



## Clinical trial results:

**A phase III, controlled, single-blind study to assess the reactogenicity, safety and immunogenicity of a booster dose of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine or Prevenar™ when co-administered with Hiberix™ at 12-18 months of age in children primed with the same vaccines in study 10PN-PD-DIT-036 (110808).**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-001506-34  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 11 January 2010 |

### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 13 December 2020   |
| First version publication date | 25 July 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Minor corrections in safety section.</li></ul> |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 112933 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00911144 |
| 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? | Yes |

Notes:

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**Results analysis stage**

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|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 17 June 2010    |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 11 January 2010 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 11 January 2010 |
| 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 safety of a booster dose of 10Pn-PD-DiT vaccine in terms of the occurrence of adverse events (AEs) with intensity grade 3, when co-administered with Hib vaccine at 12-18 months of age in children primed with the same vaccines at 2, 4 and 6 months of age in study 10PN-PD-DIT-036 (110808).

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                          | 11 June 2009 |
| 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**

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|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 450 |
| Worldwide total number of subjects   | 450                     |
| EEA total number of subjects         | 0                       |

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)  | 450 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| 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:

Two subjects enrolled in the protocol received commercial Prevenar and Hiberix vaccines instead of the clinical vaccines planned to be injected and are as such not included in the number of started subjects below.

### Period 1

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

Blinding implementation details:

This study was conducted in a single-blind manner meaning that the investigator and/or his staff were aware of the treatment assignment but the subjects' parent(s)/guardian(s) were not.

### Arms

|                              |                 |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes             |
| <b>Arm title</b>             | Synflorix Group |

Arm description:

Subjects previously primed (NCT00680914) with 3 doses of Synflorix and Hiberix in the first year of life receiving a booster dose of the same vaccines in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | GSK Biologicals' Synflorix™ (Pneumococcal vaccine GSK1024850A) |
| Investigational medicinal product code |  |
| Other name                             | Pneumococcal vaccine GSK1024850A                               |
| Pharmaceutical forms                   | Suspension for injection                                       |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

Intramuscular injection, administered as a single dose.

|  |   |
|--|---|
| Investigational medicinal product name | GSK Biologicals' Hiberix™                     |
| Investigational medicinal product code |   |
| Other name                             | Hib   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

Intramuscular injection, administered as a single dose.

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | Prevenar Group |
|------------------|----------------|

Arm description:

Subjects previously primed (NCT00680914) with 3 doses of Prevenar and Hiberix in the first year of life receiving a booster dose of Prevenar and Hiberix in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|   |   |
|---|---|
| Investigational medicinal product name                  | Wyeth-Lederle's Prevenar™                     |
| Investigational medicinal product code                  |   |
| Other name  | 7Pn   |
| Pharmaceutical forms                                    | Suspension for injection                      |
| Routes of administration                                | Intramuscular use                             |
| Dosage and administration details:                      |   |
| Intramuscular injection, administered as a single dose. |   |
| Investigational medicinal product name                  | GSK Biologicals' Hiberix™                     |
| Investigational medicinal product code                  |   |
| Other name  | Hib   |
| Pharmaceutical forms                                    | Powder and solvent for solution for injection |
| Routes of administration                                | Intramuscular use                             |
| Dosage and administration details:                      |   |
| Intramuscular injection, administered as a single dose. |   |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Synflorix Group | Prevenar Group |
|---|-----------------|----------------|
| Started   | 335             | 113            |
| Completed   | 319             | 108            |
| Not completed                                       | 16              | 5              |
| Consent withdrawn by subject                        | 16              | 5              |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the total 450 subjects enrolled in the study, 2 subjects received commercial Prevenar and Hiberix vaccines instead of the clinical vaccines planned to be injected and are as such not included in the number of subjects who started the study.

## Baseline characteristics

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Synflorix Group |
|-----------------------|-----------------|

Reporting group description:

Subjects previously primed (NCT00680914) with 3 doses of Synflorix and Hiberix in the first year of life receiving a booster dose of the same vaccines in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

|                       |                |
|-----------------------|----------------|
| Reporting group title | Prevenar Group |
|-----------------------|----------------|

Reporting group description:

Subjects previously primed (NCT00680914) with 3 doses of Prevenar and Hiberix in the first year of life receiving a booster dose of Prevenar and Hiberix in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

| Reporting group values                                | Synflorix Group | Prevenar Group | Total |
|---|-----------------|----------------|-------|
| Number of subjects                                    | 335             | 113            | 448   |
| 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: months                       |                 |                |       |
| arithmetic mean                                       | 13.6            | 13.7           |       |
| standard deviation                                    | ± 1.07          | ± 1            | -     |
| Gender categorical<br>Units: Subjects                 |                 |                |       |
| Female  | 168             | 59             | 227   |
| Male  | 167             | 54             | 221   |

## End points

### End points reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | Synflorix Group |
| Reporting group description:<br>Subjects previously primed (NCT00680914) with 3 doses of Synflorix and Hiberix in the first year of life receiving a booster dose of the same vaccines in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.   |                 |
| Reporting group title  | Prevenar Group  |
| Reporting group description:<br>Subjects previously primed (NCT00680914) with 3 doses of Prevenar and Hiberix in the first year of life receiving a booster dose of Prevenar and Hiberix in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively. |                 |

### Primary: Number of subjects reporting grade 3 adverse events

|   |  |
|---|--|
| End point title   | Number of subjects reporting grade 3 adverse events <sup>[1]</sup> |
| End point description:<br>Grade 3 adverse events are severe symptoms that prevent normal, everyday activities.  |  |
| End point type  | Primary  |
| End point timeframe:<br>Within 31 days (Day 0 - Day 30) after booster vaccination.  |  |
| Notes:<br>[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.<br>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed. |  |

| End point values            | Synflorix Group | Prevenar Group  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 332             | 113             |  |  |
| Units: Subjects             | 42              | 13              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting solicited symptoms

|  |   |
|--|---|
| End point title  | Number of subjects reporting solicited symptoms |
| End point description:<br>Solicited local symptoms assessed include pain, redness and swelling at the injection site. Solicited general symptoms assessed include drowsiness, fever (equal to or above 37.5 degrees Celsius), irritability and loss of appetite. |   |
| End point type   | Secondary                                       |
| End point timeframe:<br>Within 4 days (Days 0 to 3) after booster vaccination  |   |

| <b>End point values</b>     | Synflorix Group | Prevenar Group  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 332             | 113             |  |  |
| Units: Subjects             |                 |                 |  |  |
| Pain                        | 120             | 39              |  |  |
| Redness                     | 142             | 55              |  |  |
| Swelling                    | 97              | 35              |  |  |
| Drowsiness                  | 75              | 21              |  |  |
| Fever                       | 46              | 20              |  |  |
| Irritability                | 141             | 42              |  |  |
| Loss of appetite            | 71              | 29              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting unsolicited adverse events

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting unsolicited adverse events |
|-----------------|---|

End point description:

An unsolicited adverse event is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study. Also any "solicited" symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited adverse event.

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

End point timeframe:

Within 31 days (Days 0 to 30) after booster vaccination

| <b>End point values</b>     | Synflorix Group | Prevenar Group  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 335             | 113             |  |  |
| Units: Subjects             | 118             | 41              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting serious adverse events

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting serious adverse events |
|-----------------|---|



End point description:

Serious adverse events are medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

After booster vaccination up to study end (Month 0 to Month 1)

| End point values            | Synflorix Group | Prevenar Group  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 335             | 113             |  |  |
| Units: Subjects             | 8               | 4               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentration of antibodies against vaccine pneumococcal serotypes

|                 |  |
|-----------------|--|
| End point title | Concentration of antibodies against vaccine pneumococcal serotypes |
|-----------------|--|

End point description:

Concentrations of antibodies are measured by 22F-inhibition enzyme-linked immunosorbent assay (ELISA) and are presented as geometric mean concentrations expressed as microgram per milliliter. Vaccine pneumococcal serotypes included serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.

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

End point timeframe:

One month after booster vaccination (Month 1)

| End point values                         | Synflorix Group     | Prevenar Group         |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed              | 317                 | 102                    |  |  |
| Units: µg/mL                             |                     |                        |  |  |
| geometric mean (confidence interval 95%) |                     |                        |  |  |
| Anti-1 (n= 317, 100)                     | 4.03 (3.66 to 4.43) | 0.06 (0.05 to 0.07)    |  |  |
| Anti-4 (n= 317, 102)                     | 5.77 (5.25 to 6.34) | 12.19 (10.11 to 14.69) |  |  |
| Anti-5 (n= 317, 102)                     | 5.51 (5.08 to 5.98) | 0.19 (0.16 to 0.23)    |  |  |
| Anti-6B (n= 317, 102)                    | 2.78 (2.48 to 3.12) | 7.09 (5.82 to 8.63)    |  |  |
| Anti-7F (n= 317, 102)                    | 5.39 (4.97 to 5.85) | 0.06 (0.04 to 0.07)    |  |  |
| Anti-9V (n= 317, 102)                    | 4.99 (4.55 to 5.46) | 12.72 (10.86 to 14.88) |  |  |

|                        |                       |                        |  |  |
|------------------------|-----------------------|------------------------|--|--|
| Anti-14 (n= 316, 102)  | 7.73 (7.09 to 8.43)   | 22.22 (18.96 to 26.03) |  |  |
| Anti-18C (n= 317, 102) | 13.14 (11.9 to 14.52) | 14.53 (12.1 to 17.44)  |  |  |
| Anti-19F (n= 317, 101) | 16.89 (14.87 to 19.2) | 4.82 (3.97 to 5.85)    |  |  |
| Anti-23F (n= 317, 102) | 3.75 (3.37 to 4.16)   | 14.81 (11.61 to 18.89) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity against vaccine pneumococcal serotypes

|                 |  |
|-----------------|--|
| End point title | Opsonophagocytic activity against vaccine pneumococcal serotypes |
|-----------------|--|

End point description:

*Streptococcus pneumoniae* opsonophagocytic activity was measured by a killing-assay using a HL 60 cell line. The results are presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. Vaccine pneumococcal serotypes included serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.

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

End point timeframe:

One month after booster vaccination (Month 1)

| End point values                         | Synflorix Group           | Prevenar Group            |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed              | 151                       | 47                        |  |  |
| Units: Titer                             |                           |                           |  |  |
| geometric mean (confidence interval 95%) |                           |                           |  |  |
| Opsono-1 (n= 148, 47)                    | 363.7 (275.3 to 480.5)    | 4.7 (3.9 to 5.6)          |  |  |
| Opsono-4 (n= 149, 45)                    | 1058 (893.9 to 1252.3)    | 3717 (2759.3 to 5007)     |  |  |
| Opsono-5 (n= 150, 46)                    | 233.9 (189.8 to 288.3)    | 4 (4 to 4)                |  |  |
| Opsono-6B (n= 150, 46)                   | 546.5 (415.9 to 718)      | 3826.8 (2518 to 5815.9)   |  |  |
| Opsono-7F (n= 145, 46)                   | 5467.5 (4698.1 to 6363)   | 1038.2 (609.9 to 1767.2)  |  |  |
| Opsono-9V (n= 151, 44)                   | 1707.5 (1497.6 to 1946.8) | 5204 (3842.8 to 7047.4)   |  |  |
| Opsono-14 (n= 150, 46)                   | 1814.6 (1577.4 to 2087.5) | 3958.4 (2888.1 to 5425.4) |  |  |
| Opsono-18C (n= 147, 45)                  | 607.9 (498.2 to 741.6)    | 1723.3 (1196.4 to 2482.3) |  |  |

|                         |                           |                              |  |  |
|-------------------------|---------------------------|------------------------------|--|--|
| Opsono-19F (n= 149, 44) | 1284.5 (1027.2 to 1606.3) | 277.3 (171.6 to 448.2)       |  |  |
| Opsono-23F (n= 149, 44) | 2702.9 (2234.9 to 3268.9) | 29918.6 (17115.7 to 52298.1) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration of antibodies against cross-reactive pneumococcal serotypes 6A and 19A

|                 |  |
|-----------------|--|
| End point title | Concentration of antibodies against cross-reactive pneumococcal serotypes 6A and 19A |
|-----------------|--|

End point description:

Concentrations of antibodies are measured by 22F-inhibition ELISA and are presented as geometric mean concentrations expressed as microgram per milliliter.

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

End point timeframe:

One month after booster vaccination (Month 1)

| End point values                         | Synflorix Group     | Prevenar Group      |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 317                 | 102                 |  |  |
| Units: µg/mL                             |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| Anti-6A                                  | 0.99 (0.84 to 1.17) | 2.51 (1.79 to 3.51) |  |  |
| Anti-19A                                 | 1.54 (1.27 to 1.87) | 0.32 (0.24 to 0.43) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A

|                 |  |
|-----------------|--|
| End point title | Opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A |
|-----------------|--|

End point description:

*Streptococcus pneumoniae* opsonophagocytic activity was measured by a killing-assay using a HL 60 cell line. The results are presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions.

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

End point timeframe:

One month after booster vaccination (Month 1)

| End point values                         | Synflorix Group        | Prevenar Group           |  |  |
|--|------------------------|--------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group          |  |  |
| Number of subjects analysed              | 146                    | 44                       |  |  |
| Units: Titer                             |                        |                          |  |  |
| geometric mean (confidence interval 95%) |                        |                          |  |  |
| Opsono-6A (n= 137, 44)                   | 196.1 (134.6 to 285.9) | 1415.7 (891.2 to 2248.9) |  |  |
| Opsono-19A (n= 146, 44)                  | 64.9 (44.6 to 94.5)    | 15.5 (8.1 to 29.9)       |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration of antibodies against protein D (PD)

|   |  |
|---|--|
| End point title   | Concentration of antibodies against protein D (PD) |
| End point description:<br>Concentrations of antibodies are presented as geometric mean concentrations expressed as Enzyme-Linked Immuno-Sorbent Assay (ELISA) units per milliliter. |  |
| End point type  | Secondary  |
| End point timeframe:<br>One month after booster vaccination (Month 1)   |  |

| End point values                         | Synflorix Group           | Prevenar Group     |  |  |
|--|---------------------------|--------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group    |  |  |
| Number of subjects analysed              | 316                       | 101                |  |  |
| Units: EU/mL                             |                           |                    |  |  |
| geometric mean (confidence interval 95%) | 1288.9 (1175.6 to 1413.2) | 92 (78.3 to 108.1) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration of antibodies against polyribosyl-ribitol-phosphate (PRP)

|                 |   |
|-----------------|---|
| End point title | Concentration of antibodies against polyribosyl-ribitol-phosphate (PRP) |
|-----------------|---|

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End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as microgram per milliliter.

