# Clinical trial results:
# A phase IV, open, non-randomised, multicentre study to assess the reactogenicity and immunogenicity of a booster dose of GSK Biologicals' combined reduced-antigen-content diphtheria-tetanus, acellular pertussis and inactivated poliovirus vaccine dTpa-IPV (Boostrix-Polio) when administered in healthy subjects aged 9-13 years, 5 years after previous booster vaccination with dTpa-IPV in the study 711866/001 (dTpa-IPV-001).

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

| | |
|---|---|
| EudraCT number | 2007-003477-94 |
| Trial protocol | DE |
| Global end of trial date | 08 July 2008 |

**Results information**

| | |
|---|---|
| Result version number | v2 |
| This version publication date | 20 November 2018 |
| First version publication date | 01 May 2015 |
| Version creation reason | • Correction of full data set<br>Data correction due to a system error in EudraCT – Results |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 110947 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00635128 |
| 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) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000500-PIP01-08 |

| | |
|---|---|
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 22 April 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 July 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 July 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the incidence of grade 3 local reactions occurring during the 4-day (Day 0–Day 3) follow-up period after administration of a booster dose of dTpa-IPV vaccine in healthy children and adolescents aged 9 to 13 years, 5 years after a previous booster dose of the same vaccine in the study 711866/001 (dTpa-IPV-001).

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 22 February 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Germany: 415 |
| Worldwide total number of subjects | 415 |
| EEA total number of subjects | 415 |

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) | 415 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Boostrix-Polio Group |

Arm description:

Subjects received a single dose of Boostrix™-Polio vaccine.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix™-Polio |
| Investigational medicinal product code | |
| Other name | dTPa-IPV vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

| | |
|---|---|
| **Arm title** | Boostrix + IPV Mérieux Group |

Arm description:

Subjects received a single dose of Boostrix™ and IPV Mérieux®  vaccines, respectively.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix™ |
| Investigational medicinal product code | |
| Other name | dTPa vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

| | |
|---|---|
| Investigational medicinal product name | IPV Mérieux® |
| Investigational medicinal product code | |
| Other name | IPV vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

| **Number of subjects in period 1** | Boostrix-Polio Group | Boostrix + IPV Mérieux Group |
|---|---|---|
| Started | 351 | 64 |
| Completed | 351 | 64 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Boostrix-Polio Group |
| Reporting group description: | |
| Subjects received a single dose of Boostrix™-Polio vaccine. | |
| Reporting group title | Boostrix + IPV Mérieux Group |
| Reporting group description: | |
| Subjects received a single dose of Boostrix™ and IPV Mérieux® vaccines, respectively. | |

| Reporting group values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | Total |
|---|---|---|---|
| Number of subjects | 351 | 64 | 415 |
| Age categorical<br>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<br>Units: years | | | |
| arithmetic mean | 11.4 | 11.3 | |
| standard deviation | ± 0.97 | ± 0.72 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 169 | 32 | 201 |
| Male | 182 | 32 | 214 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Boostrix-Polio Group |
| Reporting group description: | |
| Subjects received a single dose of Boostrix™-Polio vaccine. | |
| Reporting group title | Boostrix + IPV Mérieux Group |
| Reporting group description: | |
| Subjects received a single dose of Boostrix™ and IPV Mérieux® vaccines, respectively. | |
| Subject analysis set title | All subjects |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Boostrix-Polio Group and Boostrix + IPV Mérieux Group, subjects who received one dose of dTpa-IPV vaccine and one dose of dTpa + IPV vaccines. | |

### Primary: Number of subjects with any Grade 3 local adverse events (AEs)

| | |
|---|---|
| End point title | Number of subjects with any Grade 3 local adverse events (AEs)[1] |
| End point description: | |
| Safety results are presented for all subjects. Grade 3 symptoms: symptoms that prevented normal activity. | |
| End point type | Primary |
| End point timeframe: | |
| During the 4-day follow-up period (Day 0-3) after booster vaccination | |
| 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.<br>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed. | |

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 415 | | | |
| Units: Subjects | | | | |
| Local symptoms [N=415] | 41 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with solicited local symptoms

| | |
|---|---|
| End point title | Number of subjects with solicited local symptoms |
| End point description: | |
| Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 4-day follow-up period (Day 0-3) after booster vaccination | |

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 415 | | | |
| Units: Subjects | | | | |
| Any Pain | 302 | | | |
| Any Redness | 195 | | | |
| Any Swelling | 163 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited general symptoms

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

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal, headache and temperature [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade and relationship to vaccination.

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

End point timeframe:

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

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 414 | | | |
| Units: Subjects | | | | |
| Any Fatigue | 101 | | | |
| Any Gastrointestinal | 45 | | | |
| Any Headache | 88 | | | |
| Any Temperature | 14 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (≥) 0.1 international units per milliliter (IU/mL) and ≥ 1 IU/mL

| End point title | Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (≥) 0.1 international units per milliliter (IU/mL) and ≥ 1 |
|---|---|

| | |
|---|---|
| | IU/mL |

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 336 | 62 | | |
| Units: Subjects | | | | |
| Anti-diphtheria ≥ 0.1 IU/mL Pre [N=334;62] | 298 | 53 | | |
| Anti-diphtheria ≥ 0.1 IU/mL Post [N=336;62] | 336 | 62 | | |
| Anti-diphtheria ≥ 1 IU/mL Pre [N=334;62] | 91 | 13 | | |
| Anti-diphtheria ≥ 1 IU/mL Post [N=336;62] | 308 | 55 | | |
| Anti-tetanus ≥ 0.1 IU/mL Pre [N=335;62] | 330 | 61 | | |
| Anti-tetanus ≥ 0.1 IU/mL Post [N=336;62] | 336 | 62 | | |
| Anti-tetanus ≥ 1 IU/mL Pre [N=335;62] | 181 | 35 | | |
| Anti-tetanus ≥ 1 IU/mL Post [N=336;62] | 335 | 61 | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 336 | 62 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-diphtheria Pre [N=334;62] | 0.51 (0.429 to 0.608) | 0.446 (0.305 to 0.651) | | |
| Anti-diphtheria Post [N=336;62] | 4.784 (4.302 to 5.32) | 4.153 (3.089 to 5.585) | | |
| Anti-tetanus Pre [N=335;62] | 1.197 (1.045 to 1.37) | 1.067 (0.797 to 1.429) | | |
| Anti-tetanus Post [N=336;62] | 11.81 (11.011 to 12.667) | 9.518 (7.879 to 11.498) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ 5 ELISA unit per milliliter (EL.U/ml)

| End point title | Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ 5 ELISA unit per milliliter (EL.U/ml) |
|---|---|

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 336 | 62 | | |
| Units: Subjects | | | | |
| Anti-PT Pre [N=330;62] | 134 | 21 | | |
| Anti-PT Post [N=335;62] | 334 | 59 | | |
| Anti-FHA Pre [N=333;60] | 332 | 60 | | |
| Anti-FHA Post [N=336;61] | 336 | 61 | | |
| Anti-PRN Pre [N=335;62] | 325 | 57 | | |
| Anti-PRN Post [N=336;62] | 336 | 62 | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 336 | 62 | | |
| Units: EL.U/ml | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT Pre [N=330;62] | 5.2 (4.7 to 5.9) | 4.5 (3.6 to 5.6) | | |
| Anti-PT Post [N=335;62] | 41.6 (38.1 to 45.3) | 32 (24.5 to 41.9) | | |
| Anti-FHA Pre [N=333;60] | 69.8 (62.1 to 78.4) | 70.1 (52.5 to 93.5) | | |
| Anti-FHA Post [N=336;61] | 662.7 (613.2 to 716.1) | 733.9 (610.4 to 882.5) | | |
| Anti-PRN Pre [N=335;62] | 46.8 (41.5 to 52.8) | 41.1 (30 to 56.2) | | |
| Anti-PRN Post [N=336;62] | 570.8 (527.4 to 617.7) | 460.4 (353.3 to 600) | | |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 335 | 62 | | |
| Units: Subjects | | | | |
| Anti-polio 1, Pre [N=333;62] | 329 | 60 | | |
| Anti-polio 1, Post [N=335;62] | 335 | 62 | | |
| Anti-polio 2, Pre [N=334;62] | 333 | 62 | | |
| Anti-polio 2, Post [N=335;62] | 335 | 62 | | |
| Anti-polio 3, Pre [N=334;62] | 324 | 60 | | |
| Anti-polio 3, Post [N=333;62] | 333 | 62 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers

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

End point description:

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

End point timeframe:

Prior to and one month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 335 | 62 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-polio 1, Pre [N=333;62] | 138.7 (123 to 156.4) | 128.9 (96.1 to 172.7) | | |
| Anti-polio 1, Post [N=335;62] | 1359.6 (1213.4 to 1523.3) | 1088.9 (866.5 to 1368.4) | | |
| Anti-polio 2, Pre [N=334;62] | 166.3 (149.5 to 185) | 179.2 (142.9 to 224.7) | | |
| Anti-polio 2, Post [N=335;62] | 1629.4 (1475.2 to 1799.7) | 1309.5 (1035.2 to 1656.3) | | |
| Anti-polio 3, Pre [N=334;62] | 117.2 (102.8 to 133.5) | 118.4 (83.4 to 168) | | |
| Anti-polio 3, Post [N=333;62] | 1882.4 (1687.9 to 2099.3) | 1712.5 (1329.2 to 2206.3) | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Booster vaccine response was defined as appearance of antibodies in subjects who were seronegative at the pre-vaccination time point (i.e. with concentrations < 5 EL.U/mL) or at least 2-fold increase of pre-vaccination antibody concentrations in subjects who were seropositive at the pre-vaccination time point (i.e. with concentrations < 5 EL.U/mL).

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

End point timeframe:

One month after booster vaccination

| End point values | Boostrix-Polio Group | Boostrix + IPV Mérieux Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 335 | 62 | | |
| Units: Subjects | | | | |
| Anti-PT [N=330;62] | 308 | 56 | | |
| Anti-FHA [N=333;60] | 311 | 56 | | |
| Anti-PRN [N=335;62] | 319 | 61 | | |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

AEs results are presented for all subjects. An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

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

End point timeframe:

During the 31-day (Day 0–30) follow-up period after booster vaccination

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 415 | | | |
| Units: Subjects | | | | |
| Any AEs | 64 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with serious adverse events (SAEs)

| End point title | Number of subjects with serious adverse events (SAEs) |
|---|---|

End point description:

SAEs results are presented for all subjects. Assessed SAEs include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

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

End point timeframe:

Following booster vaccination

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 415 | | | |
| Units: Subjects | | | | |
| SAEs | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local/general during the 4-day period; AEs during the 31-Day period; SAEs following booster vaccination.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | All Subjects |

Reporting group description:

Boostrix-Polio Group and Boostrix + IPV Mérieux Group, subjects who received one dose of Boostrix™ - Polio vaccine and one dose of Boostrix™ + IPV Mérieux® vaccines.

| **Serious adverse events** | All Subjects | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 415 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| **Non-serious adverse events** | All Subjects | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 302 / 415 (72.77%) | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 302 / 415 (72.77%) | | |
| occurrences (all) | 302 | | |
| Redness | | | |
| subjects affected / exposed | 195 / 415 (46.99%) | | |
| occurrences (all) | 195 | | |
| Swelling | | | |
| subjects affected / exposed | 163 / 415 (39.28%) | | |
| occurrences (all) | 163 | | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed[1] | 101 / 414 (24.40%) | | |
| occurrences (all) | 101 | | |
| Gastrointestinal | | | |
| subjects affected / exposed[2] | 45 / 414 (10.87%) | | |
| occurrences (all) | 45 | | |
| Headache | | | |
| subjects affected / exposed[3] | 88 / 414 (21.26%) | | |
| occurrences (all) | 88 | | |
| Temperature (Axillary) | | | |
| subjects affected / exposed[4] | 14 / 414 (3.38%) | | |
| occurrences (all) | 14 | | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported