



## Clinical trial results:

**An open, multicentric, post-marketing surveillance (PMS) study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals' DTPa-IPV/Hib vaccine administered at 3, 4, 5 and 18 months of age, in healthy infants.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001512-35 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 23 August 2007 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 18 April 2016 |
| First version publication date | 09 July 2015  |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 100917 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00325156 |
| 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? | Yes |

Notes:

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**Results analysis stage**

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|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 12 August 2008 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 23 August 2007 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 23 August 2007 |
| Was the trial ended prematurely?                     | No             |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety and reactogenicity of the DTPa-IPV/Hib vaccine.

Protection of trial subjects:

The vaccines were closely observed for at least 30 minutes following the administration of the study vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 02 November 2004 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                 |
|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Singapore: 2590 |
| Worldwide total number of subjects   | 2590            |
| EEA total number of subjects         | 0               |

Notes:

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**Subjects enrolled per age group**

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|                                           |      |
|-------------------------------------------|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 2590 |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 0    |
| From 65 to 84 years                       | 0    |
| 85 years and over                         | 0    |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

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

### Arms

|                                        |                        |
|----------------------------------------|------------------------|
| Arm title                              | Infanrix-IPV+Hib Group |
| Arm description: -                     |                        |
| Arm type                               | Experimental           |
| Investigational medicinal product name | Infanrix-IPV+Hib™      |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Injection              |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 3 primary doses and 1 booster dose which were administered intramuscularly into anterolateral thigh.

|                                        |                                        |
|----------------------------------------|----------------------------------------|
| Investigational medicinal product name | Rotarix™                               |
| Investigational medicinal product code |                                        |
| Other name                             |                                        |
| Pharmaceutical forms                   | Oral solution in single-dose container |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Subjects received two oral doses of Rotarix™ at 3 and 4 months of age.

| Number of subjects in period 1           | Infanrix-IPV+Hib Group |
|------------------------------------------|------------------------|
| Started                                  | 2590                   |
| Completed                                | 2478                   |
| Not completed                            | 112                    |
| Consent withdrawn by subject             | 31                     |
| Adverse event, non-fatal                 | 3                      |
| Lost to follow-up (complete vaccination) | 41                     |
| Migrated/moved from study area           | 12                     |
| Unspecified                              | 1                      |

|                                            |    |
|--------------------------------------------|----|
| Lost to follow-up (Incomplete vaccination) | 16 |
| Protocol deviation                         | 8  |

## Baseline characteristics

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Infanrix-IPV+Hib Group |
|-----------------------|------------------------|

Reporting group description: -

| Reporting group values                             | Infanrix-IPV+Hib Group | Total |  |
|----------------------------------------------------|------------------------|-------|--|
| Number of subjects                                 | 2590                   | 2590  |  |
| Age categorical                                    |                        |       |  |
| Units: Subjects                                    |                        |       |  |
| In utero                                           |                        | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) |                        | 0     |  |
| Newborns (0-27 days)                               |                        | 0     |  |
| Infants and toddlers (28 days-23 months)           |                        | 0     |  |
| Children (2-11 years)                              |                        | 0     |  |
| Adolescents (12-17 years)                          |                        | 0     |  |
| Adults (18-64 years)                               |                        | 0     |  |
| From 65-84 years                                   |                        | 0     |  |
| 85 years and over                                  |                        | 0     |  |
| Age continuous                                     |                        |       |  |
| Units: weeks                                       |                        |       |  |
| arithmetic mean                                    | 13.3                   |       |  |
| standard deviation                                 | ± 0.87                 | -     |  |
| Gender categorical                                 |                        |       |  |
| Units: Subjects                                    |                        |       |  |
| Female                                             | 1245                   | 1245  |  |
| Male                                               | 1345                   | 1345  |  |

## End points

### End points reporting groups

|                                |                        |
|--------------------------------|------------------------|
| Reporting group title          | Infanrix-IPV+Hib Group |
| Reporting group description: - |                        |

### Primary: Number of subjects reporting solicited local and general symptoms.

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Number of subjects reporting solicited local and general symptoms. <sup>[1]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

During the 4-day (Day 0-3) post-vaccination period.

Notes:

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

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

| End point values                                                 | Infanrix-IPV+Hib Group |  |  |  |
|------------------------------------------------------------------|------------------------|--|--|--|
| Subject group type                                               | Reporting group        |  |  |  |
| Number of subjects analysed                                      | 2580                   |  |  |  |
| Units: Subjects                                                  |                        |  |  |  |
| Any Pain, Across doses                                           | 855                    |  |  |  |
| Any Redness, Across doses                                        | 907                    |  |  |  |
| Any Swelling, Across doses                                       | 706                    |  |  |  |
| Any Drowsiness, Across doses                                     | 929                    |  |  |  |
| Any Fever (Axillary/ $\geq 37.5^{\circ}\text{C}$ ), Across doses | 1482                   |  |  |  |
| Any Irritability, Across doses                                   | 1217                   |  |  |  |
| Any Loss of appetite, Across doses                               | 1010                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
|-----------------|--------------------------------------------------------------------|

End point description:

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

End point timeframe:

During the 30-day follow up period (Day 0-29) after vaccination.

| End point values            | Infanrix-<br>IPV+Hib Group |  |  |  |
|-----------------------------|----------------------------|--|--|--|
| Subject group type          | Reporting group            |  |  |  |
| Number of subjects analysed | 2590                       |  |  |  |
| Units: Subjects             |                            |  |  |  |
| Any AE(s)                   | 914                        |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting large injection site swelling.

|                         |                                                             |
|-------------------------|-------------------------------------------------------------|
| End point title         | Number of subjects reporting large injection site swelling. |
| End point description:  |                                                             |
| End point type          | Secondary                                                   |
| End point timeframe:    |                                                             |
| After the booster dose. |                                                             |

| End point values            | Infanrix-<br>IPV+Hib Group |  |  |  |
|-----------------------------|----------------------------|--|--|--|
| Subject group type          | Reporting group            |  |  |  |
| Number of subjects analysed | 2540                       |  |  |  |
| Units: Subjects             |                            |  |  |  |
| Local swelling              | 10                         |  |  |  |
| Diffuse swelling            | 1                          |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any serious adverse events (SAEs).

|                                 |                                                                 |
|---------------------------------|-----------------------------------------------------------------|
| End point title                 | Number of subjects reporting any serious adverse events (SAEs). |
| End point description:          |                                                                 |
| End point type                  | Secondary                                                       |
| End point timeframe:            |                                                                 |
| During the entire study period. |                                                                 |

|                             |                            |  |  |  |
|-----------------------------|----------------------------|--|--|--|
| <b>End point values</b>     | Infanrix-<br>IPV+Hib Group |  |  |  |
| Subject group type          | Reporting group            |  |  |  |
| Number of subjects analysed | 2590                       |  |  |  |
| Units: Subjects             |                            |  |  |  |
| Any SAE(s)                  | 380                        |  |  |  |

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and general adverse events (AEs): during the 4-day (Day 0–3) after vaccination.

Unsolicited local and general AEs: during the 30-day (Day 0–29) after vaccination.

Serious adverse events (SAEs): during the entire study period.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Infanrix-IPV+Hib Group |
|-----------------------|------------------------|

Reporting group description: -

| Serious adverse events                               | Infanrix-IPV+Hib Group |  |  |
|------------------------------------------------------|------------------------|--|--|
| Total subjects affected by serious adverse events    |                        |  |  |
| subjects affected / exposed                          | 380 / 2590 (14.67%)    |  |  |
| number of deaths (all causes)                        | 0                      |  |  |
| number of deaths resulting from adverse events       | 0                      |  |  |
| Vascular disorders                                   |                        |  |  |
| Kawasaki's disease                                   |                        |  |  |
| subjects affected / exposed                          | 6 / 2590 (0.23%)       |  |  |
| occurrences causally related to treatment / all      | 0 / 6                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                  |  |  |
| Haematoma                                            |                        |  |  |
| subjects affected / exposed                          | 2 / 2590 (0.08%)       |  |  |
| occurrences causally related to treatment / all      | 0 / 2                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                  |  |  |
| General disorders and administration site conditions |                        |  |  |
| Pyrexia                                              |                        |  |  |
| subjects affected / exposed                          | 1 / 2590 (0.04%)       |  |  |
| occurrences causally related to treatment / all      | 0 / 1                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                  |  |  |
| Swelling                                             |                        |  |  |

|                                                 |                   |  |  |
|-------------------------------------------------|-------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Immune system disorders                         |                   |  |  |
| Milk allergy                                    |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Reproductive system and breast disorders        |                   |  |  |
| Balanitis                                       |                   |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Respiratory, thoracic and mediastinal disorders |                   |  |  |
| Asthma                                          |                   |  |  |
| subjects affected / exposed                     | 11 / 2590 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 11            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Bronchial hyperreactivity                       |                   |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Wheezing                                        |                   |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Asthmatic crisis                                |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Epistaxis                                       |                   |  |  |

|                                                 |                   |  |  |
|-------------------------------------------------|-------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Interstitial lung disease                       |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 1             |  |  |
| Rhinitis allergic                               |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Injury, poisoning and procedural complications  |                   |  |  |
| Head injury                                     |                   |  |  |
| subjects affected / exposed                     | 12 / 2590 (0.46%) |  |  |
| occurrences causally related to treatment / all | 0 / 12            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Foreign body trauma                             |                   |  |  |
| subjects affected / exposed                     | 3 / 2590 (0.12%)  |  |  |
| occurrences causally related to treatment / all | 0 / 3             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Thermal burn                                    |                   |  |  |
| subjects affected / exposed                     | 3 / 2590 (0.12%)  |  |  |
| occurrences causally related to treatment / all | 0 / 3             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Arthropod bite                                  |                   |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Skin laceration                                 |                   |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Accidental exposure                             |                   |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Burns second degree                             |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Overdose                                        |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Skull fracture                                  |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Subdural haemorrhage                            |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Upper limb fracture                             |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Congenital, familial and genetic disorders      |                  |  |  |
| Cryptorchism                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Laryngomalacia                                  |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Lymphangioma                                    |                  |  |  |

|                                                 |                   |  |  |
|-------------------------------------------------|-------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Cardiac disorders                               |                   |  |  |
| Cardiac aneurysm                                |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Nervous system disorders                        |                   |  |  |
| Febrile convulsion                              |                   |  |  |
| subjects affected / exposed                     | 25 / 2590 (0.97%) |  |  |
| occurrences causally related to treatment / all | 0 / 25            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Convulsion                                      |                   |  |  |
| subjects affected / exposed                     | 7 / 2590 (0.27%)  |  |  |
| occurrences causally related to treatment / all | 0 / 7             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Benign intracranial hypertension                |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Cerebral haemorrhage                            |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Blood and lymphatic system disorders            |                   |  |  |
| Idiopathic thrombocytopenic purpura             |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Lymphadenitis                                   |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| Neutropenia                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Gastrointestinal disorders                      |                  |  |  |
| Gastritis                                       |                  |  |  |
| subjects affected / exposed                     | 5 / 2590 (0.19%) |  |  |
| occurrences causally related to treatment / all | 0 / 5            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Diarrhoea                                       |                  |  |  |
| subjects affected / exposed                     | 3 / 2590 (0.12%) |  |  |
| occurrences causally related to treatment / all | 0 / 3            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Intussusception                                 |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Constipation                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Haematemesis                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Mouth ulceration                                |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Vomiting                                        |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Skin and subcutaneous tissue disorders          |                  |  |  |

|                                                 |                   |  |  |
|-------------------------------------------------|-------------------|--|--|
| Urticaria                                       |                   |  |  |
| subjects affected / exposed                     | 3 / 2590 (0.12%)  |  |  |
| occurrences causally related to treatment / all | 1 / 3             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Petechiae                                       |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Swelling face                                   |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Urticaria chronic                               |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Renal and urinary disorders                     |                   |  |  |
| Vesicoureteric reflux                           |                   |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Infections and infestations                     |                   |  |  |
| Bronchiolitis                                   |                   |  |  |
| subjects affected / exposed                     | 87 / 2590 (3.36%) |  |  |
| occurrences causally related to treatment / all | 0 / 87            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Upper respiratory tract infection               |                   |  |  |
| subjects affected / exposed                     | 47 / 2590 (1.81%) |  |  |
| occurrences causally related to treatment / all | 0 / 47            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Gastroenteritis                                 |                   |  |  |
| subjects affected / exposed                     | 45 / 2590 (1.74%) |  |  |
| occurrences causally related to treatment / all | 0 / 45            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |

|                                                 |                   |  |  |  |
|-------------------------------------------------|-------------------|--|--|--|
| Bronchitis                                      |                   |  |  |  |
| subjects affected / exposed                     | 20 / 2590 (0.77%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 20            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Gastritis viral                                 |                   |  |  |  |
| subjects affected / exposed                     | 16 / 2590 (0.62%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 16            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Urinary tract infection                         |                   |  |  |  |
| subjects affected / exposed                     | 16 / 2590 (0.62%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 16            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Escherichia urinary tract infection             |                   |  |  |  |
| subjects affected / exposed                     | 13 / 2590 (0.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 13            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Hand-foot-and-mouth disease                     |                   |  |  |  |
| subjects affected / exposed                     | 13 / 2590 (0.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 13            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Viral infection                                 |                   |  |  |  |
| subjects affected / exposed                     | 13 / 2590 (0.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 13            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Gastroenteritis viral                           |                   |  |  |  |
| subjects affected / exposed                     | 12 / 2590 (0.46%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 12            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Respiratory syncytial virus bronchiolitis       |                   |  |  |  |
| subjects affected / exposed                     | 10 / 2590 (0.39%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 10            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |  |
| Gastroenteritis rotavirus                       |                   |  |  |  |



|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 7 / 2590 (0.27%) |  |  |
| occurrences causally related to treatment / all | 0 / 7            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Herpangina                                      |                  |  |  |
| subjects affected / exposed                     | 7 / 2590 (0.27%) |  |  |
| occurrences causally related to treatment / all | 0 / 7            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Pneumonia                                       |                  |  |  |
| subjects affected / exposed                     | 7 / 2590 (0.27%) |  |  |
| occurrences causally related to treatment / all | 0 / 7            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Abscess limb                                    |                  |  |  |
| subjects affected / exposed                     | 6 / 2590 (0.23%) |  |  |
| occurrences causally related to treatment / all | 2 / 6            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Pharyngitis                                     |                  |  |  |
| subjects affected / exposed                     | 6 / 2590 (0.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 6            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Viral upper respiratory tract infection         |                  |  |  |
| subjects affected / exposed                     | 6 / 2590 (0.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 6            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Gastroenteritis salmonella                      |                  |  |  |
| subjects affected / exposed                     | 5 / 2590 (0.19%) |  |  |
| occurrences causally related to treatment / all | 0 / 5            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Lobar pneumonia                                 |                  |  |  |
| subjects affected / exposed                     | 4 / 2590 (0.15%) |  |  |
| occurrences causally related to treatment / all | 0 / 4            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Lower respiratory tract infection               |                  |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 4 / 2590 (0.15%) |  |  |
| occurrences causally related to treatment / all | 0 / 4            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Viral skin infection                            |                  |  |  |
| subjects affected / exposed                     | 4 / 2590 (0.15%) |  |  |
| occurrences causally related to treatment / all | 0 / 4            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Subcutaneous abscess                            |                  |  |  |
| subjects affected / exposed                     | 3 / 2590 (0.12%) |  |  |
| occurrences causally related to treatment / all | 0 / 3            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Bronchopneumonia                                |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Croup infectious                                |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Haematoma infection                             |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 1 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Otitis media                                    |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Perianal abscess                                |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Abscess                                         |                  |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Acarodermatitis                                 |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Bacteraemia                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Campylobacter gastroenteritis                   |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Cellulitis                                      |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Conjunctivitis viral                            |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Dengue fever                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Epstein-barr virus infection                    |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Exanthema subitum                               |                  |  |  |

|                                                 |                  |  |  |  |
|-------------------------------------------------|------------------|--|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Folliculitis                                    |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Gastroenteritis bacterial                       |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Influenza                                       |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Localised infection                             |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Lymphadenitis bacterial                         |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Necrotising fasciitis                           |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Parainfluenzae viral laryngotracheobronchitis   |                  |  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| Parotitis                                       |                  |  |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Tonsillitis                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Urinary tract infection bacterial               |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Viral pharyngitis                               |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Metabolism and nutrition disorders              |                  |  |  |
| Decreased appetite                              |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Failure to thrive                               |                  |  |  |
| subjects affected / exposed                     | 2 / 2590 (0.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Dehydration                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 2590 (0.04%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |

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

| Non-serious adverse events                            | Infanrix-IPV+Hib Group  |  |  |
|-------------------------------------------------------|-------------------------|--|--|
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 1482 / 2590<br>(57.22%) |  |  |
| General disorders and administration site conditions  |                         |  |  |
| Pain                                                  |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 855 / 2590<br>(33.01%)  |  |  |
| occurrences (all)                                     | 855                     |  |  |
| Redness                                               |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 907 / 2590<br>(35.02%)  |  |  |
| occurrences (all)                                     | 907                     |  |  |
| Swelling                                              |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 706 / 2590<br>(27.26%)  |  |  |
| occurrences (all)                                     | 706                     |  |  |
| Drowsiness                                            |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 929 / 2590<br>(35.87%)  |  |  |
| occurrences (all)                                     | 929                     |  |  |
| Fever (Axillary)                                      |                         |  |  |
| subjects affected / exposed                           | 1482 / 2590<br>(57.22%) |  |  |
| occurrences (all)                                     | 1482                    |  |  |
| Irritability                                          |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 1217 / 2590<br>(46.99%) |  |  |
| occurrences (all)                                     | 1217                    |  |  |
| Loss of appetite                                      |                         |  |  |
| alternative assessment type: Systematic               |                         |  |  |
| subjects affected / exposed                           | 1010 / 2590<br>(39.00%) |  |  |
| occurrences (all)                                     | 1010                    |  |  |
| Respiratory, thoracic and mediastinal disorders       |                         |  |  |

|                                                                                                                      |                               |  |  |
|----------------------------------------------------------------------------------------------------------------------|-------------------------------|--|--|
| Cough<br>subjects affected / exposed<br>occurrences (all)                                                            | 146 / 2590 (5.64%)<br>146     |  |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 391 / 2590<br>(15.10%)<br>391 |  |  |

## 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