



## Clinical trial results:

**Persistence of hepatitis B antibodies, immunogenicity and safety of GSK Biologicals' hepatitis B vaccine Engerix<sup>TM</sup>-B Kinder (SKF103860) challenge dose in adolescents vaccinated with four doses of Infanrix<sup>TM</sup> hexa (SB217744) during infancy.**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2013-002821-41    |
| Trial protocol           | DE                |
| Global end of trial date | 23 September 2014 |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 20 November 2018  |
| First version publication date | 10 July 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Results have been amended to account for consistency with other registries. |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 106793 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02052661 |
| 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, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 28 May 2015       |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 23 September 2014 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 23 September 2014 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the anti-HBs antibody response, in terms of subjects with antibody concentrations  $\geq 100$  mIU/ml, to a single challenge dose of HBV vaccine (Engerix-B Kinder) in subjects 12–13 years of age, previously vaccinated with four doses of Infanrix hexa in the first two years of life.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 13 January 2014 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 300 |
| Worldwide total number of subjects   | 300          |
| EEA total number of subjects         | 300          |

Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                 | 300 |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### 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 Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Engerix™-B Kinder Group |
|------------------|-------------------------|

Arm description:

Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Engerix™-B Kinder   |
| Investigational medicinal product code |   |
| Other name                             | HBV vaccine, GlaxoSmithKline (GSK) Biologicals' recombinant hepatitis B vaccine |
| Pharmaceutical forms                   | Injection   |
| Routes of administration               | Intramuscular use   |

Dosage and administration details:

Subjects received a single dose of HBV vaccine, administered intramuscularly into the deltoid of the non-dominant arm.

|                                       |                         |
|---------------------------------------|-------------------------|
| <b>Number of subjects in period 1</b> | Engerix™-B Kinder Group |
| Started                               | 300                     |
| Completed                             | 300                     |

## Baseline characteristics

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Engerix™-B Kinder Group |
|-----------------------|-------------------------|

Reporting group description:

Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

| Reporting group values                                | Engerix™-B Kinder Group | Total |  |
|---|-------------------------|-------|--|
| Number of subjects                                    | 300                     | 300   |  |
| Age categorical<br>Units: Subjects                    |                         |       |  |
| In utero  |                         | 0     |  |
| Preterm newborn infants<br>(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<br>Units: years                        |                         |       |  |
| arithmetic mean                                       | 12.3                    |       |  |
| standard deviation                                    | ± 0.5                   | -     |  |
| Gender categorical<br>Units: Subjects                 |                         |       |  |
| Female  | 150                     | 150   |  |
| Male  | 150                     | 150   |  |

## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Engerix™-B Kinder Group |
| Reporting group description:<br>Subjects who were previously primed and boosted with four doses of Infanrix™ hexa in the first two years of life, received a single dose of Engerix™-B Kinder vaccine. The vaccine was administered intramuscularly into the deltoid of the non-dominant arm. |                         |

### Primary: Anti-HBs immune response.

|   |  |
|---|--|
| End point title   | Anti-HBs immune response. <sup>[1]</sup> |
| End point description:<br>Anti-HBs immune response was defined as the number of subjects with Anti-HBs antibody concentrations $\geq 100$ mIU/ml. |  |
| End point type  | Primary                                  |
| End point timeframe:<br>One month after the single challenge dose of Engerix™-B Kinder vaccine (Month 1)  |  |

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values            | Engerix™-B Kinder Group |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 289                     |  |  |  |
| Units: Subjects             |                         |  |  |  |
| Anti-HBs                    | 272                     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib.

|   |   |
|---|---|
| End point title   | Anti-HBs antibody concentrations at 12-13 years of age, after previous vaccination with DTPa-HBV-IPV/Hib. |
| End point description:<br>Concentrations were expressed as geometric mean concentrations (GMCs) for the seropositivity cut-off of 6.2 mIU/ml. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Before (PRE) and 1 month after (POST) the single challenge dose of Engerix™-B Kinder vaccine.                         |   |