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

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End point timeframe:

One month after booster vaccination (Month 1)

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| End point values                         | Synflorix Group                | Prevenar Group             |  |  |
|--|--------------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group                | Reporting group            |  |  |
| Number of subjects analysed              | 163                            | 54                         |  |  |
| Units: µg/mL                             |                                |                            |  |  |
| geometric mean (confidence interval 95%) | 152.97<br>(130.307 to 179.575) | 99.738 (72.964 to 136.335) |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious AEs were assessed up to one month following booster vaccination (Month 1). The time frames for Other AEs reporting were 4 days and 31 days following booster vaccination for events collected by systematic and non-systematic methods, respectively.

Adverse event reporting additional description:

Subjects at risk for systematically assessed other (non-serious) adverse events has been set to the number of subjects that had returned their symptom sheet. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Prevenar Group |
|-----------------------|----------------|

Reporting group description:

Subjects previously primed (NCT00680914) with 3 doses of Prevenar and Hiberix in the first year of life receiving a booster dose of Prevenar and Hiberix in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Synflorix Group |
|-----------------------|-----------------|

Reporting group description:

Subjects previously primed (NCT00680914) with 3 doses of Synflorix and Hiberix in the first year of life receiving a booster dose of the same vaccines in the second year of life by intramuscular injection into the right and the left thigh or deltoid, respectively.

| Serious adverse events                               | Prevenar Group  | Synflorix Group |  |
|--|-----------------|-----------------|--|
| Total subjects affected by serious adverse events    |                 |                 |  |
| subjects affected / exposed                          | 4 / 113 (3.54%) | 8 / 335 (2.39%) |  |
| number of deaths (all causes)                        | 0               | 0               |  |
| number of deaths resulting from adverse events       |                 |                 |  |
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 1 / 113 (0.88%) | 0 / 335 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders               |                 |                 |  |
| Urticaria  |                 |                 |  |
| subjects affected / exposed                          | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Infections and infestations                          |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Pharyngitis                                     |                 |                 |  |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 335 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pharyngotonsillitis                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 2 / 335 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchopneumonia                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 335 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis rotavirus                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| H1N1 influenza                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hand-foot-and-mouth disease                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Otitis media acute                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Febrile convulsion                              |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 335 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Prevenar Group    | Synflorix Group    |  |
|---|-------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                   |                    |  |
| subjects affected / exposed                           | 82 / 113 (72.57%) | 243 / 335 (72.54%) |  |
| General disorders and administration site conditions  |                   |                    |  |
| Pain at the injection site                            |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 39 / 113 (34.51%) | 120 / 335 (35.82%) |  |
| occurrences (all)                                     | 39                | 120                |  |
| Redness at the injection site                         |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 55 / 113 (48.67%) | 142 / 335 (42.39%) |  |
| occurrences (all)                                     | 55                | 142                |  |
| Swelling at the injection site                        |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 35 / 113 (30.97%) | 97 / 335 (28.96%)  |  |
| occurrences (all)                                     | 35                | 97                 |  |
| Drowsiness  |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 21 / 113 (18.58%) | 75 / 335 (22.39%)  |  |
| occurrences (all)                                     | 21                | 75                 |  |
| Fever   |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 20 / 113 (17.70%) | 46 / 335 (13.73%)  |  |
| occurrences (all)                                     | 20                | 46                 |  |
| Irritability  |                   |                    |  |
| alternative assessment type: Systematic               |                   |                    |  |
| subjects affected / exposed                           | 42 / 113 (37.17%) | 141 / 335 (42.09%) |  |
| occurrences (all)                                     | 42                | 141                |  |



|  |                         |                         |  |
|--|-------------------------|-------------------------|--|
| Loss of appetite<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)   | 29 / 113 (25.66%)<br>29 | 71 / 335 (21.19%)<br>71 |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 12 / 113 (10.62%)<br>12 | 30 / 335 (8.96%)<br>30  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 10 / 113 (8.85%)<br>10  | 19 / 335 (5.67%)<br>19  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                              |
|---------------|--|
| 29 April 2009 | Comments received from the Korean FDA. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported