



## Clinical trial results:

**A phase IIIA, randomized, observer-blind, controlled, multinational consistency study to evaluate the immunogenicity and safety of GSK Biologicals' MMR vaccine (GSK209762) (Priorix) compared to Merck & Co., Inc.'s MMR vaccine (M-M-R II), as a first dose, both co-administered with Varivax, Havrix and Prevna 13 (subset of children) to healthy children 12 to 15 months of age.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-004891-12 |
| Trial protocol           | EE FI ES       |
| Global end of trial date | 16 April 2015  |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2 (current) |
| This version publication date  | 16 June 2018 |
| First version publication date | 30 July 2016 |
| Version creation reason        |              |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 115648 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01702428 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut, 89, Rixensart, Belgium, 1330   |
| Public contact               | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, (44)2089 904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, (44)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                       | 09 February 2018 |
| Is this the analysis of the primary completion data? | No               |

|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 16 April 2015 |
| 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:

1. To demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.
2. To demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of geometric mean concentrations (GMCs) for antibodies to measles, mumps and rubella viruses at Day 42.
3. To demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR (for the two pooled lots) vaccine in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.
4. To demonstrate non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR (for the two pooled lots) vaccine in terms of GMCs for antibodies to measles, mumps and rubella viruses at Day 42.
5. To demonstrate an acceptable immune response for INV\_MMR in terms of seroresponse rates to measles, mumps and rubella viruses at Day 42.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 09 November 2012 |
| 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 | Spain: 256          |
| Country: Number of subjects enrolled | Estonia: 501        |
| Country: Number of subjects enrolled | Finland: 1350       |
| Country: Number of subjects enrolled | Mexico: 394         |
| Country: Number of subjects enrolled | United States: 2515 |
| Worldwide total number of subjects   | 5016                |
| EEA total number of subjects         | 2107                |

Notes:

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**Subjects enrolled per age group**

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|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |      |
|--|------|
| wk                                       |      |
| Newborns (0-27 days)                     | 0    |
| Infants and toddlers (28 days-23 months) | 5016 |
| 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:

13 subjects from 5016 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started is 5003.

### Pre-assignment

Screening details:

Sub-cohorts for this study were as follows: • US sub-cohort: Subjects recruited in US and received INV\_MMR or COM\_MMR co-administered with Varivax (VV), Havrix (HAV) and Prevnar (PCV-13) vaccines at Visit 1 (Day 0). • Non-US sub-cohort: Subjects recruited outside US and received INV\_MMR or COM\_MMR co-administered with VV and HAV vaccines at Day 0.

### Pre-assignment period milestones

|                              |      |
|------------------------------|------|
| Number of subjects started   | 5016 |
| Number of subjects completed | 5003 |

### Pre-assignment subject non-completion reasons

|                            |                                   |
|----------------------------|-----------------------------------|
| Reason: Number of subjects | No study vaccine administered: 13 |
|----------------------------|-----------------------------------|

### Period 1

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

Blinding implementation details:

The study was conducted in a double-blind fashion, with regard to the lot-to-lot consistency evaluation of the three INV\_MMR vaccine lots and in an observer-blind fashion for the comparison of the pooled lots of INV\_MMR vaccine versus the pooled COM\_MMR vaccine lots.

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| Arm title                    | INV_MMR_L1 Group |

Arm description:

Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV\_MMR) Lot 1 (L1) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Priorix   |
| Investigational medicinal product code |   |
| Other name                             | GSK Biologicals' live attenuated measles, mumps and rubella vaccine (GSK209762) |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                   |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

|  |         |
|--|---------|
| Investigational medicinal product name | Varivax |
| Investigational medicinal product code |         |
| Other name                             |         |

|   |   |
|---|---|
| Pharmaceutical forms  | Powder and solvent for solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use  |
| Dosage and administration details:  |   |
| Subjects received 1 dose of VV vaccine which was administered subcutaneously in the triceps region of the right arm.                |   |
| Investigational medicinal product name  | Havrix  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Suspension for injection  |
| Routes of administration  | Intramuscular use   |
| Dosage and administration details:  |   |
| Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.      |   |
| Investigational medicinal product name  | Prevnar 13  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Suspension for injection  |
| Routes of administration  | Intramuscular use   |
| Dosage and administration details:  |   |
| US subjects received 1 dose of PCV-13 vaccine which was administered intramuscularly in the anterolateral region of the left thigh. |   |
| <b>Arm title</b>  | INV_MMR_L2 Group  |

Arm description:

Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV\_MMR) Lot 2 (L2) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Priorix   |
| Investigational medicinal product code |   |
| Other name                             | GSK Biologicals' live attenuated measles, mumps and rubella vaccine (GSK209762) |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                   |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

|  |   |
|--|---|
| Investigational medicinal product name | Varivax   |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Subjects received 1 dose of VV vaccine which was administered subcutaneously in the triceps region of the right arm.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Havrix                   |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Pevnar 13                |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

US subjects received 1 dose of PCV-13 vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | INV_MMR_L3 Group |
|------------------|------------------|

Arm description:

Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV\_MMR) Lot 3 (L3) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Priorix   |
| Investigational medicinal product code |   |
| Other name                             | GSK Biologicals' live attenuated measles, mumps and rubella vaccine (GSK209762) |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                   |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

|  |   |
|--|---|
| Investigational medicinal product name | Varivax   |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

Subjects received 1 dose of VV vaccine which was administered subcutaneously in the triceps region of the right arm.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Havrix                   |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Pevnar 13                |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

US subjects received 1 dose of PCV-13 vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

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

**Arm description:**

Subjects received 1 dose of COM\_MMR Lot 1 and Lot 2 co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. Pooled analysis was conducted for this group.

|  |   |
|--|---|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Varivax   |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use  |

**Dosage and administration details:**

Subjects received 1 dose of VV vaccine which was administered subcutaneously in the triceps region of the right arm.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Havrix                   |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

**Dosage and administration details:**

Subjects received 1 dose of HAV vaccine which was administered intramuscularly in the anterolateral region of the right thigh.

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

**Dosage and administration details:**

US subjects received 1 dose of PCV-13 vaccine which was administered intramuscularly in the anterolateral region of the left thigh.

|  |   |
|--|---|
| Investigational medicinal product name | M-M-R II  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Subcutaneous use                                |

**Dosage and administration details:**

Subjects received 1 dose of MMR vaccine which was administered subcutaneously in the triceps region of the left arm.

**Notes:**

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The study was conducted in a double-blind fashion, with regard to the lot-to-lot consistency evaluation of the three INV\_MMR vaccine lots and in an observer-blind fashion for the comparison of the pooled lots of INV\_MMR vaccine versus COM\_MMR vaccine.

| <b>Number of subjects in period 1<sup>[2]</sup></b> | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group |
|---|------------------|------------------|------------------|
| Started   | 1239             | 1232             | 1243             |
| Completed   | 1175             | 1162             | 1190             |
| Not completed                                       | 64               | 70               | 53               |
| Lost Health Plan                                    | 3                | 5                | -                |
| Consent withdrawn by subject                        | 21               | 23               | 14               |

|                               |    |    |    |
|-------------------------------|----|----|----|
| Adverse event, non-fatal      | 2  | -  | -  |
| Parents cannot assist to site | 1  | -  | 1  |
| Mother transferred care       | -  | 1  | -  |
| Lost to follow-up             | 33 | 41 | 37 |
| Parents too busy              | 1  | -  | -  |
| Protocol deviation            | 3  | -  | 1  |
| Lost Coverage                 | -  | -  | -  |

| Number of subjects in period<br>1 <sup>[2]</sup> | COM_MMR Group |
|--|---------------|
|  |               |
| Started  | 1289          |
| Completed  | 1232          |
| Not completed                                    | 57            |
| Lost Health Plan                                 | 2             |
| Consent withdrawn by subject                     | 10            |
| Adverse event, non-fatal                         | -             |
| Parents cannot assist to site                    | -             |
| Mother transferred care                          | -             |
| Lost to follow-up                                | 44            |
| Parents too busy                                 | -             |
| Protocol deviation                               | -             |
| Lost Coverage                                    | 1             |

Notes:

[2] - 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: 13 subjects from 5016 were allocated subject number but no study vaccine was administered. Therefore, the number of subjects started is 5003.



## Baseline characteristics

### Reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | INV_MMR_L1 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 1 (L1) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | INV_MMR_L2 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 2 (L2) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | INV_MMR_L3 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 3 (L3) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | COM_MMR Group    |
| Reporting group description:  |                  |
| Subjects received 1 dose of COM_MMR Lot 1 and Lot 2 co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. Pooled analysis was conducted for this group.                                  |                  |

| Reporting group values | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group |
|------------------------|------------------|------------------|------------------|
| Number of subjects     | 1239             | 1232             | 1243             |
| Age categorical        |                  |                  |                  |
| Units: Subjects        |                  |                  |                  |

|   |       |       |       |
|---|-------|-------|-------|
| Age continuous                          |       |       |       |
| Units: months                           |       |       |       |
| arithmetic mean                         | 12.3  | 12.3  | 12.3  |
| standard deviation                      | ± 0.7 | ± 0.7 | ± 0.7 |
| Gender categorical                      |       |       |       |
| Units: Subjects                         |       |       |       |
| Female                                  | 607   | 594   | 615   |
| Male                                    | 632   | 638   | 628   |
| Race/Ethnicity, Customized              |       |       |       |
| Units: Subjects                         |       |       |       |
| White - Arabic / North African Heritage | 5     | 6     | 2     |

|   |     |     |     |
|---|-----|-----|-----|
| Asian - Central/South Asian Heritage      | 14  | 6   | 7   |
| Other                                     | 170 | 155 | 162 |
| Native Hawaiian or Other Pacific Islander | 3   | 1   | 5   |
| American Indian or Alaskan Native         | 25  | 37  | 33  |
| White - Caucasian / European Heritage     | 932 | 938 | 944 |
| Asian - South East Asian Heritage         | 21  | 25  | 21  |
| African Heritage / African American       | 60  | 52  | 57  |
| Asian - Japanese Heritage                 | 1   | 2   | 2   |
| Asian - East Asian Heritage               | 8   | 10  | 10  |

| Reporting group values | COM_MMR Group | Total |  |
|------------------------|---------------|-------|--|
| Number of subjects     | 1289          | 5003  |  |
| Age categorical        |               |       |  |
| Units: Subjects        |               |       |  |

|   |       |      |  |
|---|-------|------|--|
| Age continuous                            |       |      |  |
| Units: months                             |       |      |  |
| arithmetic mean                           | 12.3  |      |  |
| standard deviation                        | ± 0.7 | -    |  |
| Gender categorical                        |       |      |  |
| Units: Subjects                           |       |      |  |
| Female                                    | 618   | 2434 |  |
| Male                                      | 671   | 2569 |  |
| Race/Ethnicity, Customized                |       |      |  |
| Units: Subjects                           |       |      |  |
| White - Arabic / North African Heritage   | 7     | 20   |  |
| Asian - Central/South Asian Heritage      | 9     | 36   |  |
| Other                                     | 163   | 650  |  |
| Native Hawaiian or Other Pacific Islander | 2     | 11   |  |
| American Indian or Alaskan Native         | 31    | 126  |  |
| White - Caucasian / European Heritage     | 970   | 3784 |  |
| Asian - South East Asian Heritage         | 26    | 93   |  |
| African Heritage / African American       | 70    | 239  |  |
| Asian - Japanese Heritage                 | 1     | 6    |  |
| Asian - East Asian Heritage               | 10    | 38   |  |

## End points

### End points reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | INV_MMR_L1 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 1 (L1) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | INV_MMR_L2 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 2 (L2) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | INV_MMR_L3 Group |
| Reporting group description:  |                  |
| Subjects received 1 dose of GSK's candidate combined measles, mumps and rubella (MMR) investigational vaccine (INV_MMR) Lot 3 (L3) co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. |                  |
| Reporting group title   | COM_MMR Group    |
| Reporting group description:  |                  |
| Subjects received 1 dose of COM_MMR Lot 1 and Lot 2 co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. Pooled analysis was conducted for this group.                                  |                  |
| Subject analysis set title  | INV_MMR Group    |
| Subject analysis set type   | Per protocol     |
| Subject analysis set description:   |                  |
| This group included subjects from INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.  |                  |

### Primary: Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value

|  |  |
|--|--|
| End point title  | Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value <sup>[1]</sup> |
| End point description:   |  |
| Seroreponse was defined as post-vaccination anti-measles virus antibody concentration $\geq 200$ milli International Unit/Milliliter (mIU/mL) among subjects who were seronegative (antibody concentration $< 150$ mIU/mL) before vaccination. This outcome measure is applicable to reporting groups INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 as analysis was performed on subjects who received one of the lots of INV_MMR vaccine. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Day 42  |  |
| Notes:   |  |

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of seroreponse rates. This endpoint therefore presents

the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                 | INV_MMR_L1 Group    | INV_MMR_L2 Group    | INV_MMR_L3 Group    |  |
|----------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type               | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed      | 1083                | 1069                | 1096                |  |
| Units: Percentage of subjects    |                     |                     |                     |  |
| number (confidence interval 95%) |                     |                     |                     |  |
| Anti-measles $\geq$ 150 mIU/mL   | 98.2 (97.3 to 98.9) | 98.9 (98.0 to 99.4) | 98.1 (97.1 to 98.8) |  |
| Anti-measles $\geq$ 200 mIU/mL   | 98.1 (97.1 to 98.8) | 98.6 (97.7 to 99.2) | 97.8 (96.8 to 98.6) |  |

## Statistical analyses

| Statistical analysis title  | Statistical analysis 1              |
|---|-------------------------------------|
| Statistical analysis description:   |                                     |
| Difference between groups (INV_MMR_L1 Group minus INV_MMR_L2 Group) in percentage of subjects with anti-measles antibody concentration $\geq$ 200 mIU/mL. |                                     |
| Comparison groups   | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis   | 2152                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[2]</sup>      |
| Parameter estimate  | Difference in seroresponse rate     |
| Point estimate  | -0.54                               |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | -1.69                               |
| upper limit   | 0.58                                |

Notes:

[2] - For each pair-wise comparison, the 2-sided 95% confidence interval (CI) on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to measles virus.

| Statistical analysis title  | Statistical analysis 2              |
|---|-------------------------------------|
| Statistical analysis description:   |                                     |
| Difference between groups (INV_MMR_L2 Group minus INV_MMR_L3 Group) in percentage of subjects with anti-measles antibody concentration $\geq$ 200 mIU/mL. |                                     |
| Comparison groups   | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis   | 2165                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[3]</sup>      |
| Parameter estimate  | Difference in seroresponse rate     |
| Point estimate  | 0.79                                |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | -0.35                               |
| upper limit   | 1.98                                |

Notes:

[3] - For each pair-wise comparison, the 2-sided 95% confidence interval (CI) on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to measles virus.

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 3              |
| Statistical analysis description:   |                                     |
| Difference between groups (INV_MMR_L1 Group minus INV_MMR_L3 Group) in percentage of subjects with anti-measles antibody concentration $\geq 200$ mIU/mL. |                                     |
| Comparison groups   | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis   | 2179                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[4]</sup>      |
| Parameter estimate  | Difference in seroresponse rate     |
| Point estimate  | 0.25                                |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | -0.98                               |
| upper limit   | 1.5                                 |

Notes:

[4] - For each pair-wise comparison, the 2-sided 95% confidence interval (CI) on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to measles virus.

### Primary: Anti-measles virus antibody concentrations

|   |   |
|---|---|
| End point title   | Anti-measles virus antibody concentrations <sup>[5]</sup> |
| End point description:  |   |
| Antibody concentrations were expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. This outcome measure is applicable to reporting groups INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 as analysis was performed on subjects who received one of the lots of INV_MMR vaccine. |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| At Day 42   |   |

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of geometric mean concentrations (GMCs). This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                         | INV_MMR_L1 Group          | INV_MMR_L2 Group          | INV_MMR_L3 Group          |  |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type                       | Reporting group           | Reporting group           | Reporting group           |  |
| Number of subjects analysed              | 1083                      | 1069                      | 1096                      |  |
| Units: mIU/mL                            |                           |                           |                           |  |
| geometric mean (confidence interval 95%) |                           |                           |                           |  |
| mIU/mL                                   | 2970.3 (2813.2 to 3136.2) | 3023.6 (2864.5 to 3191.6) | 3058.3 (2893.9 to 3232.0) |  |

## Statistical analyses

|  |                                     |
|--|-------------------------------------|
| <b>Statistical analysis title</b>  | Statistical analysis 1              |
| Statistical analysis description:  |                                     |
| Adjusted GMC ratio (INV_MMR_L1 Group divided by INV_MMR_L2 Group) for antibodies to measles virus at Day 42. |                                     |
| Comparison groups  | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis  | 2152                                |
| Analysis specification   | Pre-specified                       |
| Analysis type  | non-inferiority <sup>[6]</sup>      |
| Method   | ANOVA                               |
| Parameter estimate   | Adjusted GMC ratio                  |
| Point estimate   | 0.99                                |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | 0.91                                |
| upper limit  | 1.06                                |

Notes:

[6] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67;1.5] margin for antibodies to measles.

|  |                                     |
|--|-------------------------------------|
| <b>Statistical analysis title</b>  | Statistical analysis 2              |
| Statistical analysis description:  |                                     |
| Adjusted GMC ratio (INV_MMR_L1 Group divided by INV_MMR_L3 Group) for antibodies to measles virus at Day 42. |                                     |
| Comparison groups  | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis  | 2179                                |
| Analysis specification   | Pre-specified                       |
| Analysis type  | non-inferiority <sup>[7]</sup>      |
| Method   | ANOVA                               |
| Parameter estimate   | Adjusted GMC ratio                  |
| Point estimate   | 0.97                                |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | 0.9                                 |
| upper limit  | 1.05                                |

Notes:

[7] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67;1.5] margin for antibodies to measles.

|  |                                     |
|--|-------------------------------------|
| <b>Statistical analysis title</b>  | Statistical analysis 3              |
| Statistical analysis description:  |                                     |
| Adjusted GMC ratio (INV_MMR_L2 Group divided by INV_MMR_L1 Group) for antibodies to measles virus at Day 42. |                                     |
| Comparison groups  | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis  | 2152                                |
| Analysis specification   | Pre-specified                       |
| Analysis type  | non-inferiority <sup>[8]</sup>      |
| Method   | ANOVA                               |
| Parameter estimate   | Adjusted GMC ratio                  |
| Point estimate   | 1.01                                |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.94    |
| upper limit         | 1.09    |

Notes:

[8] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67;1.5] margin for antibodies to measles.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L2 Group divided by INV\_MMR\_L3 Group) for antibodies to measles virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2165                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[9]</sup>      |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 0.99                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 0.91                                |
| upper limit                             | 1.06                                |

Notes:

[9] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67;1.5] margin for antibodies to measles.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L3 Group divided by INV\_MMR\_L1 Group) for antibodies to measles virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2179                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[10]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.03                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 0.95                                |
| upper limit                             | 1.11                                |

Notes:

[10] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to measles.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L3 Group divided by INV\_MMR\_L2 Group) for antibodies to measles virus at Day 42.

|                   |                                     |
|-------------------|-------------------------------------|
| Comparison groups | INV_MMR_L2 Group v INV_MMR_L3 Group |
|-------------------|-------------------------------------|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 2165                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[11]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 1.01                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.94                            |
| upper limit                             | 1.09                            |

Notes:

[11] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to measles.

### Primary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value <sup>[12]</sup> |
|-----------------|---|

End point description:

Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration  $\geq 10$  ELISA Unit/Milliliter (EU/mL) among subjects who were seronegative (antibody concentrations  $< 5$  EU/mL) before vaccination. This outcome measure is applicable to reporting groups INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 as analysis was performed on subjects who received one of the lots of INV\_MMR vaccine.

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

End point timeframe:

At Day 42

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                 | INV_MMR_L1 Group    | INV_MMR_L2 Group    | INV_MMR_L3 Group    |  |
|----------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type               | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed      | 1062                | 1047                | 1078                |  |
| Units: Percentage of subjects    |                     |                     |                     |  |
| number (confidence interval 95%) |                     |                     |                     |  |
| Anti-mumps $\geq 5$ EU/mL        | 99.7 (99.2 to 99.9) | 99.3 (98.6 to 99.7) | 99.2 (98.4 to 99.6) |  |
| Anti-mumps $\geq 10$ EU/mL       | 98.6 (97.7 to 99.2) | 98.6 (97.6 to 99.2) | 98.0 (96.9 to 98.7) |  |

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L1 Group minus INV\_MMR\_L2 Group) in percentage of subjects with anti-mumps antibody concentration  $\geq 10$  EU/mL.



|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis | 2109                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[13]</sup>     |
| Parameter estimate                      | Difference in seroresponse rate     |
| Point estimate                          | 0.02                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -1.05                               |
| upper limit                             | 1.09                                |

Notes:

[13] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to mumps virus.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L1 Group minus INV\_MMR\_L3 Group) in percentage of subjects with anti-mumps antibody concentration  $\geq 10$  EU/mL.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2140                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[14]</sup>     |
| Parameter estimate                      | Difference in seroresponse rate     |
| Point estimate                          | 0.63                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -0.5                                |
| upper limit                             | 1.81                                |

Notes:

[14] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to mumps virus.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L2 Group minus INV\_MMR\_L3 Group) in percentage of subjects with anti-mumps antibody concentration  $\geq 10$  EU/mL.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2125                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[15]</sup>     |
| Parameter estimate                      | Difference in seroresponse rate     |
| Point estimate                          | 0.61                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -0.53                               |
| upper limit                             | 1.79                                |

Notes:

[15] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to mumps virus.

## Primary: Anti-mumps virus antibody concentration

|                 |   |
|-----------------|---|
| End point title | Anti-mumps virus antibody concentration <sup>[16]</sup> |
|-----------------|---|

End point description:

Antibody concentrations were expressed as GMCs in EU/mL. This outcome measure is applicable to reporting groups INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 as analysis was performed on subjects who received one of the lots of INV\_MMR vaccine.

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

End point timeframe:

At Day 42

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                         | INV_MMR_L1 Group    | INV_MMR_L2 Group    | INV_MMR_L3 Group    |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 1062                | 1047                | 1078                |  |
| Units: EU/mL                             |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| EU/mL                                    | 71.7 (68.3 to 75.2) | 76.9 (73.2 to 80.8) | 69.0 (65.5 to 72.7) |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L1 Group divided by INV\_MMR\_L2 Group) for antibodies to mumps virus at Day 42.

|                   |                                     |
|-------------------|-------------------------------------|
| Comparison groups | INV_MMR_L1 Group v INV_MMR_L2 Group |
|-------------------|-------------------------------------|

|   |      |
|---|------|
| Number of subjects included in analysis | 2109 |
|---|------|

|                        |               |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

|               |                                 |
|---------------|---------------------------------|
| Analysis type | non-inferiority <sup>[17]</sup> |
|---------------|---------------------------------|

|        |       |
|--------|-------|
| Method | ANOVA |
|--------|-------|

|                    |                    |
|--------------------|--------------------|
| Parameter estimate | Adjusted GMC ratio |
|--------------------|--------------------|

|                |      |
|----------------|------|
| Point estimate | 0.93 |
|----------------|------|

Confidence interval

|       |      |
|-------|------|
| level | 95 % |
|-------|------|

|       |         |
|-------|---------|
| sides | 2-sided |
|-------|---------|

|             |      |
|-------------|------|
| lower limit | 0.87 |
|-------------|------|

|             |   |
|-------------|---|
| upper limit | 1 |
|-------------|---|

Notes:

[17] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|----------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L1 Group divided by INV\_MMR\_L3 Group) for antibodies to mumps virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2140                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[18]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.04                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 0.97                                |
| upper limit                             | 1.11                                |

Notes:

[18] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L2 Group divided by INV\_MMR\_L1 Group) for antibodies to mumps virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis | 2109                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[19]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.07                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 1                                   |
| upper limit                             | 1.15                                |

Notes:

[19] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L2 Group divided by INV\_MMR\_L3 Group) for antibodies to mumps virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L3 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis | 2125                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[20]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.11                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 1.04                                |
| upper limit                             | 1.19                                |

Notes:

[20] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

| Statistical analysis title  | Statistical analysis 5              |
|---|-------------------------------------|
| Statistical analysis description:<br>Adjusted GMC ratio (INV_MMR_L3 Group divided by INV_MMR_L1 Group) for antibodies to mumps virus at Day 42. |                                     |
| Comparison groups   | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis   | 2140                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[21]</sup>     |
| Method  | ANOVA                               |
| Parameter estimate  | Adjusted GMC ratio                  |
| Point estimate  | 0.96                                |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | 0.9                                 |
| upper limit   | 1.03                                |

Notes:

[21] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

| Statistical analysis title  | Statistical analysis 6              |
|---|-------------------------------------|
| Statistical analysis description:<br>Adjusted GMC ratio (INV_MMR_L3 Group divided by INV_MMR_L2 Group) for antibodies to mumps virus at Day 42. |                                     |
| Comparison groups   | INV_MMR_L3 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis   | 2125                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[22]</sup>     |
| Method  | ANOVA                               |
| Parameter estimate  | Adjusted GMC ratio                  |
| Point estimate  | 0.9                                 |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | 0.84                                |
| upper limit   | 0.96                                |

Notes:

[22] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to mumps.

### **Primary: Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value**

|   |   |
|---|---|
| End point title   | Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value <sup>[23]</sup> |
| End point description:<br>Seroresponse was defined as post-vaccination anti-rubella virus antibody concentration $\geq 10$ International Unit/Milliliter (IU/mL) among subjects who were seronegative (antibody concentrations $< 4$ IU/mL) before vaccination. This outcome measure is applicable to reporting groups INV_MMR_L1, INV_MMR_L2 and INV_MMR_L3 as analysis was performed on subjects who received one of the lots of INV_MMR vaccine. |   |
| End point type  | Primary   |

End point timeframe:

At Day 42

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                 | INV_MMR_L1 Group    | INV_MMR_L2 Group    | INV_MMR_L3 Group    |  |
|----------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type               | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed      | 1083                | 1067                | 1095                |  |
| Units: Percentage of subjects    |                     |                     |                     |  |
| number (confidence interval 95%) |                     |                     |                     |  |
| Anti-rubella $\geq 4$ IU/mL      | 99.4 (98.8 to 99.8) | 99.7 (99.2 to 99.9) | 99.4 (98.7 to 99.7) |  |
| Anti-rubella $\geq 10$ IU/mL     | 97.2 (96.1 to 98.1) | 97.1 (95.9 to 98.0) | 97.7 (96.6 to 98.5) |  |

## Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L1 Group minus INV\_MMR\_L2 Group) in percentage of subjects with anti-rubella antibody concentration  $\geq 10$  IU/mL.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L2 Group |
| Number of subjects included in analysis | 2150                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[24]</sup>     |
| Parameter estimate                      | Difference in seroresponse rate     |
| Point estimate                          | 0.14                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -1.3                                |
| upper limit                             | 1.58                                |

Notes:

[24] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to rubella virus.

| Statistical analysis title | Statistical analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L1 Group minus INV\_MMR\_L3 Group) in percentage of subjects with anti-rubella antibody concentration  $\geq 10$  IU/mL.

|                   |                                     |
|-------------------|-------------------------------------|
| Comparison groups | INV_MMR_L1 Group v INV_MMR_L3 Group |
|-------------------|-------------------------------------|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 2178                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[25]</sup> |
| Parameter estimate                      | Difference in seroresponse rate |
| Point estimate                          | -0.49                           |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | -1.86                           |
| upper limit                             | 0.86                            |

Notes:

[25] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to rubella virus.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Difference between groups (INV\_MMR\_L2 Group minus INV\_MMR\_L3 Group) in percentage of subjects with anti-rubella antibody concentration  $\geq 10$  IU/mL.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2162                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[26]</sup>     |
| Parameter estimate                      | Difference in seroresponse rate     |
| Point estimate                          | -0.62                               |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -2.02                               |
| upper limit                             | 0.74                                |

Notes:

[26] - For each pair-wise comparison, the 2-sided 95% CI on the lot difference in seroresponse rates should be within the [-5%;5%] margin for antibodies to rubella virus.

### **Primary: Anti-rubella virus antibody concentration**

|                 |   |
|-----------------|---|
| End point title | Anti-rubella virus antibody concentration <sup>[27]</sup> |
|-----------------|---|

End point description:

Antibody concentrations were expressed as GMCs in IU/mL. This outcome measure is applicable to reporting groups INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 as analysis was performed on subjects who received one of the lots of INV\_MMR vaccine.

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

End point timeframe:

At Day 42

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the consistency of three manufacturing lots of INV\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 Groups).

| End point values                         | INV_MMR_L1 Group    | INV_MMR_L2 Group    | INV_MMR_L3 Group    |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 1083                | 1067                | 1095                |  |
| Units: IU/mL                             |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| IU/mL                                    | 57.2 (54.4 to 60.1) | 53.1 (50.5 to 55.7) | 57.0 (54.3 to 59.8) |  |

## Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L1 Group divided by INV\_MMR\_L2 Group) for antibodies to rubella virus at Day 42. .

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L2 Group v INV_MMR_L1 Group |
| Number of subjects included in analysis | 2150                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[28]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.08                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 1.01                                |
| upper limit                             | 1.15                                |

Notes:

[28] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to measles.

| Statistical analysis title | Statistical analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L1 Group divided by INV\_MMR\_L3 Group) for antibodies to rubella virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2178                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[29]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1                                   |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 0.94                                |
| upper limit                             | 1.07                                |

Notes:

[29] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to measles.

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 3              |
| Statistical analysis description:<br>Adjusted GMC ratio (INV_MMR_L2 Group divided by INV_MMR_L1 Group) for antibodies to rubella virus at Day 42. |                                     |
| Comparison groups   | INV_MMR_L2 Group v INV_MMR_L1 Group |
| Number of subjects included in analysis   | 2150                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[30]</sup>     |
| Method  | ANOVA                               |
| Parameter estimate  | Adjusted GMC ratio                  |
| Point estimate  | 0.93                                |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | 0.87                                |
| upper limit   | 0.99                                |

Notes:

[30] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to measles.

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 4              |
| Statistical analysis description:<br>Adjusted GMC ratio (INV_MMR_L2 Group divided by INV_MMR_L3 Group) for antibodies to rubella virus at Day 42. |                                     |
| Comparison groups   | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis   | 2162                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[31]</sup>     |
| Method  | ANOVA                               |
| Parameter estimate  | Adjusted GMC ratio                  |
| Point estimate  | 0.93                                |
| Confidence interval   |                                     |
| level   | 95 %                                |
| sides   | 2-sided                             |
| lower limit   | 0.87                                |
| upper limit   | 0.99                                |

Notes:

[31] - For each pair-wise comparison, the 2-sided 95% CI on the log ratio should be within the [0.67; 1.5] margin for antibodies to measles.

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 5              |
| Statistical analysis description:<br>Adjusted GMC ratio (INV_MMR_L3 Group divided by INV_MMR_L1 Group) for antibodies to rubella virus at Day 42. |                                     |
| Comparison groups   | INV_MMR_L1 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis   | 2178                                |
| Analysis specification  | Pre-specified                       |
| Analysis type   | non-inferiority <sup>[32]</sup>     |
| Method  | ANOVA                               |
| Parameter estimate  | Adjusted GMC ratio                  |
| Point estimate  | 1                                   |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.93    |
| upper limit         | 1.07    |

Notes:

[32] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to measles.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Adjusted GMC ratio (INV\_MMR\_L3 Group divided by INV\_MMR\_L2 Group) for antibodies to rubella virus at Day 42.

|   |                                     |
|---|-------------------------------------|
| Comparison groups                       | INV_MMR_L2 Group v INV_MMR_L3 Group |
| Number of subjects included in analysis | 2162                                |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | non-inferiority <sup>[33]</sup>     |
| Method                                  | ANOVA                               |
| Parameter estimate                      | Adjusted GMC ratio                  |
| Point estimate                          | 1.08                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | 1.01                                |
| upper limit                             | 1.15                                |

Notes:

[33] - For each pair-wise comparison, the 2-sided 95% CI on the lot ratio should be within the [0.67; 1.5] margin for antibodies to measles.

### **Primary: Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value in pooled MMR groups**

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value in pooled MMR groups <sup>[34]</sup> |
|-----------------|--|

End point description:

Seroresponse was defined as post-vaccination anti-measles virus antibody concentration  $\geq 200$  mIU/mL among subjects who were seronegative (antibody concentration  $< 150$  mIU/mL) before vaccination. Criteria to demonstrate an acceptable immune response for INV\_MMR in terms of seroresponse rates to measles virus at Day 42: The LL of 2-sided 95% CI for the seroresponse rate for the pooled INV\_MMR lots is  $\geq 90\%$  for antibodies to measles virus.

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

End point timeframe:

At Day 42

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                 | COM_MMR Group       | INV_MMR Group        |  |  |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type               | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed      | 1137                | 3248                 |  |  |
| Units: Percentage of subjects    |                     |                      |  |  |
| number (confidence interval 95%) |                     |                      |  |  |
| Anti-measles $\geq$ 150 mIU/mL   | 98.1 (97.1 to 98.8) | 98.4 (97.9 to 98.8)  |  |  |
| Anti-measles $\geq$ 200 mIU/mL   | 98.0 (97.0 to 98.7) | 98.2 (97.6 to 98.6)  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical analysis 1          |
|---|---------------------------------|
| Statistical analysis description:<br>Difference in percentage (INV_MMR Group minus COM_MMR Group) of subjects with anti-measles antibody concentration at Day 42. |                                 |
| Comparison groups   | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis   | 4385                            |
| Analysis specification  | Pre-specified                   |
| Analysis type   | non-inferiority <sup>[35]</sup> |
| Parameter estimate  | Difference in seroresponse rate |
| Point estimate  | 0.18                            |
| Confidence interval   |                                 |
| level   | 95 %                            |
| sides   | 2-sided                         |
| lower limit   | -0.68                           |
| upper limit   | 1.25                            |

Notes:

[35] - The Lower Limit (LL) of 2-sided 95 % CI for the difference in seroresponse (INV\_MMR Group minus COM\_MMR Group) should be  $\geq$  -5% for antibodies to measles virus.

## Primary: Anti-measles virus antibody concentrations in pooled MMR groups

|   |   |
|---|---|
| End point title   | Anti-measles virus antibody concentrations in pooled MMR groups <sup>[36]</sup> |
| End point description:<br>Antibody concentrations were expressed as GMCs in mIU/mL. |   |
| End point type  | Primary   |
| End point timeframe:<br>At Day 42   |   |

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                         | COM_MMR Group             | INV_MMR Group             |  |  |
|--|---------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group           | Subject analysis set      |  |  |
| Number of subjects analysed              | 1137                      | 3248                      |  |  |
| Units: mIU/mL                            |                           |                           |  |  |
| geometric mean (confidence interval 95%) |                           |                           |  |  |
| mIU/mL                                   | 3074.4 (2911.0 to 3246.9) | 3017.4 (2923.9 to 3113.8) |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for antibodies to measles virus at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 4385                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[37]</sup> |
| Method   | ANOVA                           |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.98                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.93                            |
| upper limit  | 1.05                            |

Notes:

[37] - The LL of the 2-sided 95% CI on GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.67$  for antibodies to measles virus.

## Primary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value in pooled MMR groups

|   |  |
|---|--|
| End point title   | Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value in pooled MMR groups <sup>[38]</sup> |
| End point description:  |  |
| Seroresponse was defined as post-vaccination anti-mumps virus antibody concentration $\geq 10$ EU/mL among subjects who were seronegative (antibody concentrations $< 5$ EU/mL) before vaccination. |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| At Day 42   |  |

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                 | COM_MMR Group       | INV_MMR Group        |  |  |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type               | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed      | 1107                | 3187                 |  |  |
| Units: Percentage of subjects    |                     |                      |  |  |
| number (confidence interval 95%) |                     |                      |  |  |
| Anti-mumps $\geq$ 5 EU/mL        | 99.3 (98.6 to 99.7) | 99.4 (99.1 to 99.6)  |  |  |
| Anti-mumps $\geq$ 10 EU/mL       | 97.6 (96.5 to 98.4) | 98.4 (97.9 to 98.8)  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| Difference in percentage (INV_MMR Group minus COM_MMR Group) of subjects with anti-mumps antibody concentration at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 4294                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[39]</sup> |
| Parameter estimate   | Difference in seroresponse rate |
| Point estimate   | 0.81                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | -0.1                            |
| upper limit  | 1.96                            |

Notes:

[39] - The LL of 2-sided 95 % CI for the difference in seroresponse (INV\_MMR Group minus COM\_MMR Group) should be  $\geq$  -5% for antibodies to mumps virus.

## Primary: Anti-mumps virus antibody concentration in pooled MMR groups

|  |  |
|--|--|
| End point title  | Anti-mumps virus antibody concentration in pooled MMR groups <sup>[40]</sup> |
| End point description:                                   |  |
| Antibody concentrations were expressed as GMCs in EU/mL. |  |
| End point type   | Primary  |
| End point timeframe:                                     |  |
| At Day 42  |  |

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                         | COM_MMR Group       | INV_MMR Group        |  |  |
|--|---------------------|----------------------|--|--|
| Subject group type                       | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed              | 1107                | 3187                 |  |  |
| Units: EU/mL                             |                     |                      |  |  |
| geometric mean (confidence interval 95%) |                     |                      |  |  |
| EU/mL                                    | 69.1 (65.7 to 72.7) | 72.4 (70.4 to 74.5)  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for antibodies to mumps virus at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 4294                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[41]</sup> |
| Method   | ANOVA                           |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 1.05                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.99                            |
| upper limit  | 1.11                            |

Notes:

[41] - The LL of the 2-sided 95% CI on GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.67$  for antibodies to mumps virus.

## Primary: Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value in pooled MMR groups

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value in pooled MMR groups <sup>[42]</sup> |
|-----------------|--|

End point description:

Seroresponse was defined as post-vaccination anti-rubella virus antibody concentration  $\geq 10$  IU/mL among subjects who were seronegative (antibody concentrations  $< 4$  IU/mL) before vaccination. Criteria to demonstrate an acceptable immune response for INV\_MMR in terms of seroresponse rates to rubella virus at Day 42: The LL of 2-sided 95% CI for the seroresponse rate for the pooled INV\_MMR lots is  $\geq 90\%$  for antibodies to rubella virus.

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

End point timeframe:

At Day 42

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                 | COM_MMR Group       | INV_MMR Group        |  |  |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type               | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed      | 1135                | 3245                 |  |  |
| Units: Percentage of subjects    |                     |                      |  |  |
| number (confidence interval 95%) |                     |                      |  |  |
| Anti-rubella $\geq$ 4 IU/mL      | 99.6 (99.0 to 99.9) | 99.5 (99.2 to 99.7)  |  |  |
| Anti-rubella $\geq$ 10 IU/mL     | 98.5 (97.6 to 99.1) | 97.3 (96.7 to 97.9)  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical analysis 1          |
|---|---------------------------------|
| Statistical analysis description:<br>Difference in percentage (INV_MMR Group minus COM_MMR Group) of subjects with anti-rubella antibody concentration at Day 42. |                                 |
| Comparison groups   | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis   | 4380                            |
| Analysis specification  | Pre-specified                   |
| Analysis type   | non-inferiority <sup>[43]</sup> |
| Parameter estimate  | Difference in seroresponse rate |
| Point estimate  | -1.15                           |
| Confidence interval   |                                 |
| level   | 95 %                            |
| sides   | 2-sided                         |
| lower limit   | -2                              |
| upper limit   | -0.15                           |

Notes:

[43] - The LL of 2-sided 95 % CI for the difference in seroresponse (INV\_MMR Group minus COM\_MMR Group) should be  $\geq$  -5% for antibodies to rubella virus.

## Primary: Anti-rubella virus antibody concentration in pooled MMR groups

|  |   |
|--|---|
| End point title  | Anti-rubella virus antibody concentration in pooled MMR |
| End point description:<br>Antibody concentrations were expressed as GMCs in IU/mL. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Day 42  |   |

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                         | COM_MMR Group       | INV_MMR Group        |  |  |
|--|---------------------|----------------------|--|--|
| Subject group type                       | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed              | 1135                | 3245                 |  |  |
| Units: IU/mL                             |                     |                      |  |  |
| geometric mean (confidence interval 95%) |                     |                      |  |  |
| IU/mL                                    | 64.0 (61.1 to 67.0) | 55.7 (54.2 to 57.3)  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for antibodies to rubella virus at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 4380                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[45]</sup> |
| Method   | ANOVA                           |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.87                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.83                            |
| upper limit  | 0.92                            |

Notes:

[45] - The LL of the 2-sided 95% CI on GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.67$  for antibodies to measles virus.

## Secondary: Percentage of subjects with an anti-Varicella Zoster Virus (VZV) antibody concentration equal to or above the cut-off value in US sub-cohort of pooled MMR groups

|   |   |
|---|---|
| End point title   | Percentage of subjects with an anti-Varicella Zoster Virus (VZV) antibody concentration equal to or above the cut-off value in US sub-cohort of pooled MMR groups <sup>[46]</sup> |
| End point description:  |   |
| Seroresponse was defined as post-vaccination anti-VZV antibody concentration $\geq 75$ mIU/mL among subjects who were seronegative (antibody concentration $< 25$ mIU/mL) before vaccination. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| At Day 42   |   |

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of seroresponse rates. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                 | COM_MMR Group       | INV_MMR Group        |  |  |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type               | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed      | 540                 | 1492                 |  |  |
| Units: Percentage of subjects    |                     |                      |  |  |
| number (confidence interval 95%) |                     |                      |  |  |
| Anti-VZV $\geq$ 25 mIU/mL        | 99.6 (98.7 to 100)  | 99.7 (99.3 to 99.9)  |  |  |
| Anti-VZV $\geq$ 75 mIU/mL        | 90.9 (88.2 to 93.2) | 92.2 (90.7 to 93.5)  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| In US sub-cohort: Difference in percentage (INV_MMR Group minus COM_MMR Group) of subjects with anti-VZV antibody concentration at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 2032                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[47]</sup> |
| Parameter estimate   | Difference in seroresponse rate |
| Point estimate   | 1.3                             |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | -1.31                           |
| upper limit  | 4.29                            |

Notes:

[47] - The LL of 2-sided 95 % CI for the difference in seroresponse (pooled INV\_MMR Group minus pooled COM\_MMR Group) should be  $\geq$  -10% for antibodies to VZV.

## Secondary: Anti-VZV virus antibody concentration in US sub-cohort of pooled MMR groups

|   |   |
|---|---|
| End point title   | Anti-VZV virus antibody concentration in US sub-cohort of pooled MMR groups <sup>[48]</sup> |
| End point description:                                    |   |
| Antibody concentrations were expressed as GMCs in mIU/mL. |   |
| End point type  | Secondary   |
| End point timeframe:                                      |   |
| At Day 42   |   |

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).



| End point values                         | COM_MMR Group          | INV_MMR Group        |  |  |
|--|------------------------|----------------------|--|--|
| Subject group type                       | Reporting group        | Subject analysis set |  |  |
| Number of subjects analysed              | 540                    | 1492                 |  |  |
| Units: mIU/mL                            |                        |                      |  |  |
| geometric mean (confidence interval 95%) |                        |                      |  |  |
| mIU/mL                                   | 167.2 (158.2 to 176.7) | 169.6 (164.3 to 175) |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:  |                                 |
| In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for antibodies to VZV virus at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 2032                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[49]</sup> |
| Method   | ANOVA                           |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 1.01                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.95                            |
| upper limit  | 1.08                            |

Notes:

[49] - The LL of the 2-sided 95% CI on GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.67$  for antibodies to VZV.

## Secondary: Percentage of subjects with an anti-HAV antibody concentration equal to or above the cut-off value in US sub-cohort of pooled MMR groups

|   |  |
|---|--|
| End point title   | Percentage of subjects with an anti-HAV antibody concentration equal to or above the cut-off value in US sub-cohort of pooled MMR groups <sup>[50]</sup> |
| End point description:  |  |
| Percentage of subjects with an Anti-HAV antibody concentration equal to or above 15 mIU/mL were reported. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| At Day 42   |  |

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to assess the immunogenicity of HAV vaccine with respect to the seroresponse rates for antibodies to HAV in the pooled INV\_MMR group in contrast to the COM\_MMR vaccine groups. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                 | COM_MMR Group       | INV_MMR Group        |  |  |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type               | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed      | 285                 | 783                  |  |  |
| Units: Percentage of subjects    |                     |                      |  |  |
| number (confidence interval 95%) |                     |                      |  |  |
| Percentage of subjects           | 87.4 (82.9 to 91.0) | 88.9 (86.5 to 91.0)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-HAV antibody concentrations in US sub-cohort of pooled MMR groups

|                 |  |
|-----------------|--|
| End point title | Anti-HAV antibody concentrations in US sub-cohort of pooled MMR groups <sup>[51]</sup> |
|-----------------|--|

End point description:

Antibody concentrations were expressed as GMCs in mIU/mL.

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

End point timeframe:

At Day 42

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                         | COM_MMR Group       | INV_MMR Group        |  |  |
|--|---------------------|----------------------|--|--|
| Subject group type                       | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed              | 285                 | 783                  |  |  |
| Units: mIU/mL                            |                     |                      |  |  |
| geometric mean (confidence interval 95%) |                     |                      |  |  |
| mIU/mL                                   | 42.4 (38.1 to 47.2) | 42.0 (39.3 to 44.8)  |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for antibodies to HAV virus at Day 42.

|                   |                               |
|-------------------|-------------------------------|
| Comparison groups | COM_MMR Group v INV_MMR Group |
|-------------------|-------------------------------|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 1068                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[52]</sup> |
| Method                                  | ANOVA                           |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.98                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.86                            |
| upper limit                             | 1.11                            |

Notes:

[52] - The LL of the 2-sided 95% CI on GMC ratio (INV\_MMR Group over COM\_MMR Group) was  $\geq 0.5$  for antibodies to HAV virus.

## Secondary: Anti-S.pneumoniae antibody concentration in US sub-cohort of pooled MMR groups

|                 |  |
|-----------------|--|
| End point title | Anti-S.pneumoniae antibody concentration in US sub-cohort of pooled MMR groups <sup>[53]</sup> |
|-----------------|--|

End point description:

Antibody concentrations were expressed as GMCs in microgram/Milliliter ( $\mu\text{g/mL}$ ).