|   |                            |  |  |  |
|---|----------------------------|--|--|--|
| <b>End point values</b>                     | Engerix™-B<br>Kinder Group |  |  |  |
| Subject group type                          | Reporting group            |  |  |  |
| Number of subjects analysed                 | 293                        |  |  |  |
| Units: mIU/mL                               |                            |  |  |  |
| geometric mean (confidence interval<br>95%) |                            |  |  |  |
| Anti-HBs, PRE [N=293]                       | 22.7 (18.5 to<br>27.9)     |  |  |  |
| Anti-HBs, POST [N=289]                      | 3502.6 (2672<br>to 4591.5) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml, $\geq 10$ mIU/ml, 10 to $< 100$ mIU/ml and $\geq 100$ mIU/ml

|                 |  |
|-----------------|--|
| End point title | Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml, $\geq 10$ mIU/ml, 10 to $< 100$ mIU/ml and $\geq 100$ mIU/ml |
|-----------------|--|

End point description:

A seropositive subject was defined as a subject with anti-HBs antibody concentrations  $\geq 6.2$  milli-international units per milliliter (mIU/ml). A seroprotected subjects was defined as a subject with anti-HBs antibody concentrations  $\geq 10$  mIU/ml.

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

End point timeframe:

Before the single challenge dose of Engerix™-B Kinder vaccine.

|                               |                            |  |  |  |
|-------------------------------|----------------------------|--|--|--|
| <b>End point values</b>       | Engerix™-B<br>Kinder Group |  |  |  |
| Subject group type            | Reporting group            |  |  |  |
| Number of subjects analysed   | 293                        |  |  |  |
| Units: Subjects               |                            |  |  |  |
| Anti-HBs $\geq 6.2$ mIU/ml    | 205                        |  |  |  |
| Anti-HBs $\geq 10$ mIU/ml     | 178                        |  |  |  |
| Anti-HBs 10 to $< 100$ mIU/ml | 116                        |  |  |  |
| Anti-HBs $\geq 100$ mIU/ml    | 62                         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml and $\geq 10$ mIU/ml

|                 |   |
|-----------------|---|
| End point title | Number of subjects with anti-HBs antibody concentrations $\geq 6.2$ mIU/ml and $\geq 10$ mIU/ml |
|-----------------|---|

End point description:

A seropositive subject was defined as a subject with anti-HBs antibody concentrations  $\geq 6.2$  mIU/ml. A seroprotected subjects was defined as a subject with anti-HBs antibody concentrations  $\geq 10$  mIU/ml.

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

End point timeframe:

1 month after the single challenge dose of Engerix™-B Kinder vaccine.

| End point values            | Engerix™-B Kinder Group |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 289                     |  |  |  |
| Units: Subjects             |                         |  |  |  |
| Anti-HBs $\geq 6.2$ mIU/ml  | 283                     |  |  |  |
| Anti-HBs $\geq 10$ mIU/ml   | 282                     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with an anamnestic response to the single challenge dose of HBV vaccine. |
|-----------------|---|

End point description:

The amnestic response to the challenge dose was defined as: for initially seronegative subjects, antibody concentration  $\geq 10$ mIU/mL; for initially seropositive subjects, antibody concentration at least four times the pre-challenge antibody concentration.

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

End point timeframe:

One month after the single challenge dose of Engerix™-B Kinder vaccine.

| End point values            | Engerix™-B Kinder Group |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 287                     |  |  |  |
| Units: Subjects             |                         |  |  |  |
| Anamnestic response         | 277                     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any solicited local symptoms.

|   |   |
|---|---|
| End point title   | Number of subjects with any solicited local symptoms. |
| End point description:<br>Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. |   |
| End point type  | Secondary   |
| End point timeframe:<br>During the 4-day (Day 0–3) follow-up period after the single challenge dose of Engerix™-B Kinder vaccine.                           |   |

|                             |                         |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| <b>End point values</b>     | Engerix™-B Kinder Group |  |  |  |
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 300                     |  |  |  |
| Units: Subjects             |                         |  |  |  |
| Pain                        | 132                     |  |  |  |
| Redness                     | 70                      |  |  |  |
| Swelling                    | 29                      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any solicited general symptoms.

|  |   |
|--|---|
| End point title  | Number of subjects with any solicited general symptoms. |
| End point description:<br>Assessed solicited general symptoms were fatigue, gastrointestinal, headache and temperature [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. |   |
| End point type   | Secondary   |
| End point timeframe:<br>During the 4-day (Day 0–3) follow-up period after the single challenge dose of Engerix™-B Kinder vaccine.  |   |

|                             |                         |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| <b>End point values</b>     | Engerix™-B Kinder Group |  |  |  |
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 300                     |  |  |  |
| Units: Subjects             |                         |  |  |  |
| Fatigue                     | 73                      |  |  |  |
| Gastrointestinal            | 34                      |  |  |  |
| Headache                    | 71                      |  |  |  |
| Temperature/(Axillary)      | 7                       |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any unsolicited adverse events (AEs).

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any unsolicited adverse events (AEs). |
|-----------------|---|

End point description:

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

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

End point timeframe:

During the 31-day (Day 0–30) follow-up period after the single challenge dose of Engerix™-B Kinder vaccine.

| End point values            | Engerix™-B<br>Kinder Group |  |  |  |
|-----------------------------|----------------------------|--|--|--|
| Subject group type          | Reporting group            |  |  |  |
| Number of subjects analysed | 300                        |  |  |  |
| Units: Subjects             |                            |  |  |  |
| Any AEs                     | 44                         |  |  |  |

## 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 include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

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

End point timeframe:

From Month 0 to Month 1

| End point values            | Engerix™-B<br>Kinder Group |  |  |  |
|-----------------------------|----------------------------|--|--|--|
| Subject group type          | Reporting group            |  |  |  |
| Number of subjects analysed | 300                        |  |  |  |
| Units: Subjects             |                            |  |  |  |
| Any SAEs                    | 2                          |  |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4-day (Day 0–3) follow-up period after vaccination

Unsolicited AEs: during the 31-day (Day 0–30) follow-up period after vaccination

SAEs: During the entire study.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Engerix™-B Kinder Group |
|-----------------------|-------------------------|

Reporting group description:

Subjects who were previously primed and boosted with four doses of DTPa-HBV-IPV/Hib in the first two years of life, received a single dose of HBV vaccine.

| Serious adverse events                            | Engerix™-B Kinder Group |  |  |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events |                         |  |  |
| subjects affected / exposed                       | 2 / 300 (0.67%)         |  |  |
| number of deaths (all causes)                     | 0                       |  |  |
| number of deaths resulting from adverse events    |                         |  |  |
| Injury, poisoning and procedural complications    |                         |  |  |
| Contusion   |                         |  |  |
| subjects affected / exposed                       | 1 / 300 (0.33%)         |  |  |
| occurrences causally related to treatment / all   | 0 / 1                   |  |  |
| deaths causally related to treatment / all        | 0 / 0                   |  |  |
| Forearm fracture                                  |                         |  |  |
| subjects affected / exposed                       | 1 / 300 (0.33%)         |  |  |
| occurrences causally related to treatment / all   | 0 / 1                   |  |  |
| deaths causally related to treatment / all        | 0 / 0                   |  |  |

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

| <b>Non-serious adverse events</b>                     | Engerix™-B Kinder Group |  |  |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 132 / 300 (44.00%)      |  |  |
| General disorders and administration site conditions  |                         |  |  |
| Pain  |                         |  |  |
| subjects affected / exposed                           | 132 / 300 (44.00%)      |  |  |
| occurrences (all)                                     | 132                     |  |  |
| Redness   |                         |  |  |
| subjects affected / exposed                           | 70 / 300 (23.33%)       |  |  |
| occurrences (all)                                     | 70                      |  |  |
| Swelling  |                         |  |  |
| subjects affected / exposed                           | 29 / 300 (9.67%)        |  |  |
| occurrences (all)                                     | 29                      |  |  |
| Fatigue   |                         |  |  |
| subjects affected / exposed                           | 73 / 300 (24.33%)       |  |  |
| occurrences (all)                                     | 73                      |  |  |
| Gastrointestinal                                      |                         |  |  |
| subjects affected / exposed                           | 34 / 300 (11.33%)       |  |  |
| occurrences (all)                                     | 34                      |  |  |
| Headache  |                         |  |  |
| subjects affected / exposed                           | 71 / 300 (23.67%)       |  |  |
| occurrences (all)                                     | 71                      |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported