



## Clinical trial results:

**A phase IV, open-label, non-randomised, multi-centre study to assess the immunogenicity and safety of Infanrix hexa? administered as primary vaccination in healthy infants born to mothers given Boostrix? during pregnancy or post-delivery in 116945 [DTPA (BOOSTRIX)-047].**

### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2014-001117-41             |
| Trial protocol           | ES CZ Outside EU/EEA FI IT |
| Global end of trial date | 07 March 2018              |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 06 April 2019 |
| First version publication date | 06 April 2019 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 201330 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02422264 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 044 8664357343, 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                       | 26 November 2018 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 07 March 2018    |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To assess the immunological response to Infanrix hexa in terms of seroprotection status for diphtheria, tetanus, hepatitis B, poliovirus and Hib antigens, and in terms of vaccine response for the pertussis antigens, one month after the last dose of the primary vaccination in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 22 January 2016 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 38      |
| Country: Number of subjects enrolled | Canada: 144        |
| Country: Number of subjects enrolled | Czech Republic: 71 |
| Country: Number of subjects enrolled | Finland: 52        |
| Country: Number of subjects enrolled | Italy: 14          |
| Country: Number of subjects enrolled | Spain: 282         |
| Worldwide total number of subjects   | 601                |
| EEA total number of subjects         | 419                |

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          | 601 |

|                           |   |
|---------------------------|---|
| months)                   |   |
| 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:

Out of 601 subjects enrolled in the study, only 592 were vaccinated.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

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

Arm description:

Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevnar 13 according to the routine national immunisation schedule.

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Infanrix hexa Prevnar 13 |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

All subjects received Infanrix hexa co-administered with Prevnar 13 at 2, 4 and 6 months or 2, 3 and 4 months, depending on the immunization schedule of the country. In some countries/regions, Prevnar 13 was given as a 2-dose schedule at 2 and 4 months of age.

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

Arm description:

Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevnar 13 according to the routine national immunisation schedule.

|  |                          |
|--|--------------------------|
| Arm type                               | Active comparator        |
| Investigational medicinal product name | Infanrix hexa Prevnar 13 |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

All subjects received Infanrix hexa co-administered with Prevnar 13 at 2, 4 and 6 months or 2, 3 and 4 months, depending on the immunization schedule of the country. In some countries/regions, Prevnar 13 was given as a 2-dose schedule at 2 and 4 months of age.

| <b>Number of subjects in period 1</b>   | dTpa Group | Control Group |
|---|------------|---------------|
| Started                                 | 296        | 305           |
| Completed                               | 291        | 301           |
| Not completed                           | 5          | 4             |
| Consent withdrawn by subject            | 1          | 2             |
| Migrated/moved from study area          | 3          | 1             |
| Subject vaccinated outside of the study | -          | 1             |
| Serious Adverse Event                   | 1          | -             |

## Baseline characteristics

### Reporting groups

|   |               |
|---|---------------|
| Reporting group title   | dTpa Group    |
| Reporting group description:  |               |
| Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule. |               |
| Reporting group title   | Control Group |
| Reporting group description:  |               |
| Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule. |               |

| Reporting group values                             | dTpa Group | Control Group | Total |
|--|------------|---------------|-------|
| Number of subjects                                 | 296        | 305           | 601   |
| Age categorical                                    |            |               |       |
| Units: Subjects                                    |            |               |       |
| In utero   | 0          | 0             | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0          | 0             | 0     |
| Newborns (0-27 days)                               | 0          | 0             | 0     |
| Infants and toddlers (28 days-23 months)           | 296        | 305           | 601   |
| Children (2-11 years)                              | 0          | 0             | 0     |
| Adolescents (12-17 years)                          | 0          | 0             | 0     |
| Adults (18-64 years)                               | 0          | 0             | 0     |
| From 65-84 years                                   | 0          | 0             | 0     |
| 85 years and over                                  | 0          | 0             | 0     |
| Age Continuous                                     |            |               |       |
| Age at Dose 1                                      |            |               |       |
| Units: Weeks                                       |            |               |       |
| arithmetic mean                                    | 8.7        | 8.9           |       |
| standard deviation                                 | ± 1.6      | ± 1.8         | -     |
| Sex: Female, Male                                  |            |               |       |
| Units: Subjects                                    |            |               |       |
| Female   | 141        | 144           | 285   |
| Male   | 155        | 161           | 316   |
| Race/Ethnicity, Customized                         |            |               |       |
| Units: Subjects                                    |            |               |       |
| African Heritage / African American                | 4          | 9             | 13    |
| Asian - East Asian Heritage                        | 2          | 0             | 2     |
| Asian - South East Asian Heritage                  | 3          | 0             | 3     |
| White - Arabic / North African Heritage            | 1          | 3             | 4     |
| White - Caucasian / European Heritage              | 268        | 285           | 553   |
| Mixed origin                                       | 18         | 8             | 26    |

## End points

### End points reporting groups

|   |               |
|---|---------------|
| Reporting group title   | dTpa Group    |
| Reporting group description:<br>Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule. |               |
| Reporting group title   | Control Group |
| Reporting group description:<br>Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule. |               |

### Primary: Number of subjects with vaccine response against Pertussis Toxoid (PT), Filamentous Haemagglutinin (FHA) and Pertactin (PRN) antigens

|  |  |
|--|--|
| End point title  | Number of subjects with vaccine response against Pertussis Toxoid (PT), Filamentous Haemagglutinin (FHA) and Pertactin (PRN) antigens <sup>[1]</sup> |
| End point description:<br>Vaccine response to the PT, FHA and PRN antigens, is defined as the appearance of antibodies in subjects who were initially seronegative (i.e., with concentrations lower than (<) the cut-off value of the assay), or at least maintenance of pre-vaccination antibody concentrations in subjects who were initially seropositive (i.e., with concentrations greater than or equal to (≥) the cut-off value of the assay). Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA, 2.187 IU/mL for anti-PRN. |  |
| End point type   | Primary  |
| End point timeframe:<br>1 month after the last dose of the 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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.  |  |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 240             | 251             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-PT antibody            | 185             | 249             |  |  |
| anti-FHA antibody           | 95              | 238             |  |  |
| anti-PRN antibody           | 90              | 225             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroprotected subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentration above or equal to the assay cut-off

|   |  |
|---|--|
| End point title   | Number of seroprotected subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentration above or equal to the assay cut-off <sup>[2]</sup> |
| End point description:<br>A seroprotected subject is a subject whose antibody concentration/titre was $\geq$ the level defining clinical protection, of 0.1 International Units per milliliter (IU/mL).   |  |
| End point type  | Primary  |
| End point timeframe:<br>1 month after the last dose of the primary vaccination  |  |
| Notes:<br>[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.<br>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed. |  |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 266             | 271             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-D antibody             | 264             | 271             |  |  |
| anti-T antibody             | 266             | 271             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroprotected subjects with anti Hepatitis B (anti-HBs) antibody concentration above or equal to the assay cut-off

|   |   |
|---|---|
| End point title   | Number of seroprotected subjects with anti Hepatitis B (anti-HBs) antibody concentration above or equal to the assay cut-off <sup>[3]</sup> |
| End point description:<br>A seroprotected subject is a subject whose antibody concentration/titre was $\geq$ to the level defining clinical protection, of 10 micro International Units per milliliter (mIU/mL).  |   |
| End point type  | Primary   |
| End point timeframe:<br>1 month after the last dose of the primary vaccination  |   |
| Notes:<br>[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.<br>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed. |   |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 253             | 263             |  |  |
| Units: Participants         | 251             | 259             |  |  |



## Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroprotected subjects with anti-poliovirus type 1, 2 and 3 antibody concentration above or equal to 8

|                 |   |
|-----------------|---|
| End point title | Number of seroprotected subjects with anti-poliovirus type 1, 2 and 3 antibody concentration above or equal to 8 <sup>[4]</sup> |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose antibody titre was  $\geq$  the level defining clinical protection, of 8 ED50.

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

End point timeframe:

1 month after the last dose of the 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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 241             | 245             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-Polio 1 antibody       | 233             | 242             |  |  |
| anti-Polio 2 antibody       | 239             | 235             |  |  |
| anti-Polio 3 antibody       | 228             | 236             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroprotected subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration above or equal to the assay cut-off

|                 |   |
|-----------------|---|
| End point title | Number of seroprotected subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration above or equal to the assay cut-off <sup>[5]</sup> |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose antibody concentration/titre was  $\geq$  the level defining clinical protection, of 0.15 micrograms per milliliter ( $\mu\text{g/mL}$ ).

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

End point timeframe:

1 month after the last dose of the primary vaccination

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

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 266             | 271             |  |  |
| Units: Participants         | 255             | 256             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-D and anti-T antibody concentrations.

|   |  |
|---|--|
| End point title   | Anti-D and anti-T antibody concentrations. |
| End point description:<br>Antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in IU/mL. |  |
| End point type  | Secondary                                  |
| End point timeframe:<br>Before the first dose of Infanrix hexa  |  |

| End point values                         | dTpa Group             | Control Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 242                    | 253                    |  |  |
| Units: IU/mL                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| anti-D antibody, before dose 1           | 0.423 (0.354 to 0.506) | 0.089 (0.076 to 0.103) |  |  |
| anti-T antibody, before dose 1           | 2.152 (1.925 to 2.406) | 0.378 (0.330 to 0.434) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations.

|  |   |
|--|---|
| End point title  | Anti-PT, anti-FHA and anti-PRN antibody concentrations. |
| End point description:<br>Anti-PT, anti-FHA and anti-PRN antibody concentrations were expressed as GMCs and measured in IU/mL. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Before the first dose of Infanrix hexa   |   |

| End point values                         | dTpa Group           | Control Group    |  |  |
|--|----------------------|------------------|--|--|
| Subject group type                       | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed              | 242                  | 253              |  |  |
| Units: IU/ml                             |                      |                  |  |  |
| geometric mean (confidence interval 95%) |                      |                  |  |  |
| anti-PT antibody                         | 11.9 (10.3 to 13.6)  | 2.2 (2.0 to 2.5) |  |  |
| anti-FHA antibody                        | 88.3 (77.7 to 100.4) | 6.6 (5.7 to 7.7) |  |  |
| anti-PRN antibody                        | 70.5 (56.1 to 88.5)  | 4.5 (3.7 to 5.4) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-D and anti-T antibody concentrations

|   |   |
|---|---|
| End point title   | Anti-D and anti-T antibody concentrations |
| End point description:<br>Antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in IU/mL. |   |
| End point type  | Secondary                                 |
| End point timeframe:<br>1 month after the last dose of the primary vaccination  |   |

| End point values                         | dTpa Group             | Control Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 266                    | 271                    |  |  |
| Units: IU/ml                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| anti-Diphtheria antibody                 | 1.747 (1.598 to 1.910) | 2.746 (2.502 to 3.015) |  |  |
| anti-Tetanus antibody                    | 2.347 (2.135 to 2.582) | 2.278 (2.069 to 2.508) |  |  |

## 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:<br>Anti-Polio type 1, 2 and 3 antibody titers were expressed as geometric mean titers (GMT). |  |
| End point type  | Secondary                                  |

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values                         | dTpa Group             | Control Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 241                    | 245                    |  |  |
| Units: Titers                            |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| anti-Polio 1 antibody                    | 432.1 (351.8 to 530.9) | 489.9 (402.6 to 596.0) |  |  |
| anti-Polio 2 antibody                    | 424.6 (342.7 to 526.2) | 388.4 (306.3 to 492.6) |  |  |
| anti-Polio 3 antibody                    | 730.6 (596.5 to 894.9) | 775.6 (645.9 to 931.3) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

End point title Anti-PRP antibody concentrations

End point description:

Anti-PRP antibody concentrations were expressed as GMCs and measured in µg/mL.

End point type Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values                         | dTpa Group             | Control Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 266                    | 271                    |  |  |
| Units: µg/mL                             |                        |                        |  |  |
| geometric mean (confidence interval 95%) | 1.862 (1.554 to 2.231) | 1.717 (1.428 to 2.064) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PT, anti-FHA, anti-PRN antibody concentrations

End point title Anti-PT, anti-FHA, anti-PRN antibody concentrations

End point description:

Anti-PT, anti-FHA, anti-PRN antibody concentrations were expressed as GMCs and measured in IU/mL.

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

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values                         | dTpa Group          | Control Group         |  |  |
|--|---------------------|-----------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed              | 266                 | 271                   |  |  |
| Units: IU/mL                             |                     |                       |  |  |
| geometric mean (confidence interval 95%) |                     |                       |  |  |
| anti-PT antibody                         | 32.7 (30.2 to 35.3) | 54.7 (51.0 to 58.6)   |  |  |
| anti-FHA antibody                        | 68.5 (63.5 to 73.9) | 103.5 (95.6 to 112.1) |  |  |
| anti-PRN antibody                        | 60.5 (54.2 to 67.6) | 92.0 (81.6 to 103.6)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-pneumococcal antibody concentrations

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

End point description:

Assessed anti-pneumococcal serotypes were (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F), expressed as GMCs and measured in µg/mL.

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

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values                         | dTpa Group          | Control Group       |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 232                 | 237                 |  |  |
| Units: µg/mL                             |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| anti-PnPS 1 antibody                     | 1.61 (1.43 to 1.80) | 1.92 (1.73 to 2.14) |  |  |
| anti-PnPS 3 antibody                     | 0.54 (0.49 to 0.60) | 0.60 (0.55 to 0.67) |  |  |
| anti-PnPS 4 antibody                     | 1.20 (1.07 to 1.35) | 1.56 (1.40 to 1.75) |  |  |
| anti-PnPS 5 antibody                     | 1.09 (0.96 to 1.24) | 1.27 (1.13 to 1.43) |  |  |

|                        |                     |                     |  |  |
|------------------------|---------------------|---------------------|--|--|
| anti-PnPS 6A antibody  | 2.16 (1.89 to 2.47) | 2.59 (2.27 to 2.95) |  |  |
| anti-PnPS 6B antibody  | 1.37 (1.12 to 1.68) | 1.44 (1.20 to 1.73) |  |  |
| anti-PnPS 7F antibody  | 2.39 (2.15 to 2.65) | 2.67 (2.43 to 2.93) |  |  |
| anti-PnPS 9V antibody  | 1.33 (1.19 to 1.50) | 1.64 (1.47 to 1.83) |  |  |
| anti-PnPS 14 antibody  | 5.70 (4.99 to 6.52) | 6.57 (5.71 to 7.56) |  |  |
| anti-PnPS 18C antibody | 1.61 (1.42 to 1.82) | 1.79 (1.59 to 2.01) |  |  |
| anti-PnPS 19A antibody | 1.61 (1.43 to 1.82) | 2.01 (1.78 to 2.27) |  |  |
| anti-PnPS 19F antibody | 2.57 (2.35 to 2.82) | 3.24 (2.92 to 3.60) |  |  |
| anti-PnPS 23F antibody | 0.86 (0.74 to 0.99) | 1.02 (0.88 to 1.17) |  |  |

## 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:<br>Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Solicited local symptoms were assessed by each and across dose. |  |
| End point type  | Secondary  |
| End point timeframe:<br>During the 4-day (Day 0-Day 3) follow-up period after each vaccination  |  |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 294             | 303             |  |  |
| Units: Participants         |                 |                 |  |  |
| Any Pain, Dose 1            | 120             | 120             |  |  |
| Any Redness, Dose 1         | 128             | 116             |  |  |
| Any Swelling, Dose 1        | 81              | 87              |  |  |
| Any Pain, Dose 2            | 109             | 101             |  |  |
| Any Redness, Dose 2         | 139             | 139             |  |  |
| Any Swelling, Dose 2        | 98              | 95              |  |  |
| Any Pain, Dose 3            | 85              | 94              |  |  |
| Any Redness, Dose 3         | 122             | 134             |  |  |
| Any Swelling, Dose 3        | 77              | 109             |  |  |
| Any Pain, Across Doses      | 175             | 184             |  |  |
| Any Redness, Across Doses   | 205             | 203             |  |  |
| Any Swelling, Across Doses  | 157             | 168             |  |  |

## 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:

Assessed solicited general symptoms were drowsiness, irritability/fussiness, loss of appetite and fever [defined as axillary route temperature  $\geq 37.5$  degrees Celsius ( $^{\circ}\text{C}$ )]. Any = occurrence of the symptom regardless of intensity grade. Solicited general symptoms were assessed by each and across dose.

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

End point timeframe:

During the 4-day (Day 0-Day 3) follow-up period after each vaccination

| End point values   | dTpa Group      | Control Group   |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type   | Reporting group | Reporting group |  |  |
| Number of subjects analysed  | 294             | 303             |  |  |
| Units: Participants  |                 |                 |  |  |
| Any Drowsiness, Dose 1   | 166             | 174             |  |  |
| Any Irritability / Fussiness, Dose 1                                     | 187             | 191             |  |  |
| Any Loss of Appetite, Dose 1   | 85              | 94              |  |  |
| Any Temperature/(Axillary) ( $\geq 37.5^{\circ}\text{C}$ ), Dose 1       | 64              | 69              |  |  |
| Any Drowsiness, Dose 2   | 142             | 149             |  |  |
| Any Irritability / Fussiness, Dose 2                                     | 182             | 194             |  |  |
| Any Loss of Appetite, Dose 2   | 69              | 94              |  |  |
| Any Temperature/(Axillary) ( $\geq 37.5^{\circ}\text{C}$ ), Dose 2       | 62              | 76              |  |  |
| Any Drowsiness, Dose 3   | 99              | 104             |  |  |
| Any Irritability / Fussiness, Dose 3                                     | 142             | 161             |  |  |
| Any Loss of Appetite, Dose 3   | 64              | 63              |  |  |
| Any Temperature/(Axillary) ( $\geq 37.5^{\circ}\text{C}$ ), Dose 3       | 52              | 47              |  |  |
| Any Drowsiness, Across Doses   | 216             | 232             |  |  |
| Any Irritability/Fussiness, Across Doses                                 | 255             | 257             |  |  |
| Any Loss of appetite, Across Doses                                       | 142             | 157             |  |  |
| Any Temperature/(Axillary) ( $\geq 37.5^{\circ}\text{C}$ ), Across Doses | 125             | 126             |  |  |

## Statistical analyses

No statistical analyses for this end point

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

|  |  |
|--|--|
| End point title  | Number of subjects with unsolicited adverse events |
| End point description:<br>An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any is defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. |  |
| End point type   | Secondary  |
| End point timeframe:<br>During the 31-day (days 0-30) follow-up period after each vaccination  |  |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 296             | 305             |  |  |
| Units: Participants         | 161             | 173             |  |  |

### 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 included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. |   |
| End point type  | Secondary   |
| End point timeframe:<br>From Day 0, prior to vaccination until the study end, at Month 3 or 5 (depending on vaccination schedule of the country)  |   |

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 296             | 305             |  |  |
| Units: Participants         | 7               | 17              |  |  |

### Statistical analyses

No statistical analyses for this end point



**Secondary: Number of seroprotected subjects against diphtheria (anti-D) and tetanus (anti-T) antibody concentration above or equal to the assay cut-off.**

|                 |   |
|-----------------|---|
| End point title | Number of seroprotected subjects against diphtheria (anti-D) and tetanus (anti-T) antibody concentration above or equal to the assay cut-off. |
|-----------------|---|

End point description:

A seroprotected subject is a subject whose antibody concentration was  $\geq$  the level defining clinical protection, of 0.1 IU/mL.

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

End point timeframe:

Before the first dose of Infanrix hexa

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 242             | 253             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-D antibody             | 200             | 110             |  |  |
| anti-T antibody             | 240             | 225             |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentration above or equal to the assay cut-off.**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentration above or equal to the assay cut-off. |
|-----------------|--|

End point description:

A seropositive subject is a subject whose antibody concentration is  $\geq$  the assay cut-off defined. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA, 2.187 IU/mL for anti-PRN

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

End point timeframe:

Before the first dose of Infanrix hexa

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 242             | 253             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-PT antibody            | 218             | 88              |  |  |
| anti-FHA antibody           | 242             | 210             |  |  |
| anti-PRN antibody           | 231             | 151             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-HBs antibody concentrations

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

End point description:

Anti-HBs antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in mIU/mL.

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

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values                         | dTpa Group                | Control Group             |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed              | 253                       | 263                       |  |  |
| Units: mIU/ml                            |                           |                           |  |  |
| geometric mean (confidence interval 95%) | 1322.8 (1116.7 to 1567.0) | 1339.2 (1132.8 to 1583.3) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with anti-PT, anti-FHA, anti-PRN antibody concentration above or equal to the assay cut-off.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with anti-PT, anti-FHA, anti-PRN antibody concentration above or equal to the assay cut-off. |
|-----------------|---|

End point description:

A seropositive subject is a subject whose antibody concentration is  $\geq$  the assay cut-off defined. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA, 2.187 IU/mL for anti-PRN

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

End point timeframe:

1 month after the last dose of the primary vaccination

| End point values            | dTpa Group      | Control Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 266             | 271             |  |  |
| Units: Participants         |                 |                 |  |  |
| anti-PT antibody            | 266             | 271             |  |  |
| anti-FHA antibody           | 266             | 271             |  |  |
| anti-PRN antibody           | 266             | 269             |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 4-day (Day 0-Day 3) and unsolicited AEs were collected during the 31-day (days 0-30) follow-up period after each vaccination. SAEs were collected from Day 0 until the study end (Month 3 or 5).

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.0   |

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Control Group |
|-----------------------|---------------|

Reporting group description:

Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

|                       |            |
|-----------------------|------------|
| Reporting group title | dTpa Group |
|-----------------------|------------|

Reporting group description:

Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

| Serious adverse events                            | Control Group    | dTpa Group      |  |
|---|------------------|-----------------|--|
| Total subjects affected by serious adverse events |                  |                 |  |
| subjects affected / exposed                       | 17 / 305 (5.57%) | 7 / 296 (2.36%) |  |
| number of deaths (all causes)                     | 0                | 0               |  |
| number of deaths resulting from adverse events    |                  |                 |  |
| Injury, poisoning and procedural complications    |                  |                 |  |
| Fall  |                  |                 |  |
| subjects affected / exposed                       | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0           |  |
| Femur fracture                                    |                  |                 |  |
| subjects affected / exposed                       | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0           |  |
| Skull fracture                                    |                  |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skull fractured base                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Wound haemorrhage                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Congenital, familial and genetic disorders      |                 |                 |  |
| Congenital cytomegalovirus infection            |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Craniosynostosis                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cryptorchism                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dandy-walker syndrome                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ear malformation                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Microcephaly                                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Altered state of consciousness                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Immune system disorders                         |                 |                 |  |
| Milk allergy                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Intestinal haemorrhage                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vomiting  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Bacterial infection                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 4 / 305 (1.31%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Candida infection                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Conjunctivitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pyelonephritis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Superinfection bacterial                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 1 / 296 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Viral infection                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                                   | Control Group      | dTpa Group         |  |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events               |                    |                    |  |
| subjects affected / exposed   | 294 / 305 (96.39%) | 292 / 296 (98.65%) |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |  |
| Haemangioma   |                    |                    |  |
| subjects affected / exposed   | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)   | 1                  | 0                  |  |
| Infantile haemangioma   |                    |                    |  |
| subjects affected / exposed   | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |  |
| occurrences (all)   | 0                  | 1                  |  |
| Vascular disorders  |                    |                    |  |
| Pallor  |                    |                    |  |
| subjects affected / exposed   | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)   | 1                  | 0                  |  |
| Peripheral coldness   |                    |                    |  |
| subjects affected / exposed   | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |  |
| occurrences (all)   | 0                  | 1                  |  |
| General disorders and administration site conditions                |                    |                    |  |
| Influenza like illness  |                    |                    |  |
| subjects affected / exposed   | 0 / 305 (0.00%)    | 3 / 296 (1.01%)    |  |
| occurrences (all)   | 0                  | 3                  |  |
| Injection site bruising   |                    |                    |  |
| subjects affected / exposed   | 2 / 305 (0.66%)    | 2 / 296 (0.68%)    |  |
| occurrences (all)   | 2                  | 2                  |  |
| Injection site mass   |                    |                    |  |
| subjects affected / exposed   | 1 / 305 (0.33%)    | 3 / 296 (1.01%)    |  |
| occurrences (all)   | 2                  | 4                  |  |
| Injection site induration   |                    |                    |  |



