



## Clinical trial results:

**A Phase IV, observer-blind, randomised, cross-over, placebo-controlled, multicentre study to assess the immunogenicity and safety of a single dose of Boostrix in pregnant women.**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-001119-38  |
| Trial protocol           | ES CZ FI IT     |
| Global end of trial date | 24 October 2017 |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 30 August 2018 |
| First version publication date | 30 August 2018 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 116945 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02377349 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 24 October 2017 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 24 October 2017 |
| Was the trial ended prematurely? | No              |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the maternally transferred antibodies against pertussis in the dTpa Group was superior to that in the Control Group in terms of geometric mean concentrations (GMCs) for the pertussis antibodies, in the cord blood sample.

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                          | 14 October 2015 |
| 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: 54      |
| Country: Number of subjects enrolled | Canada: 159        |
| Country: Number of subjects enrolled | Czech Republic: 75 |
| Country: Number of subjects enrolled | Finland: 76        |
| Country: Number of subjects enrolled | Italy: 15          |
| Country: Number of subjects enrolled | Spain: 309         |
| Worldwide total number of subjects   | 688                |
| EEA total number of subjects         | 475                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |

|                      |     |
|----------------------|-----|
| Adults (18-64 years) | 688 |
| From 65 to 84 years  | 0   |
| 85 years and over    | 0   |

## Subject disposition

### Recruitment

Recruitment details:

A total of 725 pregnant subjects were screened of which 690 were randomized to 2 groups. Of these, 2 subjects were withdrawn before vaccination. Therefore 688 subjects were enrolled: 1 subject was excluded from the statistical analysis, leaving 687 subjects that comprised the Total Vaccinated cohort.

### Pre-assignment

Screening details:

Safety was assessed for infants born to vaccinated subjects as well as safety of dTpa vaccination in the vaccinated pregnant subjects. There was also an assessment of the acceptance rate of a single dose of Boostrix among 723 eligible household contacts of the infants born to pregnant women enrolled in Spain, as part of an assessment of cocooning.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall Study (overall period)                         |
| Is this the baseline period? | Yes  |
| Allocation method            | Randomised - controlled                                |
| Blinding used                | Double blind   |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Assessor |

Blinding implementation details:

Data was collected in an observer-blind manner: the vaccine recipient and those responsible for the evaluation of any study endpoints (e.g. safety, reactogenicity) were unaware of which vaccine was administered. The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

### Arms

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

Arm description:

This group consisted of pregnant women who received a single dose of Boostrix at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of the placebo post-delivery (within 72 hours).

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | Boostrix                                       |
| Investigational medicinal product code |  |
| Other name                             | dTpa   |
| Pharmaceutical forms                   | Suspension for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose was administered as intramuscular injection into the deltoid muscle of the non-dominant arm.

|  |  |
|--|--|
| Investigational medicinal product name | Placebo for dTpa vaccine                       |
| Investigational medicinal product code |  |
| Other name                             | NaCl   |
| Pharmaceutical forms                   | Suspension for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose was administered as intramuscular injection into the deltoid muscle of the non-dominant arm.

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

Arm description:

This group consisted of pregnant women who received a single dose of placebo at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of Boostrix post-delivery (within 72 hours).

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | Placebo for dTpa vaccine                       |
| Investigational medicinal product code |  |
| Other name                             | NaCl   |
| Pharmaceutical forms                   | Suspension for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose was administered as intramuscular injection into the deltoid muscle of the non-dominant arm.

|  |  |
|--|--|
| Investigational medicinal product name | Boostrix                                       |
| Investigational medicinal product code |  |
| Other name                             | dTpa   |
| Pharmaceutical forms                   | Suspension for injection in pre-filled syringe |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose was administered as intramuscular injection into the deltoid muscle of the non-dominant arm.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | dTpa Group - Mother | Control Group - Mother |
|---|---------------------|------------------------|
| Started   | 341                 | 346                    |
| Completed   | 325                 | 335                    |
| Not completed                                       | 16                  | 11                     |
| Consent withdrawn by subject                        | 5                   | 3                      |
| Lost to follow-up (complete vaccination)            | 6                   | 5                      |
| Unspecified   | -                   | 1                      |
| Lost to follow-up (partial vaccination)             | 1                   | -                      |
| Serious Adverse Event                               | 1                   | -                      |
| Protocol deviation                                  | 3                   | 2                      |

Notes:

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

Justification: Out of 688 subjects enrolled in this trial only 687 comprised the Total Vaccinated cohort, since one subject was excluded from the statistical analysis.

## Baseline characteristics

### Reporting groups

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

Reporting group description:

This group consisted of pregnant women who received a single dose of Boostrix at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of the placebo post-delivery (within 72 hours).

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

Reporting group description:

This group consisted of pregnant women who received a single dose of placebo at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of Boostrix post-delivery (within 72 hours).

| Reporting group values             | dTpa Group - Mother | Control Group - Mother | Total |
|------------------------------------|---------------------|------------------------|-------|
| Number of subjects                 | 341                 | 346                    | 687   |
| Age categorical<br>Units: Subjects |                     |                        |       |

|   |               |               |     |
|---|---------------|---------------|-----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 32.7<br>± 4.4 | 32.5<br>± 4.3 | -   |
| Gender categorical<br>Units:  |               |               |     |
| Female  | 341           | 346           | 687 |
| Male  | 0             | 0             | 0   |
| Race/Ethnicity, Customized<br>Units: Subjects                           |               |               |     |
| African Heritage / African American                                     | 3             | 9             | 12  |
| American Indian or Alaskan Native                                       | 2             | 0             | 2   |
| Asian - Central/South Asian Heritage                                    | 3             | 0             | 3   |
| Asian - East Asian Heritage   | 4             | 1             | 5   |
| Asian - Japanese Heritage   | 1             | 0             | 1   |
| Asian - South East Asian Heritage                                       | 1             | 1             | 2   |
| White - Arabic / North African Heritage                                 | 3             | 7             | 10  |
| White - Caucasian / European Heritage                                   | 314           | 319           | 633 |
| Unspecified   | 10            | 9             | 19  |

## End points

### End points reporting groups

|  |                        |
|--|------------------------|
| Reporting group title  | dTpa Group - Mother    |
| Reporting group description:<br>This group consisted of pregnant women who received a single dose of Boostrix at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of the placebo post-delivery (within 72 hours). |                        |
| Reporting group title  | Control Group - Mother |
| Reporting group description:<br>This group consisted of pregnant women who received a single dose of placebo at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of Boostrix post-delivery (within 72 hours).     |                        |
| Subject analysis set title   | dTpa Group - Infant    |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:<br>This group consisted of infants born to mothers (from dTpa Group Mother) who received a dose of Boostrix during pregnancy.  |                        |
| Subject analysis set title   | Control Group - Infant |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:<br>This group consisted of infants born to mothers (from Control Group Mother) who received a dose of placebo during pregnancy   |                        |
| Subject analysis set title   | Household Group        |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:<br>This group consisted of eligible household contacts of the infants born to pregnant women enrolled in Spain who received a single dose of Boostrix anytime during the study.  |                        |

### Primary: Antibody concentrations against pertussis toxoid antigen (anti-PT), filamentous haemagglutinin antigen (anti-FHA) and pertactin antigen (anti-PRN) in cord blood samples

|   |  |
|---|--|
| End point title   | Antibody concentrations against pertussis toxoid antigen (anti-PT), filamentous haemagglutinin antigen (anti-FHA) and pertactin antigen (anti-PRN) in cord blood samples |
| End point description:<br>Antibody concentrations were assessed by Enzyme-linked immunosorbent assay (ELISA), tabulated as Geometric Mean Concentrations (GMCs) and expressed in International units per milliliter (IU/mL) for the following assay cut-offs: 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN. |  |
| End point type  | Primary  |
| End point timeframe:<br>At delivery - Visit 3 (anytime after 28 weeks of gestation)   |  |

| End point values                         | dTpa Group - Mother | Control Group - Mother |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed              | 291                 | 292                    |  |  |
| Units: IU/mL                             |                     |                        |  |  |
| geometric mean (confidence interval 95%) |                     |                        |  |  |

|                      |                        |                     |  |  |
|----------------------|------------------------|---------------------|--|--|
| Anti-PT (N=290;292)  | 46.9 (41.2 to 53.3)    | 5.5 (4.8 to 6.3)    |  |  |
| Anti-FHA (N=291;292) | 366.1 (329 to 407.3)   | 22.7 (19.7 to 26.2) |  |  |
| Anti-PRN (N=290;291) | 301.8 (250.9 to 362.9) | 14.6 (12.1 to 17.7) |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1                       |
|--|--|
| Statistical analysis description:  |  |
| GMC ratio between groups (dTpa Group-Mother/Control Group-Mother) to demonstrate that maternally transferred antibodies against pertussis in the dTpa Group-Mother was superior to that in the Control Group-mother, in the cord blood sample at the time of delivery. |  |
| Comparison groups  | Control Group - Mother v dTpa Group - Mother |
| Number of subjects included in analysis  | 583  |
| Analysis specification   | Pre-specified                                |
| Analysis type  | superiority <sup>[1]</sup>                   |
| Method   | 2-sample t-test                              |
| Parameter estimate   | GMC ratio                                    |
| Point estimate   | 8.47   |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided                                      |
| lower limit  | 7.02   |
| upper limit  | 10.2   |

Notes:

[1] - Criterion: The lower limit (LL) of the 95% confidence interval (CI) of the GMC ratio [dTpa Group-Mother/Control Group-Mother] for anti-PT antibodies was greater than or equal to ( $\geq$ ) 1.5.

| Statistical analysis title   | Statistical analysis 2                       |
|--|--|
| Statistical analysis description:  |  |
| GMC ratio between groups (dTpa Group-Mother/Control Group-Mother) to demonstrate that maternally transferred antibodies against pertussis in the dTpa Group-Mother was superior to that in the Control Group-mother, in the cord blood sample at the time of delivery. |  |
| Comparison groups  | Control Group - Mother v dTpa Group - Mother |
| Number of subjects included in analysis  | 583  |
| Analysis specification   | Pre-specified                                |
| Analysis type  | superiority <sup>[2]</sup>                   |
| Method   | 2-sample t-test                              |
| Parameter estimate   | GMC ratio                                    |
| Point estimate   | 16.11  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided                                      |
| lower limit  | 13.48  |
| upper limit  | 19.24  |

Notes:

[2] - Criterion: The lower limit (LL) of the 95% confidence interval (CI) of the GMC ratio [dTpa Group-Mother/Control Group-Mother] for anti-FHA antibodies was greater than or equal to ( $\geq$ ) 1.5.

| Statistical analysis title | Statistical analysis 3 |
|----------------------------|------------------------|
|----------------------------|------------------------|



**Statistical analysis description:**

GMC ratio between groups (dTpa Group-Mother/Control Group-Mother) to demonstrate that maternally transferred antibodies against pertussis in the dTpa Group-Mother was superior to that in the Control Group-mother, in the cord blood sample at the time of delivery.

|   |  |
|---|--|
| Comparison groups                       | Control Group - Mother v dTpa Group - Mother |
| Number of subjects included in analysis | 583  |
| Analysis specification                  | Pre-specified                                |
| Analysis type                           | superiority <sup>[3]</sup>                   |
| Method                                  | 2-sample t-test                              |
| Parameter estimate                      | GMC ratio                                    |
| Point estimate                          | 20.65  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided                                      |
| lower limit                             | 15.86  |
| upper limit                             | 26.88  |

**Notes:**

[3] - Criterion: The lower limit (LL) of the 95% confidence interval (CI) of the GMC ratio [dTpa Group-Mother/Control Group-Mother] for anti-PRN antibodies was greater than or equal to ( $\geq$ ) 1.5.

**Secondary: Percentage of subjects by pregnancy outcomes**

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects by pregnancy outcomes |
|-----------------|--|

**End point description:**

Pregnancy outcomes included live birth with no congenital anomalies, live birth with congenital anomalies, still birth with no congenital anomalies, still birth with congenital anomalies, elective termination with no congenital anomalies and elective termination with congenital anomalies. No subjects with still birth or elective termination of infant were reported.

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

**End point timeframe:**

From Day 0 (Visit 1) to Month 2 (Visit 4, end of the study).

| End point values                           | dTpa Group - Mother | Control Group - Mother |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                         | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed                | 341                 | 346                    |  |  |
| Units: Percentage of subjects              |                     |                        |  |  |
| number (confidence interval 95%)           |                     |                        |  |  |
| Live infant No apparent congenital anomaly | 97.4 (95 to 98.8)   | 97.4 (95.1 to 98.8)    |  |  |
| Live infant congenital anomaly             | 2.6 (1.2 to 5)      | 2.3 (1 to 4.5)         |  |  |
| Lost to follow-up                          | 0 (0 to 1.1)        | 0.3 (0 to 1.6)         |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of subjects with listed pregnancy/neonate related adverse events of interest**

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with listed pregnancy/neonate related |
|-----------------|--|

## End point description:

Listed pregnancy-related adverse events of interest/ neonate-related events of interest included gestational diabetes, pregnancy-related hypertension, premature rupture of membranes, preterm premature rupture of membranes, premature labour, premature uterine contractions, intrauterine growth restriction/poor foetal growth, pre-eclampsia, eclampsia, vaginal or intrauterine haemorrhage, maternal death, preterm birth, neonatal death, small for gestational age, neonatal hypoxic ischaemic encephalopathy and failure to thrive/growth deficiency were reported.

## End point type

Secondary

## End point timeframe:

From Day 0 (Visit 1) to Month 2 post-delivery (Visit 4, end of the study).

| End point values                                   | dTpa Group - Mother | Control Group - Mother |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                                 | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed                        | 341                 | 346                    |  |  |
| Units: Percentage of subjects                      |                     |                        |  |  |
| number (confidence interval 95%)                   |                     |                        |  |  |
| Intrauterine growth restriction/poor foetal growth | 1.5 (0.5 to 3.4)    | 0.6 (0.1 to 2.1)       |  |  |
| Pre-eclampsia                                      | 0.3 (0 to 1.6)      | 1.4 (0.5 to 3.3)       |  |  |
| Pregnancy-related hypertension                     | 1.2 (0.3 to 3)      | 1.4 (0.5 to 3.3)       |  |  |
| Premature labour                                   | 3.8 (2 to 6.4)      | 3.2 (1.6 to 5.6)       |  |  |
| Premature rupture of membranes                     | 3.8 (2 to 6.4)      | 4.3 (2.4 to 7)         |  |  |
| Premature uterine contractions                     | 0.6 (0.1 to 2.1)    | 0.9 (0.2 to 2.5)       |  |  |
| Preterm birth                                      | 3.2 (1.6 to 5.7)    | 2.6 (1.2 to 4.9)       |  |  |
| Preterm premature rupture of membranes             | 1.2 (0.3 to 3)      | 2 (0.8 to 4.1)         |  |  |
| Small for gestational age                          | 0.6 (0.1 to 2.1)    | 0.6 (0.1 to 2.1)       |  |  |
| Vaginal or intrauterine haemorrhage                | 2.6 (1.2 to 5)      | 2.9 (1.4 to 5.3)       |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Percentage of seroprotected subjects against Diphtheria antigen (anti-D), Tetanus antigen (anti-T) and of seropositive subjects against anti-PT, anti-FHA and anti-PRN**

## End point title

Percentage of seroprotected subjects against Diphtheria antigen (anti-D), Tetanus antigen (anti-T) and of seropositive subjects against anti-PT, anti-FHA and anti-PRN

## End point description:

A seroprotected subject against diphtheria and tetanus was a subject with antibody concentration  $\geq 0.1$  IU/mL. A seropositive subject was a subjects with antibody concentration  $\geq 2.693$  IU/mL for anti-PT,  $\geq 2.046$  IU/mL for anti-FHA and  $\geq 2.187$  IU/mL for anti-PRN.

## End point type

Secondary

## End point timeframe:

One month post vaccination (Day 30) during pregnancy

| <b>End point values</b>          | dTpa Group -<br>Mother | Control Group -<br>Mother |  |  |
|----------------------------------|------------------------|---------------------------|--|--|
| Subject group type               | Reporting group        | Reporting group           |  |  |
| Number of subjects analysed      | 290                    | 292                       |  |  |
| Units: Percentage of subjects    |                        |                           |  |  |
| number (confidence interval 95%) |                        |                           |  |  |
| Anti-D (N=290;289)               | 97.6 (95.1 to 99)      | 70.6 (65 to 75.8)         |  |  |
| Anti-T (N=290;292)               | 100 (98.7 to 100)      | 96.6 (93.8 to 98.3)       |  |  |
| Anti-PT (N=289;292)              | 98.6 (96.5 to 99.6)    | 61.3 (55.5 to 66.9)       |  |  |
| Anti-FHA (N=290;291)             | 100 (98.7 to 100)      | 94.5 (91.2 to 96.8)       |  |  |
| Anti-PRN (N=290;291)             | 100 (98.7 to 100)      | 84.5 (79.9 to 88.5)       |  |  |

### Statistical analyses

No statistical analyses for this end point

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

|   |  |
|---|--|
| End point title   | Anti-D, anti-T, anti-PT, anti-FHA and anti-PRN antibody concentrations |
| End point description:  |  |
| Antibody concentrations were determined by ELISA, tabulated as GMCs and expressed in IU/mL. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| One month post vaccination (Day 30) during pregnancy  |  |

| <b>End point values</b>                  | dTpa Group -<br>Mother | Control Group -<br>Mother |  |  |
|--|------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group           |  |  |
| Number of subjects analysed              | 290                    | 292                       |  |  |
| Units: IU/mL                             |                        |                           |  |  |
| geometric mean (confidence interval 95%) |                        |                           |  |  |
| Anti-D (N=290;289)                       | 2.19 (1.87 to 2.57)    | 0.23 (0.19 to 0.27)       |  |  |
| Anti-T (N=290;292)                       | 8.43 (7.72 to 9.2)     | 0.98 (0.86 to 1.11)       |  |  |
| Anti-PT (N=289;292)                      | 45.6 (40.4 to 51.5)    | 4.1 (3.6 to 4.6)          |  |  |
| Anti-FHA (N=290;291)                     | 317.5 (285 to 353.8)   | 15 (13.1 to 17.2)         |  |  |
| Anti-PRN (N=290;291)                     | 283.6 (237.1 to 339.1) | 10.5 (8.7 to 12.5)        |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with vaccine response to anti-D and anti-T

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with vaccine response to anti-D and anti-T |
|-----------------|---|

End point description:

Vaccine response for anti-D and anti-T was defined as: for initially seronegative subjects (S-) with pre-vaccination concentration below cut-off: < 0.1 IU/mL) was an antibody concentration at least four times the assay cut-off (post-vaccination concentration  $\geq$  0.4 IU/mL); for initially seropositive subjects (S+) with pre-vaccination concentration  $\geq$  0.1 IU/mL): an increase in antibody concentrations of at least four times the pre-vaccination concentration.

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

End point timeframe:

One month post vaccination (Day 30) during pregnancy

| End point values                 | dTpa Group -<br>Mother | Control Group -<br>Mother |  |  |
|----------------------------------|------------------------|---------------------------|--|--|
| Subject group type               | Reporting group        | Reporting group           |  |  |
| Number of subjects analysed      | 288                    | 291                       |  |  |
| Units: Percentage of subjects    |                        |                           |  |  |
| number (confidence interval 95%) |                        |                           |  |  |
| Anti-D, S- (N=103;83)            | 64.1 (54 to 73.3)      | 0 (0 to 4.3)              |  |  |
| Anti-D, S+ (N=184;205)           | 75 (68.1 to 81.1)      | 0 (0 to 1.8)              |  |  |
| Anti-D, Total (N=287;288)        | 71.1 (65.5 to 76.3)    | 0 (0 to 1.3)              |  |  |
| Anti-T, S- (N=12;10)             | 100 (73.5 to 100)      | 0 (0 to 30.8)             |  |  |
| Anti-T, S+ (N=276;281)           | 67.8 (61.9 to 73.2)    | 0 (0 to 1.3)              |  |  |
| Anti-T, Total (N=288;291)        | 69.1 (63.4 to 74.4)    | 0 (0 to 1.3)              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with vaccine response to anti-PT, anti-FHA and anti-PRN

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with vaccine response to anti-PT, anti-FHA and anti-PRN |
|-----------------|--|

**End point description:**

Vaccine response to PT, FHA and PRN antigens is defined as: for subjects with pre-vaccination antibody concentration below the assay cut-off (S-), post-vaccination anti-body concentration  $\geq 4$  times the assay cut-off; for subjects with pre-vaccination antibody concentration between the assay cut-off and below 4 times the assay cut-off (S+), post-vaccination antibody concentration  $\geq 4$  times the pre-vaccination antibody concentration, and for subjects with pre-vaccination antibody concentration  $\geq 4$  times the assay cut-off (S+), post-vaccination antibody concentration  $\geq 2$  times the pre-vaccination antibody concentration.

|  |           |
|--|-----------|
| End point type                                       | Secondary |
| End point timeframe:                                 |           |
| One month post vaccination (Day 30) during pregnancy |           |

| End point values                             | dTpa Group - Mother | Control Group - Mother |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                           | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed                  | 288                 | 291                    |  |  |
| Units: Percentage of subjects                |                     |                        |  |  |
| number (confidence interval 95%)             |                     |                        |  |  |
| Anti-PT, S- (N=121;107)                      | 82.6 (74.7 to 88.9) | 0.9 (0 to 5.1)         |  |  |
| Anti-PT, S+ (<4 cut-off) (N=108;117)         | 90.7 (83.6 to 95.5) | 0 (0 to 3.1)           |  |  |
| Anti-PT, S+ ( $\geq 4$ cut-off) (N=58;67)    | 93.1 (83.3 to 98.1) | 3 (0.4 to 10.4)        |  |  |
| Anti-PT, Total (N=287;291)                   | 87.8 (83.4 to 91.4) | 1 (0.2 to 3)           |  |  |
| Anti-FHA, S- (N=16;16)                       | 100 (79.4 to 100)   | 0 (0 to 20.6)          |  |  |
| Anti-FHA, S+ (<4 cut-off) (N=84;65)          | 100 (95.7 to 100)   | 0 (0 to 5.5)           |  |  |
| Anti-FHA, S+ ( $\geq 4$ cut-off) (N=188;209) | 89.9 (84.7 to 93.8) | 1.9 (0.5 to 4.8)       |  |  |
| Anti-FHA, Total (N=288;290)                  | 93.4 (89.9 to 96)   | 1.4 (0.4 to 3.5)       |  |  |
| Anti-PRN, S- (N=45;43)                       | 86.7 (73.2 to 94.9) | 0 (0 to 8.2)           |  |  |
| Anti-PRN, S+ (<4 cut-off) (N=98;86)          | 95.9 (89.9 to 98.9) | 0 (0 to 4.2)           |  |  |
| Anti-PRN, S+ ( $\geq 4$ cut-off) (N=145;161) | 86.2 (79.5 to 91.4) | 1.2 (0.2 to 4.4)       |  |  |
| Anti-PRN Total (N=288;290)                   | 89.6 (85.5 to 92.9) | 0.7 (0.1 to 2.5)       |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of seropositive subjects against anti-PT, anti-FHA and anti-PRN in the cord blood samples**

|                 |  |
|-----------------|--|
| End point title | Percentage of seropositive subjects against anti-PT, anti-FHA and anti-PRN in the cord blood samples |
|-----------------|--|

End point description:

For this assay the anti-PT, anti-FHA and anti-PRN seropositivity status was determined from the cord blood samples. The seropositivity cut-offs were the following: 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN.

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

End point timeframe:

At delivery - Visit 3 (anytime after 27 eligible weeks of gestation)

| End point values                 | dTpa Group - Mother | Control Group - Mother |  |  |
|----------------------------------|---------------------|------------------------|--|--|
| Subject group type               | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed      | 291                 | 292                    |  |  |
| Units: Percentage of subjects    |                     |                        |  |  |
| number (confidence interval 95%) |                     |                        |  |  |
| Anti-PT (N=290;292)              | 98.6 (96.5 to 99.6) | 68.8 (63.2 to 74.1)    |  |  |
| Anti-FHA (N=291;292)             | 100 (98.7 to 100)   | 96.6 (93.8 to 98.3)    |  |  |
| Anti-PRN (N=290;291)             | 99.7 (98.1 to 100)  | 88 (83.7 to 91.5)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with solicited local Adverse Events (AEs)

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with solicited local Adverse Events (AEs) |
|-----------------|--|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. "Any" = any report of the specified symptom irrespective of intensity grade. Dose 1 = pregnancy dose at Day 0 - Visit 1, Dose 2 = post-delivery dose at birth - Visit 3.

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

End point timeframe:

During the 8-day (Day 0-Day 7) follow-up period after vaccination during pregnancy

| End point values                      | dTpa Group - Mother | Control Group - Mother |  |  |
|---------------------------------------|---------------------|------------------------|--|--|
| Subject group type                    | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed           | 335                 | 343                    |  |  |
| Units: Percentage of subjects         |                     |                        |  |  |
| number (confidence interval 95%)      |                     |                        |  |  |
| Any Pain, Dose 1 (N=335;343)          | 86.3 (82.1 to 89.8) | 14.6 (11 to 18.8)      |  |  |
| Any Redness (mm), Dose 1 (N=335;343)  | 28.7 (23.9 to 33.8) | 12.8 (9.5 to 16.8)     |  |  |
| Any Swelling (mm), Dose 1 (N=335;343) | 25.1 (20.5 to 30.1) | 3.5 (1.8 to 6)         |  |  |

|                                       |                    |                     |  |  |
|---------------------------------------|--------------------|---------------------|--|--|
| Any Pain, Dose 2 (N=324;330)          | 12.7 (9.2 to 16.8) | 62.7 (57.3 to 68)   |  |  |
| Any Redness (mm), Dose 2 (N=324;330)  | 10.5 (7.4 to 14.4) | 29.7 (24.8 to 34.9) |  |  |
| Any Swelling (mm), Dose 2 (N=324;330) | 5.2 (3.1 to 8.3)   | 26.4 (21.7 to 31.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with solicited general AEs

|  |   |
|--|---|
| End point title  | Percentage of subjects with solicited general AEs |
| End point description:   |   |
| Assessed solicited general symptoms were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), headache and fever [defined as oral, axillary or tympanic temperature $\geq 37.5$ degrees Celsius ( $^{\circ}\text{C}$ ) or rectal temperature $\geq 38.0$ $^{\circ}\text{C}$ ]. "Any" = any report of the specified symptom irrespective of intensity grade. Dose 1 = pregnancy dose at Day 0 - Visit 1, Dose 2 = post-delivery dose at birth - Visit 3. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| During the 8-day (Day 0-Day 7) follow-up period after vaccination during pregnancy   |   |

| End point values  | dTpa Group - Mother | Control Group - Mother |  |  |
|---|---------------------|------------------------|--|--|
| Subject group type  | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed   | 335                 | 342                    |  |  |
| Units: Percentage of subjects   |                     |                        |  |  |
| number (confidence interval 95%)                                      |                     |                        |  |  |
| Any Fatigue, Dose 1 (N=335;342)                                       | 43.6 (38.2 to 49.1) | 36.3 (31.2 to 41.6)    |  |  |
| Any Gastrointestinal symptom, Dose 1 (N=335;342)                      | 17.9 (14 to 22.4)   | 15.2 (11.6 to 19.5)    |  |  |
| Any Headache, Dose 1 (N=335;342)                                      | 24.8 (20.2 to 29.8) | 22.8 (18.5 to 27.6)    |  |  |
| Any Temperature/(Axillary) ( $^{\circ}\text{C}$ ), Dose 1 (N=335;342) | 1.2 (0.3 to 3)      | 0.9 (0.2 to 2.5)       |  |  |
| Any Fatigue, Dose 2 (N=324;331)                                       | 40.1 (34.7 to 45.7) | 46.2 (40.8 to 51.8)    |  |  |
| Any Gastrointestinal symptom, Dose 2 (N=324;331)                      | 9.9 (6.9 to 13.7)   | 12.7 (9.3 to 16.8)     |  |  |
| Any Headache, Dose 2 (N=324;331)                                      | 23.1 (18.7 to 28.1) | 23.6 (19.1 to 28.5)    |  |  |
| Any Temperature/(Axillary) ( $^{\circ}\text{C}$ ), Dose 2 (N=324;331) | 4.6 (2.6 to 7.5)    | 9.1 (6.2 to 12.7)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with unsolicited AEs

|  |   |
|--|---|
| End point title  | Percentage of subjects with unsolicited AEs |
| End point description:<br>An unsolicited AE was any AE that was not solicited using a subject diary and that was spontaneously communicated by the subject. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. Dose 1 = pregnancy dose at Day 0 - Visit 1, Dose 2 = post-delivery dose at birth - Visit 3. |   |
| End point type   | Secondary                                   |
| End point timeframe:<br>Within 31 days (Day 0 – Day 30) after each vaccination   |   |

| End point values                       | dTpa Group - Mother | Control Group - Mother |  |  |
|--|---------------------|------------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group        |  |  |
| Number of subjects analysed            | 341                 | 346                    |  |  |
| Units: Percentage of subjects          |                     |                        |  |  |
| number (confidence interval 95%)       |                     |                        |  |  |
| Any unsolicited AE, Dose 1 (N=341;346) | 38.7 (33.5 to 44.1) | 35.5 (30.5 to 40.8)    |  |  |
| Any unsolicited AE, Dose 2 (N=336;342) | 30.7 (25.8 to 35.9) | 32.2 (27.2 to 37.4)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of infants with unsolicited AEs

|  |  |
|--|--|
| End point title  | Percentage of infants with unsolicited AEs |
| End point description:<br>An unsolicited AE was any AE that was not solicited using a subject diary and that was spontaneously communicated by the subject. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. |  |
| End point type   | Secondary                                  |
| End point timeframe:<br>From delivery to Month 2 (Visit 4, end of the study).  |  |

| End point values                 | dTpa Group - Infant  | Control Group - Infant |  |  |
|----------------------------------|----------------------|------------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set   |  |  |
| Number of subjects analysed      | 341                  | 346                    |  |  |
| Units: Percentage of subjects    |                      |                        |  |  |
| number (confidence interval 95%) |                      |                        |  |  |
| Percentage of subjects           | 26.4 (21.8 to 31.4)  | 22.3 (18.0 to 27.0)    |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with serious AEs (SAEs)

|  |  |
|--|--|
| End point title  | Number of subjects with serious AEs (SAEs) |
| End point description:<br>A SAE was any untoward medical occurrence that resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or a congenital anomaly/birth defect in the offspring of a study subject. |  |
| End point type   | Secondary                                  |
| End point timeframe:<br>From Day 0 (Visit 1) to Month 2 (Visit 4, end of the study).   |  |

| End point values            | dTpa Group -<br>Mother | Control Group -<br>Mother | dTpa Group -<br>Infant | Control Group -<br>Infant |
|-----------------------------|------------------------|---------------------------|------------------------|---------------------------|
| Subject group type          | Reporting group        | Reporting group           | Subject analysis set   | Subject analysis set      |
| Number of subjects analysed | 341                    | 346                       | 341                    | 346                       |
| Units: Participants         |                        |                           |                        |                           |
| Participants                | 51                     | 52                        | 52                     | 45                        |

| End point values            | Household<br>Group   |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 608                  |  |  |  |
| Units: Participants         |                      |  |  |  |
| Participants                | 0                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of household contacts of the infants born to pregnant women vaccinated in Spain

|   |  |
|---|--|
| End point title   | Percentage of household contacts of the infants born to pregnant women vaccinated in Spain |
| End point description:<br>This analysis assessed the vaccination status of the household contacts (who accepted, received or refused vaccination) and also the reasons for refusal (not coming to site, refused to be vaccinated, |  |

unspecified) as part of an assessment of cocooning among the eligible household contacts.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From Day 0 (Visit 1) to Month 2 (Visit 4, end of the study). |           |

| End point values                        | Household Group      |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                      | Subject analysis set |  |  |  |
| Number of subjects analysed             | 723                  |  |  |  |
| Units: Percentage of household contacts |                      |  |  |  |
| number (confidence interval 95%)        |                      |  |  |  |
| Accepted vaccination                    | 84.4 (81.5 to 86.9)  |  |  |  |
| Received vaccination                    | 84.1 (81.2 to 86.7)  |  |  |  |
| Refused vaccination                     | 15.6 (13.1 to 18.5)  |  |  |  |
| Not coming to site                      | 1.4 (0.7 to 2.5)     |  |  |  |
| Refused to be vaccinated                | 13.4 (11 to 16.1)    |  |  |  |
| Unspecified                             | 0.8 (0.3 to 1.8)     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of household contacts with SAEs

|  |  |
|--|--|
| End point title  | Percentage of household contacts with SAEs |
| End point description:   |  |
| SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. |  |
| End point type   | Secondary                                  |
| End point timeframe:   |  |
| During the 31-day (Days 0-30) follow-up period post-vaccination (Boostrix administered preferably 2 weeks before the birth of the infant, Visit 3).  |  |

| End point values              | Household Group      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 723                  |  |  |  |
| Units: Percentage of subjects |                      |  |  |  |
| Percentage of subjects        | 0                    |  |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: Days 0 - 7 following each dose; unsolicited AEs: Days 0 - 30 following each dose; SAEs: Day 0 - Month 2 (Mother Groups). Unsolicited AEs and SAEs: Day 0 - Month 2 (Infant Groups). SAEs: Days 0 - 30 post-vaccination (Household Group).

Adverse event reporting additional description:

No solicited symptoms were assessed for the Infants` Groups and Household Group.

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

### Dictionary used

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

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

### Reporting groups

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

Reporting group description:

This group consisted of pregnant women who received a single dose of Boostrix at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of the placebo post-delivery (within 72 hours).

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

Reporting group description:

This group consisted of pregnant women who received a single dose of placebo at 27-36 weeks (i.e. 27 weeks until 36 completed weeks) of gestation (Visit 1) and received a dose of Boostrix post-delivery (within 72 hours).

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

Reporting group description:

This group consisted of infants born to mothers (from Control Group Mother) who received a dose of placebo during pregnancy

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Household Group |
|-----------------------|-----------------|

Reporting group description:

This group consisted of eligible household contacts of the infants born to pregnant women enrolled in Spain who received a single dose of Boostrix anytime during the study.

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

Reporting group description:

This group consisted of infants born to mothers (from dTpa Group Mother) who received a dose of Boostrix during pregnancy.

| Serious adverse events                            | dTpa Group-Mother | Control Group-Mother | Control Group-Infant |
|---|-------------------|----------------------|----------------------|
| Total subjects affected by serious adverse events |                   |                      |                      |
| subjects affected / exposed                       | 51 / 341 (14.96%) | 52 / 346 (15.03%)    | 45 / 346 (13.01%)    |
| number of deaths (all causes)                     | 0                 | 0                    | 0                    |
| number of deaths resulting from adverse events    |                   |                      |                      |
| Vascular disorders                                |                   |                      |                      |
| Deep vein thrombosis                              |                   |                      |                      |
| subjects affected / exposed                       | 1 / 341 (0.29%)   | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences causally related to treatment / all   | 0 / 1             | 0 / 0                | 0 / 0                |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0                | 0 / 0                |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Pregnancy, puerperium and perinatal conditions  |                 |                 |                 |
| Cephalhaematoma                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Foetal distress syndrome                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Foetal growth restriction                       |                 |                 |                 |
| subjects affected / exposed                     | 3 / 341 (0.88%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gestational hypertension                        |                 |                 |                 |
| subjects affected / exposed                     | 4 / 341 (1.17%) | 4 / 346 (1.16%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 4           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hellp syndrome                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Jaundice neonatal                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Large for dates baby                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Placenta praevia haemorrhage                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                  |                  |                 |
|---|------------------|------------------|-----------------|
| Polyhydramnios                                  |                  |                  |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Postpartum haemorrhage                          |                  |                  |                 |
| subjects affected / exposed                     | 5 / 341 (1.47%)  | 7 / 346 (2.02%)  | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 7            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Pre-eclampsia                                   |                  |                  |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%)  | 5 / 346 (1.45%)  | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Premature baby                                  |                  |                  |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 9 / 346 (2.60%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 9           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Premature delivery                              |                  |                  |                 |
| subjects affected / exposed                     | 4 / 341 (1.17%)  | 4 / 346 (1.16%)  | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Premature labour                                |                  |                  |                 |
| subjects affected / exposed                     | 11 / 341 (3.23%) | 11 / 346 (3.18%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 12           | 1 / 11           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Premature rupture of membranes                  |                  |                  |                 |
| subjects affected / exposed                     | 13 / 341 (3.81%) | 17 / 346 (4.91%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 13           | 0 / 17           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Preterm premature rupture of membranes          |                  |                  |                 |
| subjects affected / exposed                     | 4 / 341 (1.17%)  | 5 / 346 (1.45%)  | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Retained placenta or membranes                  |                  |                  |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Small for dates baby                                 |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 3 / 346 (0.87%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 3           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Threatened labour                                    |                 |                 |                 |
| subjects affected / exposed                          | 2 / 341 (0.59%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine contractions during pregnancy                |                 |                 |                 |
| subjects affected / exposed                          | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                 |                 |                 |
| Pyrexia  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders             |                 |                 |                 |
| Female genital tract fistula                         |                 |                 |                 |
| subjects affected / exposed                          | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Metrorrhagia   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine atony  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine haemorrhage                             |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vaginal haemorrhage                             |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Apnoea  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Asphyxia  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Dyspnoea  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Meconium aspiration syndrome                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Neonatal asphyxia                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Neonatal respiratory depression                 |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumothorax                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pulmonary embolism                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory distress                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 4 / 346 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Transient tachypnoea of the newborn             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Investigations                                  |                 |                 |                 |
| Cardiac murmur                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Fall  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Procedural haemorrhage                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Congenital, familial and genetic disorders      |                 |                 |                 |
| Atrial septal defect                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac septal defect                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Congenital cardiovascular anomaly               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Congenital hydronephrosis                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cryptorchism                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 3 / 346 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypospadias                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Microtia  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Polydactyly                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Pyloric stenosis                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syndactyly                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Transposition of the great vessels              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Trisomy 21                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ventricular septal defect                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                               |                 |                 |                 |
| Atrioventricular block complete                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Supraventricular tachycardia                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypotonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Somnolence neonatal                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Anaemia neonatal                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Isoimmune haemolytic disease                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Gastrooesophageal reflux disease                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vomiting  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Hyperbilirubinaemia                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyperbilirubinaemia neonatal                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Jaundice  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 6 / 346 (1.73%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 6           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |                 |                 |
| Rash neonatal                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Acute kidney injury                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hydronephrosis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vesicoureteric reflux                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Amniotic cavity infection                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Beta haemolytic streptococcal infection         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchiolitis                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Endometritis decidual                           |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Enterovirus infection                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Influenza                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Mastitis  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nasopharyngitis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Neonatal infection                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Perineal infection                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory syncytial virus<br>bronchiolitis    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sepsis  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sepsis neonatal                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Superinfection bacterial                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tracheitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Upper respiratory tract infection               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Urinary tract infection                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Metabolism and nutrition disorders              |                 |                 |                 |
| Dehydration                                     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypernatraemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypocalcaemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypoglycaemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypoglycaemia neonatal                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Neonatal hypocalcaemia                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                     | Household Group | dTpa Group - Infant |  |
|---|-----------------|---------------------|--|
| Total subjects affected by serious adverse events |                 |                     |  |
| subjects affected / exposed                       | 0 / 608 (0.00%) | 52 / 341 (15.25%)   |  |
| number of deaths (all causes)                     | 0               | 0                   |  |
| number of deaths resulting from adverse events    |                 |                     |  |
| Vascular disorders                                |                 |                     |  |
| Deep vein thrombosis                              |                 |                     |  |
| subjects affected / exposed                       | 0 / 608 (0.00%) | 0 / 341 (0.00%)     |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0               |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0               |  |
| Pregnancy, puerperium and perinatal               |                 |                     |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| conditions                                      |                 |                 |  |
| Cephalhaematoma                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Foetal distress syndrome                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Foetal growth restriction                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gestational hypertension                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hellp syndrome                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Jaundice neonatal                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Large for dates baby                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Placenta praevia haemorrhage                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polyhydramnios                                  |                 |                 |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Postpartum haemorrhage                          |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Pre-eclampsia                                   |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Premature baby                                  |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 11 / 341 (3.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 11           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Premature delivery                              |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Premature labour                                |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Premature rupture of membranes                  |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Preterm premature rupture of membranes          |                 |                  |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Retained placenta or membranes                  |                 |                  |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Small for dates baby                                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 3 / 341 (0.88%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Threatened labour                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Uterine contractions during pregnancy                |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Female genital tract fistula                         |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Metrorrhagia   |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Uterine atony  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Uterine haemorrhage                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vaginal haemorrhage                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Apnoea  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Asphyxia  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meconium aspiration syndrome                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neonatal asphyxia                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neonatal respiratory depression                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumothorax                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory distress                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 5 / 341 (1.47%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 5           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Transient tachypnoea of the newborn             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Investigations                                  |                 |                 |  |
| Cardiac murmur                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Fall  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Procedural haemorrhage                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Congenital, familial and genetic disorders      |                 |                 |  |
| Atrial septal defect                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac septal defect                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Congenital cardiovascular anomaly               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Congenital hydronephrosis                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cryptorchism                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypospadias                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Microtia  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polydactyly                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Pyloric stenosis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syndactyly                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Transposition of the great vessels              |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Trisomy 21                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ventricular septal defect                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Atrioventricular block complete                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Supraventricular tachycardia                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Hypotonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Somnolence neonatal                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Anaemia neonatal                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Isoimmune haemolytic disease                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Gastrooesophageal reflux disease                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vomiting  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Hyperbilirubinaemia                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 3 / 341 (0.88%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hyperbilirubinaemia neonatal                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Jaundice  |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 8 / 341 (2.35%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 8           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Rash neonatal                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Acute kidney injury                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hydronephrosis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vesicoureteric reflux                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Amniotic cavity infection                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Beta haemolytic streptococcal infection         |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 3 / 341 (0.88%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Endometritis decidual                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Enterovirus infection                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Influenza                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mastitis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nasopharyngitis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neonatal infection                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Perineal infection                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis neonatal                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Superinfection bacterial                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tracheitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Dehydration                                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypernatraemia                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypocalcaemia                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypoglycaemia                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypoglycaemia neonatal                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neonatal hypocalcaemia                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| Non-serious adverse events  | dTpa Group-Mother  | Control Group-Mother | Control Group-Infant |
|---|--------------------|----------------------|----------------------|
| Total subjects affected by non-serious adverse events               |                    |                      |                      |
| subjects affected / exposed   | 321 / 341 (94.13%) | 303 / 346 (87.57%)   | 29 / 346 (8.38%)     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                      |                      |
| Anogenital warts  |                    |                      |                      |
| subjects affected / exposed   | 1 / 341 (0.29%)    | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)   | 1                  | 0                    | 0                    |
| Melanocytic naevus  |                    |                      |                      |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 341 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 |
| Vascular disorders                               |                      |                      |                      |
| Hot flush  |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Hypertension                                     |                      |                      |                      |
| subjects affected / exposed                      | 1 / 341 (0.29%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Hypotension                                      |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Phlebitis  |                      |                      |                      |
| subjects affected / exposed                      | 1 / 341 (0.29%)      | 2 / 346 (0.58%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 1                    | 2                    | 0                    |
| Raynaud's phenomenon                             |                      |                      |                      |
| subjects affected / exposed                      | 1 / 341 (0.29%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Thrombosis                                       |                      |                      |                      |
| subjects affected / exposed                      | 1 / 341 (0.29%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Varicose vein                                    |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Pregnancy, puerperium and perinatal conditions   |                      |                      |                      |
| Afterbirth pain                                  |                      |                      |                      |
| subjects affected / exposed                      | 17 / 341 (4.99%)     | 20 / 346 (5.78%)     | 0 / 346 (0.00%)      |
| occurrences (all)                                | 17                   | 20                   | 0                    |
| Cephalhaematoma                                  |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                    |
| Cervical dilatation                              |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Labour pain                                      |                      |                      |                      |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 2 / 341 (0.59%) | 3 / 346 (0.87%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 2               | 3               | 0               |
| Oligohydramnios                                      |                 |                 |                 |
| subjects affected / exposed                          | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 1               | 0               | 0               |
| Small for dates baby                                 |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 0               | 0               | 0               |
| Traumatic delivery                                   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 0               | 1               | 0               |
| Uterine contractions during pregnancy                |                 |                 |                 |
| subjects affected / exposed                          | 3 / 341 (0.88%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 3               | 1               | 0               |
| Uterine hypotonus                                    |                 |                 |                 |
| subjects affected / exposed                          | 3 / 341 (0.88%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 3               | 2               | 0               |
| Uterine irritability                                 |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 0               | 1               | 0               |
| General disorders and administration site conditions |                 |                 |                 |
| Asthenia   |                 |                 |                 |
| subjects affected / exposed                          | 2 / 341 (0.59%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 2               | 0               | 0               |
| Axillary pain  |                 |                 |                 |
| subjects affected / exposed                          | 2 / 341 (0.59%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 2               | 0               | 0               |
| Chills   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 0               | 1               | 0               |
| Discomfort   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                                    | 0               | 1               | 0               |
| Fatigue  |                 |                 |                 |

|                             |                    |                    |                 |
|-----------------------------|--------------------|--------------------|-----------------|
| subjects affected / exposed | 188 / 341 (55.13%) | 186 / 346 (53.76%) | 0 / 346 (0.00%) |
| occurrences (all)           | 276                | 277                | 0               |
| Granuloma                   |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 1                  | 0               |
| Hypothermia                 |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 0                  | 0               |
| Impaired healing            |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 1                  | 0               |
| Influenza like illness      |                    |                    |                 |
| subjects affected / exposed | 3 / 341 (0.88%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 3                  | 1                  | 0               |
| Injection site bruising     |                    |                    |                 |
| subjects affected / exposed | 2 / 341 (0.59%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 2                  | 1                  | 0               |
| Injection site erythema     |                    |                    |                 |
| subjects affected / exposed | 106 / 341 (31.09%) | 117 / 346 (33.82%) | 0 / 346 (0.00%) |
| occurrences (all)           | 130                | 142                | 0               |
| Injection site haematoma    |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 3 / 346 (0.87%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 3                  | 0               |
| Injection site induration   |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 0                  | 0               |
| Injection site mass         |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 0                  | 0               |
| Injection site pain         |                    |                    |                 |
| subjects affected / exposed | 290 / 341 (85.04%) | 223 / 346 (64.45%) | 0 / 346 (0.00%) |
| occurrences (all)           | 330                | 258                | 0               |
| Injection site pruritus     |                    |                    |                 |
| subjects affected / exposed | 4 / 341 (1.17%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 4                  | 1                  | 0               |
| Injection site rash         |                    |                    |                 |

|                             |                   |                   |                 |
|-----------------------------|-------------------|-------------------|-----------------|
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Injection site reaction     |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Injection site swelling     |                   |                   |                 |
| subjects affected / exposed | 91 / 341 (26.69%) | 92 / 346 (26.59%) | 0 / 346 (0.00%) |
| occurrences (all)           | 101               | 99                | 0               |
| Injection site urticaria    |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Malaise                     |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Nodule                      |                   |                   |                 |
| subjects affected / exposed | 1 / 341 (0.29%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 1                 | 0                 | 0               |
| Peripheral swelling         |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Pyrexia                     |                   |                   |                 |
| subjects affected / exposed | 20 / 341 (5.87%)  | 32 / 346 (9.25%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 20                | 33                | 0               |
| Swelling                    |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Vaccination site pain       |                   |                   |                 |
| subjects affected / exposed | 1 / 341 (0.29%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 1                 | 0                 | 0               |
| Vessel puncture site bruise |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 1                 | 0               |
| Immune system disorders     |                   |                   |                 |
| Milk allergy                |                   |                   |                 |
| subjects affected / exposed | 0 / 341 (0.00%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)           | 0                 | 0                 | 0               |



|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)    | 1 / 341 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |
| Reproductive system and breast disorders                                |                      |                      |                      |
| Breast engorgement<br>subjects affected / exposed<br>occurrences (all)  | 2 / 341 (0.59%)<br>2 | 4 / 346 (1.16%)<br>4 | 0 / 346 (0.00%)<br>0 |
| Breast inflammation<br>subjects affected / exposed<br>occurrences (all) | 2 / 341 (0.59%)<br>2 | 2 / 346 (0.58%)<br>2 | 0 / 346 (0.00%)<br>0 |
| Breast mass<br>subjects affected / exposed<br>occurrences (all)         | 0 / 341 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Breast pain<br>subjects affected / exposed<br>occurrences (all)         | 1 / 341 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |
| Cervical discharge<br>subjects affected / exposed<br>occurrences (all)  | 1 / 341 (0.29%)<br>1 | 2 / 346 (0.58%)<br>2 | 0 / 346 (0.00%)<br>0 |
| Menorrhagia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 341 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Metrorrhagia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 341 (0.00%)<br>0 | 2 / 346 (0.58%)<br>2 | 0 / 346 (0.00%)<br>0 |
| Nipple disorder<br>subjects affected / exposed<br>occurrences (all)     | 1 / 341 (0.29%)<br>1 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Nipple inflammation<br>subjects affected / exposed<br>occurrences (all) | 1 / 341 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |
| Nipple pain<br>subjects affected / exposed<br>occurrences (all)         | 1 / 341 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |
| Ovarian cyst torsion  |                      |                      |                      |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0               |
| Pelvic pain                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Perineal pain                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 3 / 346 (0.87%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 3               | 0               |
| Pruritus genital                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Suppressed lactation                            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 2               | 1               | 0               |
| Uterine pain                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Uterine prolapse                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Vaginal discharge                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Varicose veins vulval                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 2               | 0               |
| Vulvovaginal pain                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Cough   |                 |                 |                 |
| subjects affected / exposed                     | 6 / 341 (1.76%) | 7 / 346 (2.02%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 6               | 7               | 0               |
| Epistaxis                                       |                 |                 |                 |

|                                     |                  |                  |                 |
|-------------------------------------|------------------|------------------|-----------------|
| subjects affected / exposed         | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 1                | 0                | 0               |
| Grunting                            |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 0                | 0                | 0               |
| Nasal congestion                    |                  |                  |                 |
| subjects affected / exposed         | 3 / 341 (0.88%)  | 4 / 346 (1.16%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 3                | 4                | 0               |
| Nasal obstruction                   |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 0                | 1                | 0               |
| Oropharyngeal pain                  |                  |                  |                 |
| subjects affected / exposed         | 13 / 341 (3.81%) | 13 / 346 (3.76%) | 0 / 346 (0.00%) |
| occurrences (all)                   | 13               | 13               | 0               |
| Respiratory distress                |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 1 / 346 (0.29%) |
| occurrences (all)                   | 0                | 0                | 1               |
| Rhinitis allergic                   |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 0                | 3                | 0               |
| Rhinorrhoea                         |                  |                  |                 |
| subjects affected / exposed         | 2 / 341 (0.59%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 2                | 0                | 0               |
| Sinus congestion                    |                  |                  |                 |
| subjects affected / exposed         | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 1                | 0                | 0               |
| Throat irritation                   |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 0                | 1                | 0               |
| Transient tachypnoea of the newborn |                  |                  |                 |
| subjects affected / exposed         | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 2 / 346 (0.58%) |
| occurrences (all)                   | 0                | 0                | 2               |
| Upper-airway cough syndrome         |                  |                  |                 |
| subjects affected / exposed         | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                   | 1                | 0                | 0               |
| Psychiatric disorders               |                  |                  |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Affect liability                               |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Depression                                     |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Insomnia                                       |                 |                 |                 |
| subjects affected / exposed                    | 0 / 341 (0.00%) | 3 / 346 (0.87%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 0               | 3               | 0               |
| Irritability                                   |                 |                 |                 |
| subjects affected / exposed                    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences (all)                              | 0               | 0               | 1               |
| Investigations                                 |                 |                 |                 |
| Blood pressure increased                       |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Heart rate decreased                           |                 |                 |                 |
| subjects affected / exposed                    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences (all)                              | 0               | 0               | 1               |
| Injury, poisoning and procedural complications |                 |                 |                 |
| Clavicle fracture                              |                 |                 |                 |
| subjects affected / exposed                    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences (all)                              | 0               | 0               | 2               |
| Dislocation of vertebra                        |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Foreign body                                   |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Incision site pain                             |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 1               | 0               |
| Joint injury                                   |                 |                 |                 |
| subjects affected / exposed                    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0               |
| Laceration                                     |                 |                 |                 |

|                                |                 |                 |                 |
|--------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences (all)              | 0               | 0               | 1               |
| Ligament sprain                |                 |                 |                 |
| subjects affected / exposed    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Post procedural haematoma      |                 |                 |                 |
| subjects affected / exposed    | 2 / 341 (0.59%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 2               | 0               | 0               |
| Post procedural inflammation   |                 |                 |                 |
| subjects affected / exposed    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Procedural haemorrhage         |                 |                 |                 |
| subjects affected / exposed    | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Procedural headache            |                 |                 |                 |
| subjects affected / exposed    | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Procedural pain                |                 |                 |                 |
| subjects affected / exposed    | 3 / 341 (0.88%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences (all)              | 3               | 2               | 0               |
| Suture related complication    |                 |                 |                 |
| subjects affected / exposed    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Suture rupture                 |                 |                 |                 |
| subjects affected / exposed    | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 2               | 0               | 0               |
| Wound dehiscence               |                 |                 |                 |
| subjects affected / exposed    | 1 / 341 (0.29%) | 3 / 346 (0.87%) | 0 / 346 (0.00%) |
| occurrences (all)              | 1               | 3               | 0               |
| Cardiac disorders              |                 |                 |                 |
| Bradycardia                    |                 |                 |                 |
| subjects affected / exposed    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)              | 0               | 0               | 0               |
| Supraventricular extrasystoles |                 |                 |                 |
| subjects affected / exposed    | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 1 / 346 (0.29%) |
| occurrences (all)              | 0               | 0               | 1               |

|                             |                    |                    |                 |
|-----------------------------|--------------------|--------------------|-----------------|
| Nervous system disorders    |                    |                    |                 |
| Aphonia                     |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 0                  | 0               |
| Dizziness                   |                    |                    |                 |
| subjects affected / exposed | 7 / 341 (2.05%)    | 4 / 346 (1.16%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 8                  | 4                  | 0               |
| Extrapyramidal disorder     |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 0                  | 0               |
| Headache                    |                    |                    |                 |
| subjects affected / exposed | 129 / 341 (37.83%) | 126 / 346 (36.42%) | 0 / 346 (0.00%) |
| occurrences (all)           | 169                | 169                | 0               |
| Migraine                    |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 1                  | 0               |
| Migraine with aura          |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 0                  | 1                  | 0               |
| Paraesthesia                |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 1 / 346 (0.29%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 1                  | 0               |
| Paralysis                   |                    |                    |                 |
| subjects affected / exposed | 0 / 341 (0.00%)    | 0 / 346 (0.00%)    | 1 / 346 (0.29%) |
| occurrences (all)           | 0                  | 0                  | 1               |
| Restless legs syndrome      |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 0                  | 0               |
| Sciatica                    |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 2 / 346 (0.58%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 1                  | 3                  | 0               |
| Somnolence                  |                    |                    |                 |
| subjects affected / exposed | 1 / 341 (0.29%)    | 0 / 346 (0.00%)    | 0 / 346 (0.00%) |
| occurrences (all)           | 2                  | 0                  | 0               |
| Syncope                     |                    |                    |                 |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 341 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Blood and lymphatic system disorders             |                      |                      |                      |
| Anaemia  |                      |                      |                      |
| subjects affected / exposed                      | 11 / 341 (3.23%)     | 14 / 346 (4.05%)     | 0 / 346 (0.00%)      |
| occurrences (all)                                | 11                   | 14                   | 0                    |
| Anaemia of pregnancy                             |                      |                      |                      |
| subjects affected / exposed                      | 3 / 341 (0.88%)      | 3 / 346 (0.87%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 3                    | 3                    | 0                    |
| Ear and labyrinth disorders                      |                      |                      |                      |
| Deafness   |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Ear pain   |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Eye disorders                                    |                      |                      |                      |
| Conjunctival haemorrhage                         |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                    |
| Dacryostenosis acquired                          |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 0 / 346 (0.00%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                    |
| Eczema eyelids                                   |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Gastrointestinal disorders                       |                      |                      |                      |
| Abdominal discomfort                             |                      |                      |                      |
| subjects affected / exposed                      | 3 / 341 (0.88%)      | 1 / 346 (0.29%)      | 1 / 346 (0.29%)      |
| occurrences (all)                                | 3                    | 1                    | 1                    |
| Abdominal pain                                   |                      |                      |                      |
| subjects affected / exposed                      | 4 / 341 (1.17%)      | 1 / 346 (0.29%)      | 6 / 346 (1.73%)      |
| occurrences (all)                                | 5                    | 1                    | 6                    |
| Abdominal pain lower                             |                      |                      |                      |
| subjects affected / exposed                      | 0 / 341 (0.00%)      | 1 / 346 (0.29%)      | 0 / 346 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Abdominal pain upper                             |                      |                      |                      |

|                                  |                   |                   |                 |
|----------------------------------|-------------------|-------------------|-----------------|
| subjects affected / exposed      | 1 / 341 (0.29%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 1                 | 1                 | 0               |
| Constipation                     |                   |                   |                 |
| subjects affected / exposed      | 8 / 341 (2.35%)   | 10 / 346 (2.89%)  | 1 / 346 (0.29%) |
| occurrences (all)                | 8                 | 10                | 1               |
| Diarrhoea                        |                   |                   |                 |
| subjects affected / exposed      | 3 / 341 (0.88%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 3                 | 0                 | 0               |
| Dyspepsia                        |                   |                   |                 |
| subjects affected / exposed      | 4 / 341 (1.17%)   | 4 / 346 (1.16%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 4                 | 5                 | 0               |
| Flatulence                       |                   |                   |                 |
| subjects affected / exposed      | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 0                 | 1                 | 0               |
| Gastritis                        |                   |                   |                 |
| subjects affected / exposed      | 1 / 341 (0.29%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 1                 | 0                 | 0               |
| Gastrointestinal disorder        |                   |                   |                 |
| subjects affected / exposed      | 78 / 341 (22.87%) | 83 / 346 (23.99%) | 0 / 346 (0.00%) |
| occurrences (all)                | 92                | 95                | 0               |
| Gastrooesophageal reflux disease |                   |                   |                 |
| subjects affected / exposed      | 7 / 341 (2.05%)   | 6 / 346 (1.73%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 7                 | 6                 | 0               |
| Haemorrhoids                     |                   |                   |                 |
| subjects affected / exposed      | 4 / 341 (1.17%)   | 7 / 346 (2.02%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 4                 | 7                 | 0               |
| Inguinal hernia                  |                   |                   |                 |
| subjects affected / exposed      | 0 / 341 (0.00%)   | 1 / 346 (0.29%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 0                 | 1                 | 0               |
| Stomatitis                       |                   |                   |                 |
| subjects affected / exposed      | 1 / 341 (0.29%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 1                 | 0                 | 0               |
| Toothache                        |                   |                   |                 |
| subjects affected / exposed      | 2 / 341 (0.59%)   | 0 / 346 (0.00%)   | 0 / 346 (0.00%) |
| occurrences (all)                | 2                 | 0                 | 0               |
| Umbilical hernia                 |                   |                   |                 |



|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Vomiting                               |                 |                 |                 |
| subjects affected / exposed            | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 2               | 1               | 0               |
| Hepatobiliary disorders                |                 |                 |                 |
| Cholestasis of pregnancy               |                 |                 |                 |
| subjects affected / exposed            | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Hyperbilirubinaemia                    |                 |                 |                 |
| subjects affected / exposed            | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences (all)                      | 0               | 0               | 2               |
| Jaundice                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 5 / 346 (1.45%) |
| occurrences (all)                      | 0               | 0               | 5               |
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Alopecia areata                        |                 |                 |                 |
| subjects affected / exposed            | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Dermatitis                             |                 |                 |                 |
| subjects affected / exposed            | 1 / 341 (0.29%) | 2 / 346 (0.58%) | 1 / 346 (0.29%) |
| occurrences (all)                      | 1               | 2               | 1               |
| Dermatitis contact                     |                 |                 |                 |
| subjects affected / exposed            | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Erythema                               |                 |                 |                 |
| subjects affected / exposed            | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 1 / 346 (0.29%) |
| occurrences (all)                      | 2               | 1               | 1               |
| Hyperhidrosis                          |                 |                 |                 |
| subjects affected / exposed            | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Ingrowing nail                         |                 |                 |                 |
| subjects affected / exposed            | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 2 / 346 (0.58%) |
| occurrences (all)                      | 0               | 0               | 2               |
| Night sweats                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Pruritus  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Pruritus generalised                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Rash  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 1               | 0               |
| Urticaria                                       |                 |                 |                 |
| subjects affected / exposed                     | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 2               | 1               | 0               |
| Renal and urinary disorders                     |                 |                 |                 |
| Dysuria   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 2 / 346 (0.58%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 2               | 0               |
| Pyelocaliectasis                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0               |
| Renal colic                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Urethral prolapse                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Endocrine disorders                             |                 |                 |                 |
| Hypothyroidism                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Thyroid dysfunction in pregnancy                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |

|                             |                  |                  |                 |
|-----------------------------|------------------|------------------|-----------------|
| Arthralgia                  |                  |                  |                 |
| subjects affected / exposed | 3 / 341 (0.88%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 3                | 1                | 0               |
| Back pain                   |                  |                  |                 |
| subjects affected / exposed | 11 / 341 (3.23%) | 13 / 346 (3.76%) | 0 / 346 (0.00%) |
| occurrences (all)           | 11               | 14               | 0               |
| Flank pain                  |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 2 / 346 (0.58%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 2                | 0               |
| Ligament pain               |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 2 / 346 (0.58%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 2                | 0               |
| Limb discomfort             |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 1                | 0               |
| Muscle haemorrhage          |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 0                | 0               |
| Musculoskeletal stiffness   |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Myalgia                     |                  |                  |                 |
| subjects affected / exposed | 3 / 341 (0.88%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 3                | 3                | 0               |
| Neck pain                   |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 3                | 0               |
| Pain in extremity           |                  |                  |                 |
| subjects affected / exposed | 2 / 341 (0.59%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 2                | 3                | 0               |
| Infections and infestations |                  |                  |                 |
| Amniotic cavity infection   |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 1                | 0               |
| Bronchiolitis               |                  |                  |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 341 (0.00%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Bronchitis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Conjunctivitis              |                 |                 |                 |
| subjects affected / exposed | 1 / 341 (0.29%) | 3 / 346 (0.87%) | 3 / 346 (0.87%) |
| occurrences (all)           | 1               | 3               | 3               |
| Cystitis                    |                 |                 |                 |
| subjects affected / exposed | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Endometritis                |                 |                 |                 |
| subjects affected / exposed | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Fungal infection            |                 |                 |                 |
| subjects affected / exposed | 2 / 341 (0.59%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Fungal skin infection       |                 |                 |                 |
| subjects affected / exposed | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Gastroenteritis             |                 |                 |                 |
| subjects affected / exposed | 6 / 341 (1.76%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 6               | 1               | 0               |
| Gastroenteritis viral       |                 |                 |                 |
| subjects affected / exposed | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Genital herpes              |                 |                 |                 |
| subjects affected / exposed | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Genital infection           |                 |                 |                 |
| subjects affected / exposed | 1 / 341 (0.29%) | 0 / 346 (0.00%) | 0 / 346 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Genital infection fungal    |                 |                 |                 |
| subjects affected / exposed | 0 / 341 (0.00%) | 1 / 346 (0.29%) | 0 / 346 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Groin abscess               |                 |                 |                 |

|                             |                  |                  |                 |
|-----------------------------|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Herpes simplex              |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Hordeolum                   |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Influenza                   |                  |                  |                 |
| subjects affected / exposed | 2 / 341 (0.59%)  | 2 / 346 (0.58%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 2                | 2                | 0               |
| Mastitis                    |                  |                  |                 |
| subjects affected / exposed | 10 / 341 (2.93%) | 14 / 346 (4.05%) | 0 / 346 (0.00%) |
| occurrences (all)           | 10               | 14               | 0               |
| Mastitis postpartum         |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 1                | 0               |
| Nasopharyngitis             |                  |                  |                 |
| subjects affected / exposed | 7 / 341 (2.05%)  | 12 / 346 (3.47%) | 0 / 346 (0.00%) |
| occurrences (all)           | 7                | 12               | 0               |
| Nipple infection            |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Oral candidiasis            |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 0 / 346 (0.00%)  | 1 / 346 (0.29%) |
| occurrences (all)           | 0                | 0                | 1               |
| Oral herpes                 |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 2                | 0               |
| Otitis media acute          |                  |                  |                 |
| subjects affected / exposed | 0 / 341 (0.00%)  | 2 / 346 (0.58%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 0                | 2                | 0               |
| Periodontitis               |                  |                  |                 |
| subjects affected / exposed | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)           | 1                | 0                | 0               |
| Pharyngitis                 |                  |                  |                 |

|                                   |                  |                  |                 |
|-----------------------------------|------------------|------------------|-----------------|
| subjects affected / exposed       | 2 / 341 (0.59%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 2                | 3                | 0               |
| Pneumonia                         |                  |                  |                 |
| subjects affected / exposed       | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 0                | 1                | 0               |
| Postoperative abscess             |                  |                  |                 |
| subjects affected / exposed       | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 1                | 0                | 0               |
| Postoperative wound infection     |                  |                  |                 |
| subjects affected / exposed       | 2 / 341 (0.59%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 2                | 3                | 0               |
| Pyelonephritis                    |                  |                  |                 |
| subjects affected / exposed       | 0 / 341 (0.00%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 0                | 1                | 0               |
| Respiratory tract infection       |                  |                  |                 |
| subjects affected / exposed       | 2 / 341 (0.59%)  | 1 / 346 (0.29%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 2                | 1                | 0               |
| Respiratory tract infection viral |                  |                  |                 |
| subjects affected / exposed       | 2 / 341 (0.59%)  | 0 / 346 (0.00%)  | 2 / 346 (0.58%) |
| occurrences (all)                 | 2                | 0                | 2               |
| Rhinitis                          |                  |                  |                 |
| subjects affected / exposed       | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 1                | 0                | 0               |
| Sinusitis                         |                  |                  |                 |
| subjects affected / exposed       | 2 / 341 (0.59%)  | 3 / 346 (0.87%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 2                | 3                | 0               |
| Tinea pedis                       |                  |                  |                 |
| subjects affected / exposed       | 1 / 341 (0.29%)  | 0 / 346 (0.00%)  | 0 / 346 (0.00%) |
| occurrences (all)                 | 1                | 0                | 0               |
| Upper respiratory tract infection |                  |                  |                 |
| subjects affected / exposed       | 11 / 341 (3.23%) | 13 / 346 (3.76%) | 1 / 346 (0.29%) |
| occurrences (all)                 | 12               | 13               | 1               |
| Urinary tract infection           |                  |                  |                 |
| subjects affected / exposed       | 8 / 341 (2.35%)  | 10 / 346 (2.89%) | 0 / 346 (0.00%) |
| occurrences (all)                 | 8                | 11               | 0               |
| Vaginal infection                 |                  |                  |                 |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 341 (0.29%)<br>1 | 2 / 346 (0.58%)<br>2 | 0 / 346 (0.00%)<br>0 |
| Vulvovaginal candidiasis<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 341 (0.29%)<br>1 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Vulvovaginal mycotic infection<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 341 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Cow's milk intolerance<br>subjects affected / exposed<br>occurrences (all) | 0 / 341 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |
| Fluid retention<br>subjects affected / exposed<br>occurrences (all)  | 0 / 341 (0.00%)<br>0 | 1 / 346 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 |
| Iron deficiency<br>subjects affected / exposed<br>occurrences (all)  | 1 / 341 (0.29%)<br>1 | 0 / 346 (0.00%)<br>0 | 0 / 346 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>   | Household Group      | dTpa Group - Infant  |  |
|---|----------------------|----------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed  | 0 / 608 (0.00%)      | 33 / 341 (9.68%)     |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Anogenital warts<br>subjects affected / exposed<br>occurrences (all) | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Melanocytic naevus<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Vascular disorders<br>Hot flush<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Hypotension   |                      |                      |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Phlebitis                                      |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Raynaud's phenomenon                           |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Thrombosis                                     |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Varicose vein                                  |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Pregnancy, puerperium and perinatal conditions |                 |                 |  |
| Afterbirth pain                                |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Cephalhaematoma                                |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                              | 0               | 1               |  |
| Cervical dilatation                            |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Labour pain                                    |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Oligohydramnios                                |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Small for dates baby                           |                 |                 |  |
| subjects affected / exposed                    | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                              | 0               | 1               |  |
| Traumatic delivery                             |                 |                 |  |



|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Uterine contractions during pregnancy                |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Uterine hypotonus                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Uterine irritability                                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| General disorders and administration site conditions |                 |                 |  |
| Asthenia   |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Axillary pain  |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Chills   |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Discomfort   |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Fatigue  |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Granuloma  |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Hypothermia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                                    | 0               | 1               |  |
| Impaired healing                                     |                 |                 |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Influenza like illness      |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site bruising     |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site erythema     |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site haematoma    |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site induration   |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site mass         |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site pain         |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site pruritus     |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site rash         |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site reaction     |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site swelling     |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site urticaria    |                 |                 |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 1 / 341 (0.29%)<br>1 |  |
| Nodule<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Swelling<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Vaccination site pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Vessel puncture site bruise<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Immune system disorders<br>Milk allergy<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 608 (0.00%)<br>0 | 1 / 341 (0.29%)<br>1 |  |
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Reproductive system and breast disorders<br>Breast engorgement<br>subjects affected / exposed<br>occurrences (all) | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Breast inflammation  |                      |                      |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Breast mass                 |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Breast pain                 |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Cervical discharge          |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Menorrhagia                 |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Metrorrhagia                |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Nipple disorder             |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Nipple inflammation         |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Nipple pain                 |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Ovarian cyst torsion        |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 1 / 341 (0.29%) |
| occurrences (all)           | 0               | 1               |
| Pelvic pain                 |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Perineal pain               |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Pruritus genital            |                 |                 |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Suppressed lactation                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Uterine pain                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Uterine prolapse                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Vaginal discharge                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Varicose veins vulval                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Vulvovaginal pain                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Cough   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Epistaxis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Grunting  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Nasal congestion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Nasal obstruction                               |                 |                 |  |

|                                     |                 |                 |  |
|-------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Oropharyngeal pain                  |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Respiratory distress                |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Rhinitis allergic                   |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Rhinorrhoea                         |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Sinus congestion                    |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Throat irritation                   |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Transient tachypnoea of the newborn |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Upper-airway cough syndrome         |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Psychiatric disorders               |                 |                 |  |
| Affect lability                     |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Depression                          |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Insomnia                            |                 |                 |  |
| subjects affected / exposed         | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| Irritability<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Investigations<br>Blood pressure increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Heart rate decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Injury, poisoning and procedural complications<br>Clavicle fracture<br>subjects affected / exposed<br>occurrences (all) | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Dislocation of vertebra<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Foreign body<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Incision site pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Joint injury<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Laceration<br>subjects affected / exposed<br>occurrences (all)  | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Ligament sprain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Post procedural haematoma<br>subjects affected / exposed<br>occurrences (all)   | 0 / 608 (0.00%)<br>0 | 0 / 341 (0.00%)<br>0 |  |
| Post procedural inflammation  |                      |                      |  |

|                                |                 |                 |  |
|--------------------------------|-----------------|-----------------|--|
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Procedural haemorrhage         |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Procedural headache            |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Procedural pain                |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Suture related complication    |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Suture rupture                 |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Wound dehiscence               |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Cardiac disorders              |                 |                 |  |
| Bradycardia                    |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)              | 0               | 1               |  |
| Supraventricular extrasystoles |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Nervous system disorders       |                 |                 |  |
| Aphonia                        |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Dizziness                      |                 |                 |  |
| subjects affected / exposed    | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)              | 0               | 0               |  |
| Extrapyramidal disorder        |                 |                 |  |



|                                      |                 |                 |  |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Headache                             |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Migraine                             |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Migraine with aura                   |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Paraesthesia                         |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Paralysis                            |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Restless legs syndrome               |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Sciatica                             |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Somnolence                           |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Syncope                              |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Blood and lymphatic system disorders |                 |                 |  |
| Anaemia                              |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |
| Anaemia of pregnancy                 |                 |                 |  |
| subjects affected / exposed          | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                    | 0               | 0               |  |

|  |  |  |  |
|--|--|--|--|
| Ear and labyrinth disorders<br>Deafness<br>subjects affected / exposed<br>occurrences (all)<br><br>Ear pain<br>subjects affected / exposed<br>occurrences (all)  | <br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0   | <br><br>0 / 341 (0.00%)<br>0<br><br>0 / 341 (0.00%)<br>0   |  |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)<br><br>Dacryostenosis acquired<br>subjects affected / exposed<br>occurrences (all)<br><br>Eczema eyelids<br>subjects affected / exposed<br>occurrences (all)   | <br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0   | <br><br>1 / 341 (0.29%)<br>1<br><br>2 / 341 (0.59%)<br>2<br><br>0 / 341 (0.00%)<br>0   |  |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain lower<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia | <br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0<br><br>0 / 608 (0.00%)<br>0 | <br><br>0 / 341 (0.00%)<br>0<br><br>9 / 341 (2.64%)<br>9<br><br>0 / 341 (0.00%)<br>0<br><br>0 / 341 (0.00%)<br>0<br><br>1 / 341 (0.29%)<br>1<br><br>0 / 341 (0.00%)<br>0 |  |

|                                  |                 |                 |  |
|----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Flatulence                       |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Gastritis                        |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Gastrointestinal disorder        |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Gastrooesophageal reflux disease |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                | 0               | 1               |  |
| Haemorrhoids                     |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Inguinal hernia                  |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Stomatitis                       |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Toothache                        |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Umbilical hernia                 |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Vomiting                         |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |
| Hepatobiliary disorders          |                 |                 |  |
| Cholestasis of pregnancy         |                 |                 |  |
| subjects affected / exposed      | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                | 0               | 0               |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| Hyperbilirubinaemia                    |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences (all)                      | 0               | 2               |  |
| Jaundice                               |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 2 / 341 (0.59%) |  |
| occurrences (all)                      | 0               | 2               |  |
| Skin and subcutaneous tissue disorders |                 |                 |  |
| Alopecia areata                        |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Dermatitis                             |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 4 / 341 (1.17%) |  |
| occurrences (all)                      | 0               | 4               |  |
| Dermatitis contact                     |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Erythema                               |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Hyperhidrosis                          |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Ingrowing nail                         |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Night sweats                           |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Pruritus                               |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Pruritus generalised                   |                 |                 |  |
| subjects affected / exposed            | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                      | 0               | 0               |  |
| Rash                                   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Urticaria                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Renal and urinary disorders                     |                 |                 |  |
| Dysuria   |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Pyelocaliectasis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Renal colic                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Urethral prolapse                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Endocrine disorders                             |                 |                 |  |
| Hypothyroidism                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Thyroid dysfunction in pregnancy                |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Arthralgia                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Flank pain                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Ligament pain                                   |                 |                 |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Limb discomfort             |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Muscle haemorrhage          |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)           | 0               | 1               |  |
| Musculoskeletal stiffness   |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Myalgia                     |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Neck pain                   |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Pain in extremity           |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Infections and infestations |                 |                 |  |
| Amniotic cavity infection   |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Bronchiolitis               |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)           | 0               | 1               |  |
| Bronchitis                  |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Conjunctivitis              |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 7 / 341 (2.05%) |  |
| occurrences (all)           | 0               | 8               |  |
| Cystitis                    |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Endometritis                |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Fungal infection            |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Fungal skin infection       |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Gastroenteritis             |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 1 / 341 (0.29%) |
| occurrences (all)           | 0               | 1               |
| Gastroenteritis viral       |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Genital herpes              |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Genital infection           |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Genital infection fungal    |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Groin abscess               |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Herpes simplex              |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hordeolum                   |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Influenza                   |                 |                 |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)           | 0               | 0               |

|                               |                 |                 |
|-------------------------------|-----------------|-----------------|
| Mastitis                      |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Mastitis postpartum           |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Nasopharyngitis               |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Nipple infection              |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Oral candidiasis              |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 1 / 341 (0.29%) |
| occurrences (all)             | 0               | 1               |
| Oral herpes                   |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Otitis media acute            |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Periodontitis                 |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Pharyngitis                   |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Pneumonia                     |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Postoperative abscess         |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |
| Postoperative wound infection |                 |                 |
| subjects affected / exposed   | 0 / 608 (0.00%) | 0 / 341 (0.00%) |
| occurrences (all)             | 0               | 0               |



|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| Pyelonephritis                     |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Respiratory tract infection        |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Respiratory tract infection viral  |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Rhinitis                           |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Sinusitis                          |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Tinea pedis                        |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Upper respiratory tract infection  |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 3 / 341 (0.88%) |  |
| occurrences (all)                  | 0               | 3               |  |
| Urinary tract infection            |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Vaginal infection                  |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Vulvovaginal candidiasis           |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Vulvovaginal mycotic infection     |                 |                 |  |
| subjects affected / exposed        | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Cow's milk intolerance             |                 |                 |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 608 (0.00%) | 1 / 341 (0.29%) |  |
| occurrences (all)           | 0               | 1               |  |
| Fluid retention             |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Iron deficiency             |                 |                 |  |
| subjects affected / exposed | 0 / 608 (0.00%) | 0 / 341 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |

## **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