



## Clinical trial results:

**A phase III, open-label study to assess the immunogenicity and reactogenicity of GSK Biologicals' combined diphtheria-tetanus-acellular pertussis-inactivated poliovirus and Haemophilus influenzae type b (DTPa-IPV/Hib) vaccine administered as a three-dose primary vaccination course at 3, 4.5 and 6 months of age and a booster dose at 18 months of age in healthy infants in Russia**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-005577-43 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date |                |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 27 October 2018 |
| First version publication date | 27 October 2018 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 116194 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02858440 |
| 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 Disclosure Advisor, GlaxoSmithKline Biologicals, (44) 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Disclosure Advisor, 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**

|  |                 |
|--|-----------------|
| Analysis stage                                       | Interim         |
| Date of interim/final analysis                       | 24 October 2017 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 October 2017 |
| Global end of trial reached?                         | No              |

Notes:

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**General information about the trial**

Main objective of the trial:

To assess the immune response to the study vaccine in terms of seroprotection status for diphtheria, tetanus, Hib and poliovirus types 1, 2 and 3 antigens, and in terms of seropositivity to the pertussis antigens, one month after the third dose of primary vaccination.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 13 September 2016 |
| 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 | Russian Federation: 235 |
| Worldwide total number of subjects   | 235                     |
| EEA total number of subjects         | 0                       |

Notes:

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**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)  | 235 |
| 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:

Results for Booster Epoch are not yet available

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 235 |
| Number of subjects completed | 235 |

### Period 1

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

### Arms

|           |                    |
|-----------|--------------------|
| Arm title | DTPa-IPV/Hib Group |
|-----------|--------------------|

Arm description:

All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

|  |  |
|--|--|
| Arm type                               | Experimental                                       |
| Investigational medicinal product name | Infanrix-IPV/Hib                                   |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and suspension for suspension for injection |
| Routes of administration               | Intramuscular use                                  |

Dosage and administration details:

Subjects received Infanrix-IPV/Hib three-dose primary vaccination course at 3, 4.5 and 6 months of age and a booster dose at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

|                                       |                    |
|---------------------------------------|--------------------|
| <b>Number of subjects in period 1</b> | DTPa-IPV/Hib Group |
| Started                               | 235                |
| Completed                             | 229                |
| Not completed                         | 6                  |
| The child left for another region     | 1                  |
| Consent withdrawal                    | 3                  |
| Lost to follow-up                     | 2                  |



## Baseline characteristics

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | DTPa-IPV/Hib Group |
|-----------------------|--------------------|

Reporting group description:

All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

| Reporting group values | DTPa-IPV/Hib Group | Total |  |
|------------------------|--------------------|-------|--|
| Number of subjects     | 235                | 235   |  |
| Age categorical        |                    |       |  |
| Units: Subjects        |                    |       |  |

|  |       |     |  |
|--|-------|-----|--|
| Age continuous   |       |     |  |
| Baseline characteristics are reported only for the Primary Epoch; results for Booster Epoch are not yet available. |       |     |  |
| Units: weeks   |       |     |  |
| arithmetic mean  | 14.1  |     |  |
| standard deviation   | ± 1.2 | -   |  |
| Gender categorical   |       |     |  |
| Baseline characteristics are reported only for the Primary Epoch; results for Booster Epoch are not yet available. |       |     |  |
| Units: Subjects  |       |     |  |
| Male   | 124   | 124 |  |
| Female   | 111   | 111 |  |
| Race/Ethnicity, Customized   |       |     |  |
| Baseline characteristics are reported only for the Primary Epoch; results for Booster Epoch are not yet available. |       |     |  |
| Units: Subjects  |       |     |  |
| White - Caucasian / European Heritage  | 235   | 235 |  |

## End points

### End points reporting groups

|   |                    |
|---|--------------------|
| Reporting group title   | DTPa-IPV/Hib Group |
| Reporting group description:<br>All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side. |                    |

### Primary: Percentage of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T), post primary vaccination

|  |  |
|--|--|
| End point title  | Percentage of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T), post primary vaccination <sup>[1]</sup> |
| End point description:<br>A seroprotected subject is a subject whose anti-D and anti-T antibody concentration was greater than or equal to ( $\geq$ ) 0.1 IU/mL.   |  |
| End point type   | Primary  |
| End point timeframe:<br>At Visit 4 (i.e. one month after 3rd dose of primary 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 scope of this end point was descriptive, no statistical hypothesis test was performed. |  |

|                                  |                    |  |  |  |
|----------------------------------|--------------------|--|--|--|
| <b>End point values</b>          | DTPa-IPV/Hib Group |  |  |  |
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 176                |  |  |  |
| Units: Percentage of subjects    |                    |  |  |  |
| number (confidence interval 95%) |                    |  |  |  |
| Anti-D antibody $\geq$ 0.1 IU/mL | 100 (97.9 to 100)  |  |  |  |
| Anti-T antibody $\geq$ 0.1 IU/mL | 100 (97.9 to 100)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post primary vaccination

|   |  |
|---|--|
| End point title   | Percentage of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post primary vaccination <sup>[2]</sup> |
| End point description:<br>A seroprotected subject is a subject whose anti-poliovirus types 1, 2 and 3 antibody titer was $\geq$ 8 ED50. |  |
| End point type  | Primary  |
| End point timeframe:<br>At Visit 4 (i.e. one month after 3rd dose of primary vaccination)   |  |

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 end point was descriptive, no statistical hypothesis test was performed.

| End point values                    | DTPa-IPV/Hib Group |  |  |  |
|-------------------------------------|--------------------|--|--|--|
| Subject group type                  | Reporting group    |  |  |  |
| Number of subjects analysed         | 151                |  |  |  |
| Units: Percentage of subjects       |                    |  |  |  |
| number (confidence interval 95%)    |                    |  |  |  |
| Anti-Polio 1 antibody $\geq$ 8 ED50 | 100 (97.6 to 100)  |  |  |  |
| Anti-Polio 2 antibody $\geq$ 8 ED50 | 100 (97.6 to 100)  |  |  |  |
| Anti-Polio 3 antibody $\geq$ 8 ED50 | 99.3 (96.4 to 100) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of seroprotected subjects for anti-polyribosyl ribitol phosphate (anti-PRP), post primary vaccination

|                 |   |
|-----------------|---|
| End point title | Percentage of seroprotected subjects for anti-polyribosyl ribitol phosphate (anti-PRP), post primary vaccination <sup>[3]</sup> |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose anti-PRP antibody concentration was  $\geq$  0.15  $\mu$ g/mL.

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

End point timeframe:

At Visit 4 (i.e. one month after 3rd dose of primary vaccination)

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 end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | DTPa-IPV/Hib Group  |  |  |  |
|--|---------------------|--|--|--|
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 182                 |  |  |  |
| Units: Percentage of subjects            |                     |  |  |  |
| number (confidence interval 95%)         |                     |  |  |  |
| Anti-PRP antibody $\geq$ 0.15 $\mu$ g/mL | 98.4 (95.3 to 99.7) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of seropositive subjects for anti-pertussis (anti- PT), anti-

**filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN), post primary vaccination**

|                 |   |
|-----------------|---|
| End point title | Percentage of seropositive subjects for anti-pertussis (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN), post primary vaccination <sup>[4]</sup> |
|-----------------|---|

End point description:

A seropositive subject is a subject whose antibody concentration was  $\geq 2.046$  IU/mL for anti-FHA,  $\geq 2.187$  IU/mL for anti-PRN and  $\geq 2.693$  IU/mL for anti-PT.

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

End point timeframe:

At Visit 4 (i.e. one month after 3rd dose of primary vaccination)

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 end point was descriptive, no statistical hypothesis test was performed.

| End point values                     | DTPa-IPV/Hib Group  |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 176                 |  |  |  |
| Units: Percentage of subjects        |                     |  |  |  |
| number (confidence interval 95%)     |                     |  |  |  |
| Anti-FHA antibody $\geq 2.046$ IU/mL | 99.4 (96.9 to 100)  |  |  |  |
| Anti-PRN antibody $\geq 2.187$ IU/mL | 99.4 (96.9 to 100)  |  |  |  |
| Anti-PT antibody $\geq 2.693$ IU/mL  | 98.9 (96.0 to 99.9) |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of seroprotected subjects for anti-D and anti-T, post booster vaccination**

|                 |  |
|-----------------|--|
| End point title | Percentage of seroprotected subjects for anti-D and anti-T, post booster vaccination |
|-----------------|--|

End point description:

A seroprotected subject is a subject whose anti-D and anti-T antibody concentration is  $\geq 0.1$  IU/mL. Results for Booster Epoch are not yet available.

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

End point timeframe:

At Visit 6 (i.e. one month after booster vaccination)



|                               |                    |  |  |  |
|-------------------------------|--------------------|--|--|--|
| <b>End point values</b>       | DTPa-IPV/Hib Group |  |  |  |
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 0 <sup>[5]</sup>   |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |

Notes:

[5] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post booster vaccination

|                 |   |
|-----------------|---|
| End point title | Percentage of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post booster vaccination |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose anti-poliovirus types 1, 2 and 3 antibody titer is  $\geq 8$  ED50. Results for Booster Epoch are not yet available.

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

End point timeframe:

At Visit 6 (i.e. one month after booster vaccination)

|                               |                    |  |  |  |
|-------------------------------|--------------------|--|--|--|
| <b>End point values</b>       | DTPa-IPV/Hib Group |  |  |  |
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 0 <sup>[6]</sup>   |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |

Notes:

[6] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of seroprotected subjects for anti-PRP, post booster vaccination

|                 |   |
|-----------------|---|
| End point title | Percentage of seroprotected subjects for anti-PRP, post booster vaccination |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose anti-PRP antibody concentration is  $\geq 0.15$  µg/mL. Results for Booster Epoch are not yet available.

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

End point timeframe:

At Visit 6 (i.e. one month after booster vaccination)

|                               |                    |  |  |  |
|-------------------------------|--------------------|--|--|--|
| <b>End point values</b>       | DTPa-IPV/Hib Group |  |  |  |
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 0 <sup>[7]</sup>   |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |

Notes:

[7] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of seropositive subjects for anti- PT, anti-FHA and anti-PRN, post booster vaccination

|                 |   |
|-----------------|---|
| End point title | Percentage of seropositive subjects for anti- PT, anti-FHA and anti-PRN, post booster vaccination |
|-----------------|---|

End point description:

A seropositive subject is a subject whose antibody concentration is  $\geq 2.046$  IU/mL for anti-FHA,  $\geq 2.187$  IU/mL for anti-PRN and  $\geq 2.693$  IU/mL for anti-PT. Results for Booster Epoch are not yet available.

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

End point timeframe:

At Visit 6 (i.e. one month after booster vaccination)

|                               |                    |  |  |  |
|-------------------------------|--------------------|--|--|--|
| <b>End point values</b>       | DTPa-IPV/Hib Group |  |  |  |
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 0 <sup>[8]</sup>   |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |

Notes:

[8] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentrations for anti-D and anti-T, post primary vaccination

|                 |   |
|-----------------|---|
| End point title | Antibody concentrations for anti-D and anti-T, post primary vaccination |
|-----------------|---|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). GMCs were expressed as International Units per milliliter (IU/mL).

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

End point timeframe:

At Visit 4 (i.e. one month after 3rd dose of primary vaccination)

|  |                     |  |  |  |
|--|---------------------|--|--|--|
| <b>End point values</b>                  | DTPa-IPV/Hib Group  |  |  |  |
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 176                 |  |  |  |
| Units: IU/mL                             |                     |  |  |  |
| geometric mean (confidence interval 95%) |                     |  |  |  |
| Anti-D antibody                          | 3.24 (2.84 to 3.68) |  |  |  |
| Anti-T antibody                          | 3.14 (2.81 to 3.51) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentrations for anti-D and anti-T, post booster vaccination

|                        |  |
|------------------------|--|
| End point title        | Antibody concentrations for anti-D and anti-T, post booster vaccination                |
| End point description: | Concentrations are expressed as GMCs. Results for Booster Epoch are not yet available. |
| End point type         | Secondary  |
| End point timeframe:   | At Visit 6 (i.e. one month after booster vaccination)                                  |

|  |                    |  |  |  |
|--|--------------------|--|--|--|
| <b>End point values</b>                  | DTPa-IPV/Hib Group |  |  |  |
| Subject group type                       | Reporting group    |  |  |  |
| Number of subjects analysed              | 0 <sup>[9]</sup>   |  |  |  |
| Units: IU/mL                             |                    |  |  |  |
| geometric mean (confidence interval 95%) | ( to )             |  |  |  |

Notes:

[9] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody titers for anti-polio types 1, 2 and 3, post primary vaccination

|                        |   |
|------------------------|---|
| End point title        | Antibody titers for anti-polio types 1, 2 and 3, post primary vaccination |
| End point description: | Titers were expressed as geometric mean titres (GMTs).                    |
| End point type         | Secondary   |
| End point timeframe:   | At Visit 4 (i.e. one month after 3rd dose of primary vaccination)         |

| End point values                         | DTPa-IPV/Hib Group      |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                       | Reporting group         |  |  |  |
| Number of subjects analysed              | 151                     |  |  |  |
| Units: Titers                            |                         |  |  |  |
| geometric mean (confidence interval 95%) |                         |  |  |  |
| Anti-Polio 1 antibody                    | 613.9 (505.5 to 745.5)  |  |  |  |
| Anti-Polio 2 antibody                    | 591.6 (487.3 to 718.3)  |  |  |  |
| Anti-Polio 3 antibody                    | 827.4 (674.7 to 1014.6) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody titers for anti-polio types 1, 2 and 3, post booster vaccination

|                        |  |
|------------------------|--|
| End point title        | Antibody titers for anti-polio types 1, 2 and 3, post booster vaccination      |
| End point description: | Titers are expressed as GMTs. Results for Booster Epoch are not yet available. |
| End point type         | Secondary  |
| End point timeframe:   | At Visit 6 (i.e. one month after booster vaccination)                          |

| End point values                         | DTPa-IPV/Hib Group |  |  |  |
|--|--------------------|--|--|--|
| Subject group type                       | Reporting group    |  |  |  |
| Number of subjects analysed              | 0 <sup>[10]</sup>  |  |  |  |
| Units: Titers                            |                    |  |  |  |
| geometric mean (confidence interval 99%) | ( to )             |  |  |  |

Notes:

[10] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentration for anti-PRP, post primary vaccination

|                        |   |
|------------------------|---|
| End point title        | Antibody concentration for anti-PRP, post primary vaccination                               |
| End point description: | Concentration was expressed as GMC. GMC was expressed as micrograms per milliliter (µg/mL). |

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| At Visit 4 (i.e. one month after 3rd dose of primary vaccination) |           |

|  |                     |  |  |  |
|--|---------------------|--|--|--|
| <b>End point values</b>                  | DTPa-IPV/Hib Group  |  |  |  |
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 182                 |  |  |  |
| Units: µg/mL                             |                     |  |  |  |
| geometric mean (confidence interval 95%) |                     |  |  |  |
| µg/mL                                    | 2.97 (2.48 to 3.54) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentration for anti-PRP, post booster vaccination

|   |   |
|---|---|
| End point title   | Antibody concentration for anti-PRP, post booster vaccination |
| End point description:  |   |
| Concentration is expressed as GMC. Results for Booster Epoch are not yet available. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| At Visit 6 (i.e. one month after booster vaccination)                               |   |

|  |                    |  |  |  |
|--|--------------------|--|--|--|
| <b>End point values</b>                  | DTPa-IPV/Hib Group |  |  |  |
| Subject group type                       | Reporting group    |  |  |  |
| Number of subjects analysed              | 0 <sup>[11]</sup>  |  |  |  |
| Units: µg/mL                             |                    |  |  |  |
| geometric mean (confidence interval 95%) | ( to )             |  |  |  |

Notes:

[11] - Results for Booster Epoch are not yet available.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post primary vaccination

|                 |  |
|-----------------|--|
| End point title | Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post primary vaccination |
|-----------------|--|

End point description:

Concentrations were expressed as GMCs.

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

End point timeframe:

At Visit 4 (i.e. one month after 3rd dose of primary vaccination)

| End point values                         | DTPa-IPV/Hib Group     |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 176                    |  |  |  |
| Units: IU/mL                             |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| Anti-FHA antibody                        | 120.2 (107.0 to 135.1) |  |  |  |
| Anti-PRN antibody                        | 166.1 (146.8 to 187.8) |  |  |  |
| Anti-PT antibody                         | 65.0 (57.7 to 73.2)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post booster vaccination

|                 |  |
|-----------------|--|
| End point title | Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post booster vaccination |
|-----------------|--|

End point description:

Concentrations are expressed as GMCs. Results for Booster Epoch are not yet available.

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

End point timeframe:

At Visit 6 (i.e. one month after booster vaccination)

| End point values                         | DTPa-IPV/Hib Group |  |  |  |
|--|--------------------|--|--|--|
| Subject group type                       | Reporting group    |  |  |  |
| Number of subjects analysed              | 0 <sup>[12]</sup>  |  |  |  |
| Units: IU/mL                             |                    |  |  |  |
| geometric mean (confidence interval 95%) | ( to )             |  |  |  |

Notes:

[12] - Results for Booster Epoch are not yet available.

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of subjects with any solicited local adverse events (AEs) following each dose of primary vaccination**

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|                 |   |
|-----------------|---|
| End point title | Number of subjects with any solicited local adverse events (AEs) following each dose of primary vaccination |
|-----------------|---|

End point description:

Assessed solicited local AEs were pain, redness and swelling at injection site. Any = Occurrence of the AE regardless of the intensity grade.

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

End point timeframe:

During the 4-day follow-up period after each primary vaccination dose

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| End point values             | DTPa-IPV/Hib Group |  |  |  |
|------------------------------|--------------------|--|--|--|
| Subject group type           | Reporting group    |  |  |  |
| Number of subjects analysed  | 232                |  |  |  |
| Units: Participants          |                    |  |  |  |
| Any Pain, Dose 1             | 58                 |  |  |  |
| Any Redness, Dose 1          | 83                 |  |  |  |
| Any Swelling, Dose 1         | 45                 |  |  |  |
| Any Pain, Dose 2 (N=229)     | 47                 |  |  |  |
| Any Redness, Dose 2 (N=229)  | 89                 |  |  |  |
| Any Swelling, Dose 2 (N=229) | 58                 |  |  |  |
| Any Pain, Dose 3 (N=226)     | 50                 |  |  |  |
| Any Redness, Dose 3 (N=226)  | 96                 |  |  |  |
| Any Swelling, Dose 3 (N=226) | 63                 |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of subjects with any solicited local AEs following booster vaccination**

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|                 |   |
|-----------------|---|
| End point title | Number of subjects with any solicited local AEs following booster vaccination |
|-----------------|---|

End point description:

Assessed solicited local AEs are pain, redness and swelling at injection site. Any = Occurrence of the AE regardless of the intensity grade. Results for Booster Epoch are not yet available.

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

End point timeframe:

During the 4-day follow-up period after booster vaccination dose

---

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | DTPa-IPV/Hib Group |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 0 <sup>[13]</sup>  |  |  |  |
| Units: Participants         |                    |  |  |  |

Notes:

[13] - Results for Booster Epoch are not yet available.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any solicited general AEs following each dose of primary vaccination

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any solicited general AEs following each dose of primary vaccination |
|-----------------|--|

End point description:

Assessed solicited general AEs were drowsiness, irritability/fussiness, loss of appetite and fever. Any = Occurrence of the AE regardless of the intensity grade. Any fever = Fever (axillary)  $\geq 37.5^{\circ}\text{C}$ .

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

End point timeframe:

During the 4-day follow-up period after each primary vaccination dose

|   |                    |  |  |  |
|---|--------------------|--|--|--|
| <b>End point values</b>   | DTPa-IPV/Hib Group |  |  |  |
| Subject group type  | Reporting group    |  |  |  |
| Number of subjects analysed                                       | 232                |  |  |  |
| Units: Participants   |                    |  |  |  |
| Any Drowsiness, Dose 1  | 82                 |  |  |  |
| Any Irritability / Fussiness, Dose 1                              | 100                |  |  |  |
| Any Loss Of Appetite, Dose 1                                      | 33                 |  |  |  |
| Any Temperature/(Axillary) ( $^{\circ}\text{C}$ ), Dose 1         | 14                 |  |  |  |
| Any Drowsiness, Dose 2 (N=230)                                    | 69                 |  |  |  |
| Any Irritability / Fussiness, Dose 2 (N=230)                      | 104                |  |  |  |
| Any Loss Of Appetite, Dose 2 (N=230)                              | 34                 |  |  |  |
| Any Temperature/(Axillary) ( $^{\circ}\text{C}$ ), Dose 2 (N=230) | 32                 |  |  |  |
| Any Drowsiness, Dose 3 (N=225)                                    | 65                 |  |  |  |
| Any Irritability / Fussiness, Dose 3 (N=225)                      | 106                |  |  |  |
| Any Loss Of Appetite, Dose 3 (N=225)                              | 43                 |  |  |  |
| Any Temperature/(Axillary) ( $^{\circ}\text{C}$ ), Dose 3 (N=225) | 28                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point



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**Secondary: Number of subjects with any solicited general AEs following booster vaccination**

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|                 |   |
|-----------------|---|
| End point title | Number of subjects with any solicited general AEs following booster vaccination |
|-----------------|---|

End point description:

Assessed solicited general AEs are drowsiness, irritability/fussiness, loss of appetite and fever. Any = Occurrence of the AE regardless of the intensity grade. Any fever = Fever (axillary)  $\geq 37.5^{\circ}\text{C}$ . Results for Booster Epoch are not yet available.

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

End point timeframe:

During the 4-day follow-up period after booster vaccination dose

---

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | DTPa-IPV/Hib Group |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 0 <sup>[14]</sup>  |  |  |  |
| Units: Participants         |                    |  |  |  |

Notes:

[14] - Results for Booster Epoch are not yet available.

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of subjects with unsolicited AEs following each dose of primary vaccination**

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|                 |  |
|-----------------|--|
| End point title | Number of subjects with unsolicited AEs following each dose of primary vaccination |
|-----------------|--|

End point description:

Unsolicited AE was defined as any AE reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of the AE regardless of the intensity grade.

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

End point timeframe:

During the 31-day follow-up period after each primary vaccination dose

---

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | DTPa-IPV/Hib Group |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 235                |  |  |  |
| Units: Participants         |                    |  |  |  |
| Participants                | 41                 |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

### Secondary: Number of subjects with unsolicited AEs following booster vaccination

|   |   |
|---|---|
| End point title   | Number of subjects with unsolicited AEs following booster vaccination |
| End point description:<br>Unsolicited AE is defined as any AE reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of the AE regardless of the intensity grade. Results for Booster Epoch are not yet available. |   |
| End point type  | Secondary   |
| End point timeframe:<br>During the 31-day follow-up period after booster vaccination dose   |   |

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | DTPa-IPV/Hib Group |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 0 <sup>[15]</sup>  |  |  |  |
| Units: Participants         |                    |  |  |  |

Notes:

[15] - Results for Booster Epoch are not yet available.

### 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:<br>SAEs assessed include any untoward medical occurrences that resulted in death, were life threatening, required hospitalisation or prolongation of existing hospitalisation or resulted in disability/incapacity. Any = Occurrence of the AE regardless of the intensity grade. SAEs are reported only for the Primary Epoch; results for Booster Epoch are not yet available. |   |
| End point type  | Secondary   |
| End point timeframe:<br>From Day 0 up to Visit 4 (i.e. one month after 3rd dose of primary vaccination)   |   |

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | DTPa-IPV/Hib Group |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 235                |  |  |  |
| Units: Participants         |                    |  |  |  |
| Participants                | 1                  |  |  |  |

### Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local & general AEs: during the 4-day follow-up period after each primary & booster vaccination. Unsolicited AEs: during the 31-day follow-up period after each primary & booster vaccination. SAEs: from Day 0 up to Visit 4.

Adverse event reporting additional description:

Solicited local and general AEs, unsolicited AEs and SAEs are reported only for the Primary Epoch; results for Booster Epoch are not yet available.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | DTPa-IPV/Hib Group |
|-----------------------|--------------------|

Reporting group description:

All subjects received three doses of primary vaccination of the study vaccine, DTPa-IPV/Hib, at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

| Serious adverse events                            | DTPa-IPV/Hib Group |  |  |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events |                    |  |  |
| subjects affected / exposed                       | 1 / 235 (0.43%)    |  |  |
| number of deaths (all causes)                     | 0                  |  |  |
| number of deaths resulting from adverse events    | 0                  |  |  |
| Gastrointestinal disorders                        |                    |  |  |
| Proctitis   |                    |  |  |
| subjects affected / exposed                       | 1 / 235 (0.43%)    |  |  |
| occurrences causally related to treatment / all   | 1 / 1              |  |  |
| deaths causally related to treatment / all        | 0 / 0              |  |  |
| Anal fistula                                      |                    |  |  |
| subjects affected / exposed                       | 1 / 235 (0.43%)    |  |  |
| occurrences causally related to treatment / all   | 1 / 1              |  |  |
| deaths causally related to treatment / all        | 0 / 0              |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | DTPa-IPV/Hib Group |  |  |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 190 / 235 (80.85%) |  |  |
| Congenital, familial and genetic disorders            |                    |  |  |
| Developmental hip dysplasia                           |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Cardiac disorders                                     |                    |  |  |
| Cardiovascular disorder                               |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Nervous system disorders                              |                    |  |  |
| Autonomic nervous system imbalance                    |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Dystonia  |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Hydrocephalus   |                    |  |  |
| subjects affected / exposed                           | 2 / 235 (0.85%)    |  |  |
| occurrences (all)                                     | 2                  |  |  |
| Idiopathic intracranial hypertension                  |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Motor dysfunction                                     |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Poor quality sleep                                    |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Somnolence  |                    |  |  |
| subjects affected / exposed                           | 122 / 235 (51.91%) |  |  |
| occurrences (all)                                     | 216                |  |  |
| Tremor  |                    |  |  |
| subjects affected / exposed                           | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |

|  |                    |  |  |
|--|--------------------|--|--|
| Blood and lymphatic system disorders                 |                    |  |  |
| Anaemia  |                    |  |  |
| subjects affected / exposed                          | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                    | 1                  |  |  |
| General disorders and administration site conditions |                    |  |  |
| Injection site erythema                              |                    |  |  |
| subjects affected / exposed                          | 122 / 235 (51.91%) |  |  |
| occurrences (all)                                    | 268                |  |  |
| Injection site pain                                  |                    |  |  |
| subjects affected / exposed                          | 77 / 235 (32.77%)  |  |  |
| occurrences (all)                                    | 155                |  |  |
| Injection site swelling                              |                    |  |  |
| subjects affected / exposed                          | 83 / 235 (35.32%)  |  |  |
| occurrences (all)                                    | 166                |  |  |
| Pyrexia  |                    |  |  |
| subjects affected / exposed                          | 55 / 235 (23.40%)  |  |  |
| occurrences (all)                                    | 78                 |  |  |
| Immune system disorders                              |                    |  |  |
| Food allergy   |                    |  |  |
| subjects affected / exposed                          | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                    | 1                  |  |  |
| Hypersensitivity                                     |                    |  |  |
| subjects affected / exposed                          | 2 / 235 (0.85%)    |  |  |
| occurrences (all)                                    | 2                  |  |  |
| Gastrointestinal disorders                           |                    |  |  |
| Constipation   |                    |  |  |
| subjects affected / exposed                          | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                    | 2                  |  |  |
| Flatulence   |                    |  |  |
| subjects affected / exposed                          | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                    | 1                  |  |  |
| Infantile colic                                      |                    |  |  |
| subjects affected / exposed                          | 1 / 235 (0.43%)    |  |  |
| occurrences (all)                                    | 2                  |  |  |
| Regurgitation  |                    |  |  |

|   |                           |  |  |
|---|---------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 235 (0.43%)<br>1      |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 1 / 235 (0.43%)<br>1      |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)      | 2 / 235 (0.85%)<br>2      |  |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis allergic<br>subjects affected / exposed<br>occurrences (all) | 1 / 235 (0.43%)<br>1      |  |  |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)   | 1 / 235 (0.43%)<br>2      |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 4 / 235 (1.70%)<br>4      |  |  |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)  | 1 / 235 (0.43%)<br>1      |  |  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 1 / 235 (0.43%)<br>1      |  |  |
| Psychiatric disorders<br>Agitation<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 235 (0.43%)<br>1      |  |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)  | 150 / 235 (63.83%)<br>310 |  |  |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 235 (0.85%)<br>2      |  |  |

|                                   |                 |  |  |
|-----------------------------------|-----------------|--|--|
| Ear infection                     |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Nasopharyngitis                   |                 |  |  |
| subjects affected / exposed       | 2 / 235 (0.85%) |  |  |
| occurrences (all)                 | 2               |  |  |
| Pharyngitis                       |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Respiratory tract infection       |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Respiratory tract infection viral |                 |  |  |
| subjects affected / exposed       | 3 / 235 (1.28%) |  |  |
| occurrences (all)                 | 4               |  |  |
| Rhinitis                          |                 |  |  |
| subjects affected / exposed       | 9 / 235 (3.83%) |  |  |
| occurrences (all)                 | 10              |  |  |
| Tracheitis                        |                 |  |  |
| subjects affected / exposed       | 2 / 235 (0.85%) |  |  |
| occurrences (all)                 | 2               |  |  |
| Tracheobronchitis                 |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Upper respiratory tract infection |                 |  |  |
| subjects affected / exposed       | 3 / 235 (1.28%) |  |  |
| occurrences (all)                 | 4               |  |  |
| Urinary tract infection           |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Varicella                         |                 |  |  |
| subjects affected / exposed       | 1 / 235 (0.43%) |  |  |
| occurrences (all)                 | 1               |  |  |
| Viral infection                   |                 |  |  |
| subjects affected / exposed       | 3 / 235 (1.28%) |  |  |
| occurrences (all)                 | 3               |  |  |



|  |                          |  |  |
|--|--------------------------|--|--|
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 74 / 235 (31.49%)<br>110 |  |  |
|--|--------------------------|--|--|

## **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