|                             |                    |                    |
|-----------------------------|--------------------|--------------------|
| subjects affected / exposed | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |
| occurrences (all)           | 0                  | 1                  |
| Injection site swelling     |                    |                    |
| subjects affected / exposed | 169 / 305 (55.41%) | 157 / 296 (53.04%) |
| occurrences (all)           | 292                | 256                |
| Injection site nodule       |                    |                    |
| subjects affected / exposed | 1 / 305 (0.33%)    | 1 / 296 (0.34%)    |
| occurrences (all)           | 1                  | 1                  |
| Pyrexia                     |                    |                    |
| subjects affected / exposed | 139 / 305 (45.57%) | 133 / 296 (44.93%) |
| occurrences (all)           | 208                | 203                |
| Thirst                      |                    |                    |
| subjects affected / exposed | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |
| occurrences (all)           | 0                  | 1                  |
| Vaccination site erythema   |                    |                    |
| subjects affected / exposed | 2 / 305 (0.66%)    | 0 / 296 (0.00%)    |
| occurrences (all)           | 2                  | 0                  |
| Vaccination site pain       |                    |                    |
| subjects affected / exposed | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |
| occurrences (all)           | 0                  | 1                  |
| Vaccination site swelling   |                    |                    |
| subjects affected / exposed | 1 / 305 (0.33%)    | 1 / 296 (0.34%)    |
| occurrences (all)           | 1                  | 1                  |
| Vessel puncture site bruise |                    |                    |
| subjects affected / exposed | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |
| occurrences (all)           | 1                  | 0                  |
| Injection site erythema     |                    |                    |
| subjects affected / exposed | 203 / 305 (66.56%) | 205 / 296 (69.26%) |
| occurrences (all)           | 389                | 389                |
| Injection site pain         |                    |                    |
| subjects affected / exposed | 184 / 305 (60.33%) | 175 / 296 (59.12%) |
| occurrences (all)           | 315                | 314                |
| Irritability postvaccinal   |                    |                    |
| subjects affected / exposed | 257 / 305 (84.26%) | 255 / 296 (86.15%) |
| occurrences (all)           | 546                | 511                |
| Immune system disorders     |                    |                    |

|  |  |  |  |
|--|--|--|--|
| Milk allergy<br>subjects affected / exposed<br>occurrences (all)   | 2 / 305 (0.66%)<br>2   | 1 / 296 (0.34%)<br>1   |  |
| Reproductive system and breast disorders<br>Genital labial adhesions<br>subjects affected / exposed<br>occurrences (all)   | 0 / 305 (0.00%)<br>0   | 1 / 296 (0.34%)<br>1   |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Choking<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasal congestion<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all) | 13 / 305 (4.26%)<br>14<br><br>1 / 305 (0.33%)<br>1<br><br>6 / 305 (1.97%)<br>6<br><br>5 / 305 (1.64%)<br>5 | 6 / 296 (2.03%)<br>6<br><br>0 / 296 (0.00%)<br>0<br><br>0 / 296 (0.00%)<br>0<br><br>3 / 296 (1.01%)<br>3 |  |
| Psychiatric disorders<br>Emotional distress<br>subjects affected / exposed<br>occurrences (all)<br><br>Irritability<br>subjects affected / exposed<br>occurrences (all)  | 1 / 305 (0.33%)<br>1<br><br>3 / 305 (0.98%)<br>3   | 0 / 296 (0.00%)<br>0<br><br>2 / 296 (0.68%)<br>2   |  |
| Investigations<br>Body temperature increased<br>subjects affected / exposed<br>occurrences (all)   | 2 / 305 (0.66%)<br>2   | 2 / 296 (0.68%)<br>2   |  |
| Injury, poisoning and procedural complications<br>Arthropod bite<br>subjects affected / exposed<br>occurrences (all)<br><br>Bite   | 0 / 305 (0.00%)<br>0   | 1 / 296 (0.34%)<br>1   |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences (all)                          | 0               | 1               |  |
| Fall                                       |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Foreign body in gastrointestinal tract     |                 |                 |  |
| subjects affected / exposed                | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences (all)                          | 0               | 1               |  |
| Head injury                                |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 1 / 296 (0.34%) |  |
| occurrences (all)                          | 1               | 1               |  |
| Injury                                     |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Road traffic accident                      |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Thermal burn                               |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Vaccination complication                   |                 |                 |  |
| subjects affected / exposed                | 0 / 305 (0.00%) | 2 / 296 (0.68%) |  |
| occurrences (all)                          | 0               | 2               |  |
| Congenital, familial and genetic disorders |                 |                 |  |
| Congenital torticollis                     |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Phimosis                                   |                 |                 |  |
| subjects affected / exposed                | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences (all)                          | 0               | 1               |  |
| Nervous system disorders                   |                 |                 |  |
| Aphonia                                    |                 |                 |  |
| subjects affected / exposed                | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| External hydrocephalus                     |                 |                 |  |

|  |                           |                           |  |
|--|---------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 305 (0.00%)<br>0      | 1 / 296 (0.34%)<br>1      |  |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)   | 232 / 305 (76.07%)<br>427 | 216 / 296 (72.97%)<br>407 |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)    | 1 / 305 (0.33%)<br>1      | 0 / 296 (0.00%)<br>0      |  |
| Eye disorders<br>Dacryostenosis acquired<br>subjects affected / exposed<br>occurrences (all)           | 2 / 305 (0.66%)<br>2      | 1 / 296 (0.34%)<br>1      |  |
| Eye discharge<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 305 (0.66%)<br>2      | 0 / 296 (0.00%)<br>0      |  |
| Eye irritation<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 305 (0.33%)<br>1      | 1 / 296 (0.34%)<br>1      |  |
| Eye swelling<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 305 (0.33%)<br>1      | 0 / 296 (0.00%)<br>0      |  |
| Pupils unequal<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 305 (0.33%)<br>1      | 0 / 296 (0.00%)<br>0      |  |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all) | 1 / 305 (0.33%)<br>1      | 0 / 296 (0.00%)<br>0      |  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 305 (0.00%)<br>0      | 1 / 296 (0.34%)<br>1      |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 305 (0.33%)<br>1      | 1 / 296 (0.34%)<br>1      |  |
| Abnormal faeces  |                           |                           |  |

|                                  |                 |                 |
|----------------------------------|-----------------|-----------------|
| subjects affected / exposed      | 1 / 305 (0.33%) | 0 / 296 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Change of bowel habit            |                 |                 |
| subjects affected / exposed      | 1 / 305 (0.33%) | 0 / 296 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Constipation                     |                 |                 |
| subjects affected / exposed      | 9 / 305 (2.95%) | 8 / 296 (2.70%) |
| occurrences (all)                | 10              | 9               |
| Diarrhoea                        |                 |                 |
| subjects affected / exposed      | 2 / 305 (0.66%) | 8 / 296 (2.70%) |
| occurrences (all)                | 2               | 8               |
| Flatulence                       |                 |                 |
| subjects affected / exposed      | 1 / 305 (0.33%) | 1 / 296 (0.34%) |
| occurrences (all)                | 1               | 1               |
| Enteritis                        |                 |                 |
| subjects affected / exposed      | 1 / 305 (0.33%) | 0 / 296 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Gastric disorder                 |                 |                 |
| subjects affected / exposed      | 1 / 305 (0.33%) | 0 / 296 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Gastrooesophageal reflux disease |                 |                 |
| subjects affected / exposed      | 6 / 305 (1.97%) | 8 / 296 (2.70%) |
| occurrences (all)                | 6               | 8               |
| Gingival pain                    |                 |                 |
| subjects affected / exposed      | 1 / 305 (0.33%) | 4 / 296 (1.35%) |
| occurrences (all)                | 1               | 5               |
| Haematochezia                    |                 |                 |
| subjects affected / exposed      | 3 / 305 (0.98%) | 0 / 296 (0.00%) |
| occurrences (all)                | 3               | 0               |
| Infantile colic                  |                 |                 |
| subjects affected / exposed      | 2 / 305 (0.66%) | 2 / 296 (0.68%) |
| occurrences (all)                | 2               | 2               |
| Infrequent bowel movements       |                 |                 |
| subjects affected / exposed      | 0 / 305 (0.00%) | 1 / 296 (0.34%) |
| occurrences (all)                | 0               | 1               |
| Odynophagia                      |                 |                 |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed            | 0 / 305 (0.00%)  | 1 / 296 (0.34%)  |  |
| occurrences (all)                      | 0                | 1                |  |
| Mucous stools                          |                  |                  |  |
| subjects affected / exposed            | 0 / 305 (0.00%)  | 1 / 296 (0.34%)  |  |
| occurrences (all)                      | 0                | 1                |  |
| Oral mucosal erythema                  |                  |                  |  |
| subjects affected / exposed            | 0 / 305 (0.00%)  | 1 / 296 (0.34%)  |  |
| occurrences (all)                      | 0                | 1                |  |
| Regurgitation                          |                  |                  |  |
| subjects affected / exposed            | 1 / 305 (0.33%)  | 0 / 296 (0.00%)  |  |
| occurrences (all)                      | 1                | 0                |  |
| Sandifer's syndrome                    |                  |                  |  |
| subjects affected / exposed            | 1 / 305 (0.33%)  | 0 / 296 (0.00%)  |  |
| occurrences (all)                      | 1                | 0                |  |
| Teething                               |                  |                  |  |
| subjects affected / exposed            | 14 / 305 (4.59%) | 14 / 296 (4.73%) |  |
| occurrences (all)                      | 16               | 21               |  |
| Toothache                              |                  |                  |  |
| subjects affected / exposed            | 1 / 305 (0.33%)  | 2 / 296 (0.68%)  |  |
| occurrences (all)                      | 1                | 2                |  |
| Umbilical hernia                       |                  |                  |  |
| subjects affected / exposed            | 0 / 305 (0.00%)  | 1 / 296 (0.34%)  |  |
| occurrences (all)                      | 0                | 1                |  |
| Vomiting                               |                  |                  |  |
| subjects affected / exposed            | 4 / 305 (1.31%)  | 6 / 296 (2.03%)  |  |
| occurrences (all)                      | 4                | 6                |  |
| Skin and subcutaneous tissue disorders |                  |                  |  |
| Acne                                   |                  |                  |  |
| subjects affected / exposed            | 1 / 305 (0.33%)  | 0 / 296 (0.00%)  |  |
| occurrences (all)                      | 1                | 0                |  |
| Dermatitis                             |                  |                  |  |
| subjects affected / exposed            | 8 / 305 (2.62%)  | 1 / 296 (0.34%)  |  |
| occurrences (all)                      | 8                | 1                |  |
| Dermatitis atopic                      |                  |                  |  |
| subjects affected / exposed            | 6 / 305 (1.97%)  | 4 / 296 (1.35%)  |  |
| occurrences (all)                      | 7                | 4                |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Dermatitis diaper                               |                 |                 |  |
| subjects affected / exposed                     | 4 / 305 (1.31%) | 3 / 296 (1.01%) |  |
| occurrences (all)                               | 4               | 3               |  |
| Dry skin  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                               | 1               | 0               |  |
| Dyshidrotic eczema                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 305 (0.00%) | 1 / 296 (0.34%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Eczema  |                 |                 |  |
| subjects affected / exposed                     | 5 / 305 (1.64%) | 5 / 296 (1.69%) |  |
| occurrences (all)                               | 5               | 5               |  |
| Erythema  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 1 / 296 (0.34%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Rash  |                 |                 |  |
| subjects affected / exposed                     | 9 / 305 (2.95%) | 4 / 296 (1.35%) |  |
| occurrences (all)                               | 9               | 4               |  |
| Rash erythematous                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 0 / 296 (0.00%) |  |
| occurrences (all)                               | 1               | 0               |  |
| Rash macular                                    |                 |                 |  |
| subjects affected / exposed                     | 2 / 305 (0.66%) | 0 / 296 (0.00%) |  |
| occurrences (all)                               | 2               | 0               |  |
| Seborrhoeic dermatitis                          |                 |                 |  |
| subjects affected / exposed                     | 2 / 305 (0.66%) | 2 / 296 (0.68%) |  |
| occurrences (all)                               | 2               | 2               |  |
| Urticaria                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 1 / 296 (0.34%) |  |
| occurrences (all)                               | 1               | 2               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Head deformity                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 305 (0.33%) | 1 / 296 (0.34%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Pain in extremity                               |                 |                 |  |

|                               |                  |                 |  |
|-------------------------------|------------------|-----------------|--|
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Positional plagiocephaly      |                  |                 |  |
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Posture abnormal              |                  |                 |  |
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Torticollis                   |                  |                 |  |
| subjects affected / exposed   | 0 / 305 (0.00%)  | 2 / 296 (0.68%) |  |
| occurrences (all)             | 0                | 2               |  |
| Epiphysiolysis                |                  |                 |  |
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Infections and infestations   |                  |                 |  |
| Adenoiditis                   |                  |                 |  |
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Bronchiolitis                 |                  |                 |  |
| subjects affected / exposed   | 11 / 305 (3.61%) | 5 / 296 (1.69%) |  |
| occurrences (all)             | 12               | 5               |  |
| Campylobacter gastroenteritis |                  |                 |  |
| subjects affected / exposed   | 0 / 305 (0.00%)  | 1 / 296 (0.34%) |  |
| occurrences (all)             | 0                | 1               |  |
| Bronchitis                    |                  |                 |  |
| subjects affected / exposed   | 5 / 305 (1.64%)  | 4 / 296 (1.35%) |  |
| occurrences (all)             | 6                | 4               |  |
| Candida nappy rash            |                  |                 |  |
| subjects affected / exposed   | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |  |
| occurrences (all)             | 1                | 0               |  |
| Candida infection             |                  |                 |  |
| subjects affected / exposed   | 0 / 305 (0.00%)  | 2 / 296 (0.68%) |  |
| occurrences (all)             | 0                | 2               |  |
| Conjunctivitis                |                  |                 |  |
| subjects affected / exposed   | 13 / 305 (4.26%) | 6 / 296 (2.03%) |  |
| occurrences (all)             | 14               | 6               |  |



|                             |                  |                 |
|-----------------------------|------------------|-----------------|
| Croup infectious            |                  |                 |
| subjects affected / exposed | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |
| occurrences (all)           | 1                | 0               |
| Ear infection               |                  |                 |
| subjects affected / exposed | 10 / 305 (3.28%) | 6 / 296 (2.03%) |
| occurrences (all)           | 12               | 6               |
| Enterovirus infection       |                  |                 |
| subjects affected / exposed | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |
| occurrences (all)           | 1                | 0               |
| Erythema infectiosum        |                  |                 |
| subjects affected / exposed | 0 / 305 (0.00%)  | 1 / 296 (0.34%) |
| occurrences (all)           | 0                | 1               |
| Exanthema subitum           |                  |                 |
| subjects affected / exposed | 3 / 305 (0.98%)  | 1 / 296 (0.34%) |
| occurrences (all)           | 3                | 1               |
| Eye infection               |                  |                 |
| subjects affected / exposed | 0 / 305 (0.00%)  | 1 / 296 (0.34%) |
| occurrences (all)           | 0                | 2               |
| Fungal skin infection       |                  |                 |
| subjects affected / exposed | 0 / 305 (0.00%)  | 1 / 296 (0.34%) |
| occurrences (all)           | 0                | 1               |
| Furuncle                    |                  |                 |
| subjects affected / exposed | 1 / 305 (0.33%)  | 0 / 296 (0.00%) |
| occurrences (all)           | 1                | 0               |
| Gastroenteritis             |                  |                 |
| subjects affected / exposed | 8 / 305 (2.62%)  | 5 / 296 (1.69%) |
| occurrences (all)           | 8                | 5               |
| Gastroenteritis viral       |                  |                 |
| subjects affected / exposed | 1 / 305 (0.33%)  | 3 / 296 (1.01%) |
| occurrences (all)           | 1                | 3               |
| Hand-foot-and-mouth disease |                  |                 |
| subjects affected / exposed | 2 / 305 (0.66%)  | 0 / 296 (0.00%) |
| occurrences (all)           | 2                | 0               |
| Impetigo                    |                  |                 |
| subjects affected / exposed | 0 / 305 (0.00%)  | 1 / 296 (0.34%) |
| occurrences (all)           | 0                | 1               |

|                                   |                  |                  |
|-----------------------------------|------------------|------------------|
| Influenza                         |                  |                  |
| subjects affected / exposed       | 1 / 305 (0.33%)  | 0 / 296 (0.00%)  |
| occurrences (all)                 | 1                | 0                |
| Laryngitis                        |                  |                  |
| subjects affected / exposed       | 3 / 305 (0.98%)  | 3 / 296 (1.01%)  |
| occurrences (all)                 | 3                | 3                |
| Nail infection                    |                  |                  |
| subjects affected / exposed       | 0 / 305 (0.00%)  | 1 / 296 (0.34%)  |
| occurrences (all)                 | 0                | 1                |
| Nasopharyngitis                   |                  |                  |
| subjects affected / exposed       | 15 / 305 (4.92%) | 20 / 296 (6.76%) |
| occurrences (all)                 | 17               | 21               |
| Oral candidiasis                  |                  |                  |
| subjects affected / exposed       | 2 / 305 (0.66%)  | 4 / 296 (1.35%)  |
| occurrences (all)                 | 2                | 4                |
| Oral fungal infection             |                  |                  |
| subjects affected / exposed       | 1 / 305 (0.33%)  | 0 / 296 (0.00%)  |
| occurrences (all)                 | 1                | 0                |
| Otitis media                      |                  |                  |
| subjects affected / exposed       | 3 / 305 (0.98%)  | 0 / 296 (0.00%)  |
| occurrences (all)                 | 3                | 0                |
| Pharyngitis                       |                  |                  |
| subjects affected / exposed       | 1 / 305 (0.33%)  | 1 / 296 (0.34%)  |
| occurrences (all)                 | 1                | 1                |
| Otitis media acute                |                  |                  |
| subjects affected / exposed       | 2 / 305 (0.66%)  | 3 / 296 (1.01%)  |
| occurrences (all)                 | 3                | 3                |
| Pharyngotonsillitis               |                  |                  |
| subjects affected / exposed       | 1 / 305 (0.33%)  | 1 / 296 (0.34%)  |
| occurrences (all)                 | 1                | 1                |
| Respiratory tract infection       |                  |                  |
| subjects affected / exposed       | 9 / 305 (2.95%)  | 4 / 296 (1.35%)  |
| occurrences (all)                 | 12               | 5                |
| Respiratory tract infection viral |                  |                  |
| subjects affected / exposed       | 8 / 305 (2.62%)  | 4 / 296 (1.35%)  |
| occurrences (all)                 | 8                | 4                |

|   |                    |                    |  |
|---|--------------------|--------------------|--|
| Rhinitis                                |                    |                    |  |
| subjects affected / exposed             | 8 / 305 (2.62%)    | 2 / 296 (0.68%)    |  |
| occurrences (all)                       | 8                  | 2                  |  |
| Tonsillitis                             |                    |                    |  |
| subjects affected / exposed             | 0 / 305 (0.00%)    | 1 / 296 (0.34%)    |  |
| occurrences (all)                       | 0                  | 1                  |  |
| Upper respiratory tract infection       |                    |                    |  |
| subjects affected / exposed             | 32 / 305 (10.49%)  | 36 / 296 (12.16%)  |  |
| occurrences (all)                       | 38                 | 41                 |  |
| Urinary tract infection                 |                    |                    |  |
| subjects affected / exposed             | 2 / 305 (0.66%)    | 3 / 296 (1.01%)    |  |
| occurrences (all)                       | 2                  | 3                  |  |
| Varicella zoster virus infection        |                    |                    |  |
| subjects affected / exposed             | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)                       | 1                  | 0                  |  |
| Varicella                               |                    |                    |  |
| subjects affected / exposed             | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)                       | 1                  | 0                  |  |
| Viral infection                         |                    |                    |  |
| subjects affected / exposed             | 1 / 305 (0.33%)    | 1 / 296 (0.34%)    |  |
| occurrences (all)                       | 1                  | 1                  |  |
| Viral rash                              |                    |                    |  |
| subjects affected / exposed             | 2 / 305 (0.66%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)                       | 2                  | 0                  |  |
| Viral upper respiratory tract infection |                    |                    |  |
| subjects affected / exposed             | 1 / 305 (0.33%)    | 0 / 296 (0.00%)    |  |
| occurrences (all)                       | 1                  | 0                  |  |
| Metabolism and nutrition disorders      |                    |                    |  |
| Decreased appetite                      |                    |                    |  |
| subjects affected / exposed             | 157 / 305 (51.48%) | 142 / 296 (47.97%) |  |
| occurrences (all)                       | 252                | 219                |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 06 September 2016 | <p>Given the fact that only infants born from mothers vaccinated in the previous study (116945 [DTPA (BOOSTRIX)-047] can be enrolled in the current study, the enrolment in DTPA (BOOSTRIX)-047 study has an impact on this current study (e.g. cohorts to be investigated). Initially, the DTPA (BOOSTRIX)-047 study was opened only in countries using 3-dose primary vaccination series against diphtheria, tetanus and pertussis in infants. Nevertheless, the 2-dose primary vaccination schedule in infants is also meaningful for different regions in the world (e.g. Europe). It was therefore decided to open the DTPA (BOOSTRIX)-047, and therefore the current study to countries using 2-dose primary vaccination series in infants with the aim to increase the scientific value of the study and generate clinical data in diverse infant vaccination schedules.</p> <p>The notion of end of study was added and Section 11.5 describing the posting of information on public registry was revised accordingly.</p> <p>The names and functions of the contributing authors have been updated. The name of GSK Biologicals' Global Vaccines Clinical Laboratories (GVCL) department has been updated to Clinical Laboratory Sciences (CLS) and the name of outsourced laboratory (Quest Diagnostic laboratory is now called Q<sup>2</sup> Solutions) has also been updated. In addition, minor updates including typos, abbreviations, clarifications of wording were done throughout the document.</p> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported