



Clinical trial results:

A phase II, observer-blind, randomized study to evaluate the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' combined DSSITGDPa-HBV-IPV/Hib vaccine containing diphtheria toxoid from the Statens Serum Institute (SSI) of Denmark and tetanus toxoid from GSK Biologicals' Kft [GD], compared to the currently licensed GSK Biologicals' DTPa-HBV-IPV/Hib vaccine (Infanrix hexa) when administered to healthy infants at 2, 3 and 4 months of age.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-000554-46 |
| Trial protocol | FI |
| Global end of trial date | 31 May 2007 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 02 May 2016 |
| First version publication date | 03 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 106786 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00376779 |
| 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 Advisor Call Center, GlaxoSmithKline Biologicals, 004 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Advisor Call Center, GlaxoSmithKline Biologicals, 004 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:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 August 2007 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 May 2007 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 May 2007 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of the DSSITGDPa-HBV-IPV/Hib vaccine (preservative-free formulation) in terms of antibody response to all vaccine antigens is non-inferior to that of the DTPa-HBV-IPV/Hib vaccine, one month after a three-dose primary vaccination course.

Protection of trial subjects:

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 | 12 October 2006 |
| 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 | Finland: 455 |
| Worldwide total number of subjects | 455 |
| EEA total number of subjects | 455 |

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) | 455 |
| 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:

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 (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Preservative-Free Formulation Group |

Arm description:

Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DSSITGDPa-HBV-IPV/Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

| | |
|------------------|---|
| Arm title | Preservative-Containing Formulation Group |
|------------------|---|

Arm description:

Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DSSITGDPa-HBV-IPV/Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

| | |
|------------------|---------------------|
| Arm title | Infanrix-hexa Group |
|------------------|---------------------|

Arm description:

Subjects received the licensed formulation of DTPa-HBV-IPV/Hib.

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

| | |
|--|-------------------|
| Investigational medicinal product name | Infanrix hexa |
| Investigational medicinal product code | |
| Other name | DTPa-HBV-IPV/Hib |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered intramuscularly into the anterolateral quadrant of the right thigh according to a 3-dose vaccination schedule at 2, 3 and 4 months of age.

| Number of subjects in period 1 | Preservative-Free Formulation Group | Preservative- Containing Formulation Group | Infanrix-hexa Group |
|--------------------------------|--|--|---------------------|
| | | | |
| Started | 153 | 150 | 152 |
| Completed | 151 | 148 | 152 |
| Not completed | 2 | 2 | 0 |
| Consent withdrawn by subject | - | 1 | - |
| Adverse event, non-fatal | 1 | 1 | - |
| Migrated/moved from study area | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Preservative-Free Formulation Group |
| Reporting group description: | |
| Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib. | |
| Reporting group title | Preservative-Containing Formulation Group |
| Reporting group description: | |
| Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib. | |
| Reporting group title | Infanrix-hexa Group |
| Reporting group description: | |
| Subjects received the licensed formulation of DTPa-HBV-IPV/Hib. | |

| Reporting group values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group |
|---|-------------------------------------|---|---------------------|
| Number of subjects | 153 | 150 | 152 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: weeks | | | |
| arithmetic mean | 9.9 | 10 | 10.1 |
| standard deviation | ± 1.51 | ± 1.45 | ± 1.35 |
| Gender categorical Units: Subjects | | | |
| Female | 68 | 75 | 64 |
| Male | 85 | 75 | 88 |

| Reporting group values | Total | | |
|--|----------------------------|--|--|
| Number of subjects | 455 | | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) | 0 0 0 0 0 0 | | |

| | | | |
|----------------------|-----|--|--|
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: weeks | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 207 | | |
| Male | 248 | | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Preservative-Free Formulation Group |
| Reporting group description: Subjects received the preservative-free (PF) formulation of DSSITGDPa-HBV-IPV/Hib. | |
| Reporting group title | Preservative-Containing Formulation Group |
| Reporting group description: Subjects received the preservative-containing (PC) formulation of DSSITGDPa-HBV-IPV/Hib. | |
| Reporting group title | Infanrix-hexa Group |
| Reporting group description: Subjects received the licensed formulation of DTPa-HBV-IPV/Hib. | |

Primary: Number of subjects with anti-diphtheria (Anti-D) [by Vero-cell neutralization assay] antibody concentrations equal to or above (\geq) 0.016 international units per milliliter (IU/mL)

| | |
|------------------------|---|
| End point title | Number of subjects with anti-diphtheria (Anti-D) [by Vero-cell neutralization assay] antibody concentrations equal to or above (\geq) 0.016 international units per milliliter (IU/mL) ^[1] |
| End point description: | |

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: One month after the third dose of vaccine (POST) | |

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 | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 145 | |
| Units: Subjects | | | | |
| Anti-diphtheria, POST | 135 | 133 | 145 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-tetanus toxoids (Anti-TT) antibody concentrations \geq 0.1 IU/mL

| | |
|------------------------|--|
| End point title | Number of subjects with anti-tetanus toxoids (Anti-TT) antibody concentrations \geq 0.1 IU/mL ^[2] |
| End point description: | |

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

End point timeframe:

One month after the third dose of vaccine (POST)

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 | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 146 | |
| Units: Subjects | | | | |
| Anti-tetanus, POST | 138 | 134 | 146 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations ≥ 10.0 mili-international units per illilitre (mIU/mL)

| | |
|-----------------|--|
| End point title | Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentrations ≥ 10.0 mili-international units per illilitre (mIU/mL) ^[3] |
|-----------------|--|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

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 | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 135 | 131 | 143 | |
| Units: Subjects | | | | |
| Anti-HBs, POST | 125 | 125 | 141 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polio type 1, 2 and 3 antibody titers ≥ 8

| | |
|-----------------|--|
| End point title | Number of subjects with anti-polio type 1, 2 and 3 antibody titers ≥ 8 ^[4] |
|-----------------|--|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

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 | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|------------------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 131 | 123 | 130 | |
| Units: Subjects | | | | |
| Anti-Polio 1, POST [N=128;123;121] | 119 | 114 | 117 | |
| Anti-Polio 2, POST [N=121;119;130] | 90 | 95 | 99 | |
| Anti-Polio 3, POST [N=131;122;128] | 126 | 116 | 125 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 $\mu\text{g/mL}$

| | |
|-----------------|---|
| End point title | Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 $\mu\text{g/mL}$ ^[5] |
|-----------------|---|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

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 | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 145 | |
| Units: Subjects | | | | |
| Anti-PRP, POST | 132 | 129 | 138 | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ^[6] |
|-----------------|--|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 146 | |
| Units: EL.U/ml | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, POST [N=138;134;146] | 59.2 (54.2 to 64.5) | 49.6 (44.9 to 54.8) | 67.4 (61.9 to 73.3) | |
| Anti-FHA, POST [N=138;134;146] | 135 (120.7 to 151.1) | 137.5 (122.8 to 154) | 200.3 (181.1 to 221.5) | |
| Anti-PRN, POST [N=138;134;146] | 68.6 (59.8 to 78.6) | 75.3 (64.6 to 87.7) | 119.9 (105.5 to 136.2) | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ^[7] |
|-----------------|--|

End point description:

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

End point timeframe:

Before the first dose of the vaccine (PRE)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 140 | 139 | 145 | |
| Units: EL.U/ml | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, PRE [N=140;139;145] | 3.4 (3 to 3.8) | 3.7 (3.3 to 4.2) | 3.4 (3.1 to 3.8) | |
| Anti-FHA, PRE [N=138;139;143] | 11.2 (9.3 to 13.4) | 8.8 (7.3 to 10.6) | 10 (8.5 to 11.8) | |
| Anti-PRN, PRE [N=140;139;145] | 5.8 (4.9 to 7) | 5.8 (4.9 to 7) | 4.9 (4.2 to 5.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

| | |
|-----------------|---|
| End point title | Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) |
|-----------------|---|

End point description:

Vaccine response defined as appearance of antibodies in subjects who were initially seronegative (i.e. with concentrations < cut-off value) or at least maintenance of pre-vaccination antibody concentrations in subjects who were initially seropositive (i.e. with concentrations ≥ cut-off value), taking into consideration the decreasing maternal antibodies.

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

End point timeframe:

One month after the third dose of vaccine (POST)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--------------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 134 | 131 | 142 | |
| Units: Subjects | | | | |
| Anti-PT, POST [N=134;131;142] | 132 | 127 | 141 | |
| Anti-FHA, POST [N=133;131;140] | 126 | 124 | 139 | |
| Anti-PRN, POST [N=134;131;142] | 120 | 121 | 137 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (Anti-DT) antibody concentrations ≥ 0.1 IU/mL

| | |
|-----------------|--|
| End point title | Number of subjects with anti-diphtheria (Anti-DT) antibody concentrations ≥ 0.1 IU/mL |
|-----------------|--|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 146 | |
| Units: Subjects | | | | |
| Anti-diphtheria, POST | 136 | 134 | 146 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

Before the first dose (PRE) and one month after the third dose of the vaccine (POST)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 140 | 139 | 146 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-diphtheria, PRE [N=140;139;145] | 0.174 (0.144 to 0.21) | 0.227 (0.184 to 0.282) | 0.183 (0.148 to 0.226) | |
| Anti-diphtheria, POST [N=138;134;146] | 0.51 (0.441 to 0.59) | 0.513 (0.445 to 0.592) | 0.75 (0.658 to 0.854) | |
| Anti-tetanus, PRE [N=140;139;145] | 0.654 (0.562 to 0.76) | 0.71 (0.606 to 0.833) | 0.708 (0.627 to 0.8) | |
| Anti-tetanus, POST [N=138;134;146] | 1.423 (1.28 to 1.582) | 1.438 (1.296 to 1.596) | 1.758 (1.591 to 1.941) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

| | |
|--|----------------------------------|
| End point title | Anti-HBs antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| One month after the third dose of vaccine (POST) | |

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 135 | 131 | 143 | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs, POST | 166.1 (131.6 to 209.5) | 173.4 (140.3 to 214.3) | 299 (254.1 to 351.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 antibody titers

| | |
|-----------------|--|
| End point title | Anti-polio type 1, 2 and 3 antibody titers |
|-----------------|--|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 131 | 123 | 130 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1, POST [N=128;123;121] | 36.8 (29.8 to 45.4) | 41.8 (33.5 to 52.1) | 74.6 (57.5 to 96.7) | |
| Anti-Polio 2, POST [N=121;119;130] | 21.5 (16.4 to 28.1) | 16.9 (13.5 to 21.1) | 22.4 (17.6 to 28.5) | |
| Anti-Polio 3, POST [N=131;122;128] | 51.4 (41.4 to 63.9) | 67 (52.1 to 86.1) | 113.9 (85.6 to 151.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP concentrations

| | |
|-----------------|-------------------------|
| End point title | Anti-PRP concentrations |
|-----------------|-------------------------|

End point description:

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

End point timeframe:

One month after the third dose of vaccine (POST)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|--|-------------------------------------|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 138 | 134 | 145 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP, POST [N=138;134;145] | 1.174 (0.961 to 1.435) | 1.098 (0.894 to 1.349) | 1.661 (1.326 to 2.081) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with solicited local symptoms |
|-----------------|--|

End point description:

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

End point timeframe:

Within 8 days (Day 0-Day 7) after each vaccine dose

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|---|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 153 | 150 | 152 | |
| Units: Subjects | | | | |
| Any Pain Dose 1 [N=153;150;152] | 55 | 38 | 48 | |
| Any Redness Dose 1 [N=153;150;152] | 41 | 33 | 37 | |
| Any Swelling Dose 1 [N=153;150;152] | 36 | 28 | 32 | |
| Any Pain Dose 2 [N=152;149;152] | 34 | 27 | 35 | |
| Any Redness Dose 2 [N=152;149;152] | 46 | 66 | 73 | |
| Any Swelling Dose 2 [N=152;149;152] | 33 | 36 | 46 | |
| Any Pain Dose 3 [N=151;148;152] | 17 | 16 | 24 | |
| Any Redness Dose 3 [N=151;148;152] | 49 | 53 | 67 | |
| Any Swelling Dose 3 [N=151;148;152] | 32 | 31 | 44 | |
| Any Pain Across doses [N=153;150;152] | 73 | 52 | 65 | |
| Any Redness Across doses [N=153;150;152] | 81 | 89 | 97 | |
| Any Swelling Across doses [N=153;150;152] | 62 | 65 | 75 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with solicited general symptoms |
|-----------------|--|

End point description:

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

End point timeframe:

Within 8 days (Day 0-Day 7) after each vaccine dose

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|---|-------------------------------------|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 153 | 150 | 152 | |
| Units: Subjects | | | | |
| Any Drowsiness Dose 1 [N=153;150;152] | 88 | 82 | 85 | |
| Any Fever Dose 1 [N=153;150;152] | 29 | 30 | 24 | |
| Any Irritability Dose 1 [N=153;150;152] | 114 | 102 | 112 | |
| Any Loss of appetite Dose 1 [N=153;150;152] | 45 | 32 | 32 | |
| Any Drowsiness Dose 2 [N=152;149;152] | 55 | 55 | 63 | |
| Any Fever Dose 2 [N=152;149;152] | 29 | 17 | 34 | |
| Any Irritability Dose 2 [N=152;149;152] | 87 | 85 | 99 | |
| Any Loss of appetite Dose 2 [N=152;149;152] | 28 | 32 | 19 | |
| Any Drowsiness Dose 3 [N=151;148;152] | 47 | 44 | 47 | |
| Any Fever Dose 3 [N=151;148;152] | 24 | 17 | 36 | |
| Any Irritability Dose 3 [N=151;148;152] | 74 | 68 | 82 | |
| Any Loss of appetite Dose 3 [N=151;148;152] | 28 | 25 | 20 | |
| Any Drowsiness Across doses [N=153;150;152] | 111 | 105 | 103 | |
| Any Fever Across doses [N=153;150;152] | 58 | 51 | 67 | |
| Any Irritability Across doses [N=153;150;152] | 140 | 128 | 135 | |
| Any Loss of appetite Across doses [N=153;150;152] | 66 | 58 | 51 | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Within 31 days (Day 0-Day 30)

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|---|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 153 | 150 | 152 | |
| Units: Subjects | | | | |
| AEs | 111 | 110 | 117 | |

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:

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

End point timeframe:

During the entire study period

| End point values | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group | |
|-----------------------------|---|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 153 | 150 | 152 | |
| Units: Subjects | | | | |
| SAEs | 2 | 5 | 5 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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 | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Preservative-Free Formulation Group |
|-----------------------|-------------------------------------|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | Preservative-Containing Formulation Group |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | Infanrix-hexa Group |
|-----------------------|---------------------|

Reporting group description: -

| Serious adverse events | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group |
|--|-------------------------------------|---|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 153 (1.31%) | 5 / 150 (3.33%) | 5 / 152 (3.29%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Overdose | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 0 / 150 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Listless | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 150 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 0 / 150 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 150 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 0 / 150 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 0 / 150 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 150 (0.67%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Preservative-Free Formulation Group | Preservative-Containing Formulation Group | Infanrix-hexa Group |
|---|-------------------------------------|---|---------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 111 / 153 (72.55%) | 110 / 150 (73.33%) | 117 / 152 (76.97%) |
| General disorders and administration site conditions | | | |
| Injection site induration | | | |
| subjects affected / exposed | 10 / 153 (6.54%) | 18 / 150 (12.00%) | 19 / 152 (12.50%) |
| occurrences (all) | 10 | 18 | 19 |
| Pyrexia | | | |
| subjects affected / exposed | 15 / 153 (9.80%) | 18 / 150 (12.00%) | 11 / 152 (7.24%) |
| occurrences (all) | 15 | 18 | 11 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 15 / 153 (9.80%) | 16 / 150 (10.67%) | 9 / 152 (5.92%) |
| occurrences (all) | 15 | 16 | 9 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 153 (7.84%) | 6 / 150 (4.00%) | 21 / 152 (13.82%) |
| occurrences (all) | 12 | 6 | 21 |
| Constipation | | | |

| | | | |
|--|-------------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 5 / 153 (3.27%) 5 | 11 / 150 (7.33%) 11 | 4 / 152 (2.63%) 4 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 8 / 153 (5.23%) 8 | 13 / 150 (8.67%) 13 | 9 / 152 (5.92%) 9 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 5 / 153 (3.27%) 5 | 9 / 150 (6.00%) 9 | 10 / 152 (6.58%) 10 |
| Infections and infestations Rhinitis subjects affected / exposed occurrences (all) | 28 / 153 (18.30%) 28 | 23 / 150 (15.33%) 23 | 22 / 152 (14.47%) 22 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 35 / 153 (22.88%) 35 | 16 / 150 (10.67%) 16 | 22 / 152 (14.47%) 22 |
| Otitis media subjects affected / exposed occurrences (all) | 6 / 153 (3.92%) 6 | 12 / 150 (8.00%) 12 | 13 / 152 (8.55%) 13 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 16 November 2006 | <p>Amendment 2</p> <p>GSK Biologicals is currently validating new providers of the diphtheria toxoid (Statens Serum Institute [SSI], Denmark) and of the tetanus toxoid (GSK Biologicals Korlatolt Felelossegu Tarsasag [Kft] in Gödöllő [GD], Hungary) for inclusion in DTPa based vaccines. The purpose of this study is to demonstrate that the immunogenicity of the hexavalent DSSITGDPa-HBV-IPV/Hib vaccine containing diphtheria toxoid provided by the Statens Serum Institute of Denmark (DSSI) and tetanus toxoid provided by GSK Biologicals Kft in Gödöllő (TGD) is non-inferior to the immunogenicity of the currently licensed formulation of the vaccine. The vaccine will be administered as a primary vaccination course to healthy infants at 2, 3 and 4 months of age and its safety and reactogenicity will also be assessed. Two formulations of the DSSITGDPa-HBV-IPV/Hib vaccine will be evaluated: one in which the vaccine will be manufactured according to the new preservative-free process and the other in which the vaccine will be manufactured with preservative as the currently licensed formulation.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported