name | Engerix-B |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 3 doses administered intramuscularly into the upper arm (deltoid muscle) region. | |
| Investigational medicinal product name | Havrix 1440 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 3 doses administered intramuscularly into the upper arm (deltoid muscle) region. | |

| Number of subjects in period 6^[3] | Twinrix Adult Group | Twinrix Junior Group |
|-----------------------------------------------------|---------------------|----------------------|
| Started | 8 | 11 |
| Completed | 7 | 11 |
| Not completed | 1 | 0 |
| Pregnancy | 1 | - |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only 8 subjects in the Twinrix Adult Group and 11 subjects in the Twinrix Junior Group were eligible to receive the challenge dose.

Baseline characteristics

Reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |

| Reporting group values | Twinrix Adult Group | Twinrix Junior Group | Total |
|-------------------------------------------------------------------------|---------------------|----------------------|-------|
| Number of subjects | 99 | 111 | 210 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 24.5 ± 1.06 | 24.5 ± 1.05 | - |
| Gender categorical Units: Subjects | | | |
| Female | 49 | 52 | 101 |
| Male | 50 | 59 | 109 |

Subject analysis sets

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Subject analysis set title | Twinrix Adult Group (Year 12) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The baseline measure data here corresponds to Year 12. The analysis Population includes all subjects that returned for the Year 12 follow up time point. | |
| Subject analysis set title | Twinrix Junior Group (Year 12) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The baseline measure data here corresponds to Year 12. The analysis Population includes all subjects that returned for the Year 12 follow up time point. | |
| Subject analysis set title | Twinrix Adult Group (Year 13) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The baseline measure data here corresponds to Year 13. The analysis Population includes all subjects that returned for the Year 13 follow up time point. | |
| Subject analysis set title | Twinrix Junior Group (Year 13) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The baseline measure data here corresponds to Year 13. The analysis Population includes all subjects that returned for the Year 13 follow up time point. | |
| Subject analysis set title | Twinrix Adult Group (Year 14) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 14. The analysis Population includes all subjects that returned for the Year 14 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 14) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 14. The analysis Population includes all subjects that returned for the Year 14 follow up time point.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Twinrix Adult Group (Year 15) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 15. The analysis Population includes all subjects that returned for the Year 15 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 15) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 15. The analysis Population includes all subjects that returned for the Year 15 follow up time point.

| | |
|----------------------------|--------------------------------------------|
| Subject analysis set title | Twinrix Adult Group (challenge dose epoch) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to the challenge dose epoch. The analysis Population includes all subjects that were administrated a challenge dose.

| | |
|----------------------------|---------------------------------------------|
| Subject analysis set title | Twinrix Junior Group (challenge dose epoch) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to the challenge dose epoch. The analysis Population includes all subjects that were administrated a challenge dose.

| Reporting group values | Twinrix Adult Group (Year 12) | Twinrix Junior Group (Year 12) | Twinrix Adult Group (Year 13) |
|------------------------------------|-------------------------------|--------------------------------|-------------------------------|
| Number of subjects | 101 | 109 | 102 |
| Age categorical Units: Subjects | | | |

| | | | |
|---------------------------------------|--------|--------|--------|
| Age continuous Units: years | | | |
| arithmetic mean | 25.4 | 25.4 | 26.40 |
| standard deviation | ± 1.06 | ± 1.04 | ± 1.07 |
| Gender categorical Units: Subjects | | | |
| Female | 50 | 50 | 50 |
| Male | 51 | 59 | 52 |

| Reporting group values | Twinrix Junior Group (Year 13) | Twinrix Adult Group (Year 14) | Twinrix Junior Group (Year 14) |
|------------------------------------|--------------------------------|-------------------------------|--------------------------------|
| Number of subjects | 113 | 100 | 113 |
| Age categorical Units: Subjects | | | |

| | | | |
|--------------------------------|--------|--------|--------|
| Age continuous Units: years | | | |
| arithmetic mean | 26.40 | 27.40 | 27.40 |
| standard deviation | ± 1.06 | ± 1.11 | ± 1.05 |

| | | | |
|---------------------------------------|----|----|----|
| Gender categorical Units: Subjects | | | |
| Female | 53 | 49 | 53 |
| Male | 60 | 51 | 60 |

| | | | |
|------------------------------------|----------------------------------|-----------------------------------|--------------------------------------------------|
| Reporting group values | Twinrix Adult Group (Year 15) | Twinrix Junior Group (Year 15) | Twinrix Adult Group (challenge dose epoch) |
| Number of subjects | 98 | 111 | 8 |
| Age categorical Units: Subjects | | | |

| | | | |
|---------------------------------------|--------|--------|-------|
| Age continuous Units: years | | | |
| arithmetic mean | 28.4 | 28.3 | 29.4 |
| standard deviation | ± 1.15 | ± 1.09 | ± 1.2 |
| Gender categorical Units: Subjects | | | |
| Female | 47 | 52 | 4 |
| Male | 51 | 59 | 4 |

| | | | |
|------------------------------------|---------------------------------------------------|--|--|
| Reporting group values | Twinrix Junior Group (challenge dose epoch) | | |
| Number of subjects | 11 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|---------------------------------------|-------|--|--|
| Age continuous Units: years | | | |
| arithmetic mean | 29.4 | | |
| standard deviation | ± 1.3 | | |
| Gender categorical Units: Subjects | | | |
| Female | 7 | | |
| Male | 4 | | |

End points

End points reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Adult Group |
| Reporting group description: Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study. | |
| Reporting group title | Twinrix Junior Group |
| Reporting group description: Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study. | |
| Subject analysis set title | Twinrix Adult Group (Year 12) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 12. The analysis Population includes all subjects that returned for the Year 12 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 12) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 12. The analysis Population includes all subjects that returned for the Year 12 follow up time point.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Twinrix Adult Group (Year 13) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 13. The analysis Population includes all subjects that returned for the Year 13 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 13) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 13. The analysis Population includes all subjects that returned for the Year 13 follow up time point.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Twinrix Adult Group (Year 14) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 14. The analysis Population includes all subjects that returned for the Year 14 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 14) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 14. The analysis Population includes all subjects that returned for the Year 14 follow up time point.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Twinrix Adult Group (Year 15) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 15. The analysis Population includes all subjects that returned for the Year 15 follow up time point.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Twinrix Junior Group (Year 15) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to Year 15. The analysis Population includes all subjects that returned for the Year 15 follow up time point.

| | |
|----------------------------|--------------------------------------------|
| Subject analysis set title | Twinrix Adult Group (challenge dose epoch) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to the challenge dose epoch. The analysis Population includes all subjects that were administrated a challenge dose.

| | |
|----------------------------|---------------------------------------------|
| Subject analysis set title | Twinrix Junior Group (challenge dose epoch) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The baseline measure data here corresponds to the challenge dose epoch. The analysis Population includes all subjects that were administrated a challenge dose.

Primary: Number of Subjects With Anti-Hepatitis A (HAV) Antibody Concentrations Equal to or Above the Cut-Off Value

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Anti-Hepatitis A (HAV) Antibody Concentrations Equal to or Above the Cut-Off Value ^[1] |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-HAV antibody cut-off value assessed was ≥ 15 milli-International Units per milliliter (mIU/mL).

| | | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|--|--|
| End point type | Primary | | | |
| End point timeframe: | | | | |
| At Year 11, 12, 13, 14 and 15 after the first vaccine dose of the two-dose or three-dose primary vaccination in study HAB-084 | | | | |
| 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 endpoint was descriptive, no statistical analyses were conducted. | | | | |
| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 78 | 92 | | |
| Units: Subjects | | | | |
| Year 11 | 78 | 92 | | |
| Year 12 | 75 | 90 | | |
| Year 13 | 76 | 92 | | |
| Year 14 | 75 | 91 | | |
| Year 15 | 74 | 88 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HAV antibody concentrations

| | | | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|------------------------|--|--|
| End point title | Anti-HAV antibody concentrations ^[2] | | | |
| End point description: | | | | |
| Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. The analysis was performed on anti-HAV seropositive subjects. Seropositive subjects are subjects with anti-HAV antibody concentrations >= 15 mIU/mL. | | | | |
| End point type | Primary | | | |
| End point timeframe: | | | | |
| At Year 11, 12, 13, 14 and 15 after the first vaccine dose of two-dose or three-dose primary vaccination in study HAB-084 | | | | |
| 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 endpoint was descriptive, no statistical analyses were conducted. | | | | |
| | | | | |
| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 78 | 92 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Year 11 (N= 78; 92) | 360.5 (292 to 445.1) | 257.2 (215.1 to 307.5) | | |
| Year 12 (N= 75; 90) | 450.8 (359.6 to 565.1) | 335.6 (279 to 403.6) | | |
| Year 13 (N= 77; 92) | 401.5 (328.2 to 491.1) | 293.6 (244.2 to 352.9) | | |

| | | | | |
|---------------------|------------------------|------------------------|--|--|
| Year 14 (N= 75; 91) | 388 (309.2 to 487) | 291.4 (240.6 to 352.9) | | |
| Year 15 (N= 74; 88) | 387.5 (306.6 to 489.8) | 299.4 (247.6 to 362) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-Hepatitis B Surface Antigen (HBs) Antibody Concentrations Equal to or Above the Cut-Off Values

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Anti-Hepatitis B Surface Antigen (HBs) Antibody Concentrations Equal to or Above the Cut-Off Values ^[3] |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-HBs antibody cut-off values assessed were ≥ 6.2 mIU/mL and ≥ 10 mIU/mL. Note: A decrease in the specificity of the anti-HB ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following complete retesting and reanalysis for years 11 to 13. Results of year 14 and year 15 were only analysed by ChemiLuminescence ImmunoAssay (CLIA).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At Year 11, 12, 13, 14 and 15 after the first vaccine dose of the two-dose or three-dose primary vaccination in study HAB-084

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 endpoint was descriptive, no statistical analyses were conducted.

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 78 | 92 | | |
| Units: Subjects | | | | |
| Year 11 [6.2 mIU/mL] (N = 78;91) | 68 | 79 | | |
| Year 12 [6.2 mIU/mL] (N = 75;90) | 64 | 80 | | |
| Year 13 [6.2 mIU/mL] (N = 77;92) | 65 | 83 | | |
| Year 14 [6.2 mIU/mL] (N= 75;91) | 66 | 80 | | |
| Year 15 [6.2 mIU/mL] (N= 74;88) | 62 | 79 | | |
| Year 11 [10 mIU/mL] (N = 78;91) | 64 | 75 | | |
| Year 12 [10 mIU/mL] (N = 75;90) | 62 | 76 | | |
| Year 13 [10 mIU/mL] (N = 77;92) | 62 | 77 | | |
| Year 14 [10 mIU/mL] (N= 75;91) | 62 | 73 | | |
| Year 15 [10 mIU/mL] (N= 74;88) | 60 | 72 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HBs antibody concentrations

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| End point title | Anti-HBs antibody concentrations ^[4] |
| End point description: | |
| Antibodies concentrations are expressed as Geometric Mean concentrations (GMCs) in mIU/mL. The analysis was performed on anti-HBs seropositive subjects. Seropositive subjects are subjects with anti-HBs antibody concentrations ≥ 6.2 mIU/mL. Note: A decrease in the specificity of the anti-HB ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following complete retesting and reanalysis for years 11 to 13. Results of year 14 and year 15 were only analysed by CLIA. | |
| End point type | Primary |
| End point timeframe: | |
| At Year 11, 12, 13, 14 and 15 after the first vaccine dose of a two-dose or a three-dose primary vaccination in study HAB-084 | |
| 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 endpoint was descriptive, no statistical analyses were conducted. | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|------------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 78 | 92 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Year 11 (N = 78;91) | 88 (63.2 to 122.5) | 75.2 (55.6 to 101.8) | | |
| Year 12 (N = 75;90) | 93.3 (66.2 to 131.6) | 77 (56.1 to 105.7) | | |
| Year 13 (N = 77;92) | 92.4 (65.9 to 129.5) | 70.1 (51.2 to 96) | | |
| Year 14 (N= 75;91) | 81.8 (57.5 to 116.4) | 70.2 (51 to 96.8) | | |
| Year 15 (N= 74;88) | 87.2 (61 to 124.5) | 69.6 (50 to 96.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HBs anamnestic response

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|
| End point title | Anti-HBs anamnestic response ^[5] |
| End point description: | |
| Anamnestic response was defined as: Anti-HBs antibody concentrations ≥ 10 mIU/mL at one month post-challenge dose in subjects seronegative at the pre-challenge time-points. At least a 4-fold increase in anti-HBs antibody concentrations, at one month post-challenge dose in subjects seropositive at the pre-challenge time-points. | |
| End point type | Primary |
| End point timeframe: | |
| One month after the challenge dose | |
| 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 endpoint was descriptive, no statistical analyses were conducted. | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| ANTI-HBS ANAMNESTIC RESPONSE | 8 | 10 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection

| | |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Since the last long-term follow-up visit up to Year 11

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 99 | 111 | | |
| Units: Subjects | | | | |
| SAE (s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection

| | |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Since the last long-term follow-up visit up to Year 12

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 101 | 109 | | |
| Units: Subjects | | | | |
| SAE (s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection |
| End point description: SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above. | |
| End point type | Secondary |
| End point timeframe: Since the last long-term follow-up visit up to Year 13 | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 102 | 113 | | |
| Units: Subjects | | | | |
| SAE (s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection |
| End point description: SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed | |

above.

| | |
|--------------------------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Since the last long-term follow-up visit up to Year 14 | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 113 | | |
| Units: Subjects | | | | |
| SAE(s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection

| | |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting Serious Adverse Events (SAEs) or Hepatitis A or B Infection |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

| | |
|--------------------------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Since the last long-term follow-up visit up to Year 15 | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 98 | 111 | | |
| Units: Subjects | | | | |
| SAE(s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis A (HAV) antibody concentrations equal to or above the cut-off value

| | |
|-----------------|---------------------------------------------------------|
| End point title | Number of subjects with anti-hepatitis A (HAV) antibody |
|-----------------|---------------------------------------------------------|

| |
|----------------------------------------------------|
| concentrations equal to or above the cut-off value |
|----------------------------------------------------|

End point description:

Anti-HAV antibody cut-off value assessed was ≥ 15 milli-International Units per milliliter (mIU/mL).
Note: Since none of the subjects were seronegative for anti-HAV antibody concentration at the pre-challenge time point, subjects received only the HBV vaccine as the challenge dose.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Before (PRE) the challenge dose

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| PRE (N = 8;11) | 8 | 11 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HAV antibody concentrations

| | |
|-----------------|----------------------------------|
| End point title | Anti-HAV antibody concentrations |
|-----------------|----------------------------------|

End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. The analysis was performed on anti-HAV seropositive subjects. Seropositive subjects are subjects with anti-HAV antibody concentrations ≥ 15 mIU/mL.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Before (PRE) the challenge dose

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|------------------------------------------|------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| PRE (N =8;11) | 270.9 (173.8 to 422.3) | 201.3 (123.1 to 329) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with anti-hepatitis B surface antigen (HBs) antibody concentrations equal to or above the cut-off values |
| End point description: Anti-HBs antibody cut-off values assessed were ≥ 6.2 mIU/mL and ≥ 10 mIU/mL. | |
| End point type | Secondary |
| End point timeframe: Before (PRE) and one month after (POST) the challenge dose | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| PRE [6.2 MIU/ML] (N = 8;11) | 0 | 2 | | |
| POST [6.2 MIU/ML] (N = 8;11) | 8 | 11 | | |
| PRE [10 MIU/ML] (N = 8;11) | 0 | 1 | | |
| POST [10 MIU/ML] (N = 8;11) | 8 | 10 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| End point title | Anti-HBs antibody concentrations |
| End point description: Antibody concentrations are expressed as Geometric Mean concentrations (GMCs) in mIU/mL. The analysis was performed on anti-HBs seropositive subjects. Seropositive subjects are subjects with anti-HBs antibody concentrations ≥ 6.2 mIU/mL. | |
| End point type | Secondary |
| End point timeframe: Before (PRE) and one month after (POST) the challenge dose | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|------------------------------------------|---------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| PRE (N= 8;11) | 3.1 (3.1 to 3.1) | 4.1 (2.5 to 6.9) | | |
| POST (N= 8;11) | 3022.8 (407.8 to 22405.5) | 1433.1 (324.5 to 6328.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local adverse events

| | |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Number of subjects reporting any and grade 3 solicited local adverse events |
|-----------------|-----------------------------------------------------------------------------|

End point description:

Solicited local symptoms assessed 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 50 millimeters (mm) of injection site.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 4-day (Day 0 to Day 3) follow-up period after the challenge dose

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| ANY PAIN | 5 | 4 | | |
| GRADE 3 PAIN | 0 | 0 | | |
| ANY REDNESS | 1 | 2 | | |
| GRADE 3 REDNESS | 0 | 0 | | |
| ANY SWELLING | 0 | 0 | | |
| GRADE 3 SWELLING | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

| | |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms |
|-----------------|----------------------------------------------------------------------------------|

End point description:

Solicited general symptoms assessed were fatigue, gastrointestinal symptoms, headache and fever (axillary temperature). Gastrointestinal symptoms included nausea, vomiting, diarrhoea and/or abdominal pain. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature > 39.5°C. Related = general symptoms which were assessed by the investigator as causally related to vaccination.

| | |
|-----------------------------------------------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the 4-day (Day 0 to Day 3) follow-up period after the challenge dose | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| ANY FATIGUE | 3 | 3 | | |
| GRADE 3 FATIGUE | 0 | 0 | | |
| RELATED FATIGUE | 3 | 3 | | |
| ANY GASTROINTESTINAL SYMPTOMS | 1 | 1 | | |
| GRADE 3 GASTROINTESTINAL SYMPTOMS | 0 | 0 | | |
| RELATED GASTROINTESTINAL SYMPTOMS | 1 | 1 | | |
| ANY HEADACHE | 1 | 2 | | |
| GRADE 3 HEADACHE | 0 | 0 | | |
| RELATED HEADACHE | 1 | 2 | | |
| ANY TEMPERATURE | 0 | 0 | | |
| GRADE 3 TEMPERATURE | 0 | 0 | | |
| RELATED TEMPERATURE | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related unsolicited symptoms

| | |
|-----------------|----------------------------------------------------------------------------|
| End point title | Number of subjects reporting any, grade 3 and related unsolicited symptoms |
|-----------------|----------------------------------------------------------------------------|

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. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. Grade 3 = AE that prevented normal activity. Related = AE 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) follow-up period after the challenge dose

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| ANY AE(S) | 4 | 0 | | |
| GRADE 3 AE(S) | 0 | 0 | | |
| RELATED AE(S) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Serious Adverse Events (SAEs)

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| End point title | Number of subjects with Serious Adverse Events (SAEs) |
| End point description: | |
| Serious adverse events (SAEs) assessed included medical occurrences that resulted in death, were 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. | |
| End point type | Secondary |
| End point timeframe: | |
| One month after the administration of the challenge dose (Month 0 to Month 1) | |

| End point values | Twinrix Adult Group | Twinrix Junior Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 11 | | |
| Units: Subjects | | | | |
| SAE(S) | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Year 15 of the long-term follow-up. SAEs: one month post challenge dose, solicited symptoms: during the 4-day (Days 0-3) post challenge dose and unsolicited AEs: within the 31-day (Days 0-30) post challenge dose.

Adverse event reporting additional description:

No Serious Adverse Events (SAEs) related to primary vaccination or to lack of vaccine efficacy were reported during this long-term follow-up study up to Year 15. Other (non-serious) adverse events were not assessed for the long-term follow-up phase (up to Year 15) as per protocol.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 17 |

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | Twinrix Adult Group |
|-----------------------|---------------------|

Reporting group description:

Subjects received 2 doses of Twinrix Adult intramuscularly according to a 0, 6 month schedule in the primary study.

| | |
|-----------------------|----------------------|
| Reporting group title | Twinrix Junior Group |
|-----------------------|----------------------|

Reporting group description:

Subjects received 3 doses of Twinrix Junior (= half dose Twinrix Adult) intramuscularly according to a 0, 1, 6 month schedule in the primary study.

| Serious adverse events | Twinrix Adult Group | Twinrix Junior Group | |
|---------------------------------------------------|---------------------|----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 11 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| ABORTION SPONTANEOUS | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 11 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Twinrix Adult Group | Twinrix Junior Group | |
|-------------------------------------------------------|---------------------|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | 7 / 11 (63.64%) | |
| Nervous system disorders | | | |
| HEADACHE (solicited) | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 11 (18.18%) | |
| occurrences (all) | 1 | 2 | |
| HEADACHE (unsolicited) | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 0 / 11 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| General disorders and administration site conditions | | | |
| PAIN | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | 4 / 11 (36.36%) | |
| occurrences (all) | 5 | 4 | |
| REDNESS | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 11 (18.18%) | |
| occurrences (all) | 1 | 2 | |
| FATIGUE | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 3 / 11 (27.27%) | |
| occurrences (all) | 3 | 3 | |
| Gastrointestinal disorders | | | |
| GASTROINTESTINAL SYMPTOMS | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 11 (9.09%) | |
| occurrences (all) | 1 | 1 | |

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