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

End point timeframe:

At Day 42

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results for this end point were tabulated to demonstrate the non-inferiority of INV\_MMR (for the three pooled lots) compared to COM\_MMR vaccine in terms of GMCs. This endpoint therefore presents the results for groups applicable for this analysis (i.e., INV\_MMR and COM\_MMR Groups).

| End point values                         | COM_MMR Group          | INV_MMR Group          |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Subject analysis set   |  |  |
| Number of subjects analysed              | 266                    | 759                    |  |  |
| Units: $\mu\text{g/mL}$                  |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| anti-PnPS 1 antibody (N = 266; 759)      | 2.425 (2.195 to 2.679) | 2.257 (2.121 to 2.402) |  |  |
| anti-PnPS 3 antibody (N = 265; 758)      | 0.496 (0.454 to 0.542) | 0.506 (0.481 to 0.533) |  |  |
| anti-PnPS 4 antibody (N = 266; 753)      | 1.872 (1.676 to 2.091) | 1.618 (1.518 to 1.725) |  |  |
| anti-PnPS 5 antibody (N = 266; 757)      | 2.280 (2.085 to 2.493) | 2.106 (1.991 to 2.228) |  |  |
| anti-PnPS 6A antibody (N = 266; 759)     | 5.743 (5.233 to 6.304) | 5.840 (5.508 to 6.192) |  |  |
| anti-PnPS 6B antibody (N = 266; 758)     | 5.838 (5.239 to 6.505) | 5.872 (5.504 to 6.265) |  |  |
| anti-PnPS 7F antibody (N = 266; 758)     | 3.814 (3.484 to 4.176) | 3.691 (3.489 to 3.905) |  |  |
| anti-PnPS 9V antibody (N = 266; 759)     | 2.282 (2.065 to 2.521) | 2.318 (2.183 to 2.461) |  |  |
| anti-PnPS 14 antibody (N = 266; 757)     | 7.053 (6.368 to 7.811) | 6.578 (6.155 to 7.029) |  |  |

|                                       |                        |                        |  |  |
|---------------------------------------|------------------------|------------------------|--|--|
| anti-PnPS 18C antibody (N = 265; 759) | 2.217 (1.990 to 2.470) | 2.102 (1.973 to 2.241) |  |  |
| anti-PnPS 19A antibody (N = 265; 759) | 4.821 (4.372 to 5.317) | 4.731 (4.461 to 5.017) |  |  |
| anti-PnPS 19F antibody (N = 266; 759) | 4.260 (3.872 to 4.687) | 4.251 (4.013 to 4.504) |  |  |
| anti-PnPS 23F antibody (N = 256; 742) | 2.291 (2.025 to 2.592) | 2.198 (2.051 to 2.355) |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical analysis 1          |
|--|---------------------------------|
| Statistical analysis description:<br>In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for anti-PnPS 1 antibody at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 1025                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[54]</sup> |
| Method   | ANCOVA                          |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.94                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.85                            |
| upper limit  | 1.05                            |

Notes:

[54] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

| Statistical analysis title   | Statistical analysis 2          |
|--|---------------------------------|
| Statistical analysis description:<br>In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for anti-PnPS 3 antibody at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 1025                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[55]</sup> |
| Method   | ANCOVA                          |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.99                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.91                            |
| upper limit  | 1.08                            |

Notes:

[55] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

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

**Statistical analysis description:**

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 4 antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[56]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.88                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.79                            |
| upper limit                             | 0.98                            |

**Notes:**

[56] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 4 |
|-----------------------------------|------------------------|

**Statistical analysis description:**

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 5 antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[57]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.92                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.83                            |
| upper limit                             | 1.01                            |

**Notes:**

[57] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 5 |
|-----------------------------------|------------------------|

**Statistical analysis description:**

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 6A antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[58]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 1.01                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.92    |
| upper limit         | 1.11    |

Notes:

[58] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 6B antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[59]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.98                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.89                            |
| upper limit                             | 1.09                            |

Notes:

[59] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 7F antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[60]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.94                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.86                            |
| upper limit                             | 1.03                            |

Notes:

[60] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 9V antibody at Day 42.

|                   |                               |
|-------------------|-------------------------------|
| Comparison groups | COM_MMR Group v INV_MMR Group |
|-------------------|-------------------------------|

|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[61]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.99                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.9                             |
| upper limit                             | 1.08                            |

Notes:

[61] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 14 antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[62]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.91                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.81                            |
| upper limit                             | 1.02                            |

Notes:

[62] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 10 |
|-----------------------------------|-------------------------|

Statistical analysis description:

In US sub-cohort: Adjusted GMC ratio (INV\_MMR Group divided by COM\_MMR Group) for anti-PnPS 18C antibody at Day 42.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[63]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.92                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.84                            |
| upper limit                             | 1.02                            |

Notes:

[63] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

| Statistical analysis title   | Statistical analysis 11         |
|--|---------------------------------|
| Statistical analysis description:<br>In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for anti-PnPS 19A antibody at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 1025                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[64]</sup> |
| Method   | ANCOVA                          |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.97                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.87                            |
| upper limit  | 1.07                            |

Notes:

[64] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

| Statistical analysis title   | Statistical analysis 12         |
|--|---------------------------------|
| Statistical analysis description:<br>In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for anti-PnPS 19F antibody at Day 42. |                                 |
| Comparison groups  | COM_MMR Group v INV_MMR Group   |
| Number of subjects included in analysis  | 1025                            |
| Analysis specification   | Pre-specified                   |
| Analysis type  | non-inferiority <sup>[65]</sup> |
| Method   | ANCOVA                          |
| Parameter estimate   | Adjusted GMC ratio              |
| Point estimate   | 0.96                            |
| Confidence interval  |                                 |
| level  | 95 %                            |
| sides  | 2-sided                         |
| lower limit  | 0.87                            |
| upper limit  | 1.06                            |

Notes:

[65] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

| Statistical analysis title   | Statistical analysis 13       |
|--|-------------------------------|
| Statistical analysis description:<br>In US sub-cohort: Adjusted GMC ratio (INV_MMR Group divided by COM_MMR Group) for anti-PnPS 23F antibody at Day 42. |                               |
| Comparison groups  | COM_MMR Group v INV_MMR Group |



|   |                                 |
|---|---------------------------------|
| Number of subjects included in analysis | 1025                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | non-inferiority <sup>[66]</sup> |
| Method                                  | ANCOVA                          |
| Parameter estimate                      | Adjusted GMC ratio              |
| Point estimate                          | 0.95                            |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | 0.85                            |
| upper limit                             | 1.06                            |

Notes:

[66] - The LL of the 2-sided 95% CI for GMC ratio (INV\_MMR Group over COM\_MMR Group) should be  $\geq 0.5$  for antibodies to for antibodies to PS serotypes.

## Secondary: Number of subjects with any solicited local adverse events (AEs)

|   |  |
|---|--|
| End point title   | Number of subjects with any solicited local adverse events (AEs) |
| End point description:  |  |
| Assessed solicited local AEs were pain, redness and swelling. Any = Occurrence of the symptom regardless of intensity grade or relation to vaccination. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| During the 4-days (Days 0-3) post-vaccination period  |  |

| End point values            | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|-----------------------------|------------------|------------------|------------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed | 1186             | 1175             | 1194             | 1242            |
| Units: Participants         |                  |                  |                  |                 |
| Any Pain                    | 331              | 315              | 273              | 349             |
| Any Redness                 | 296              | 273              | 301              | 313             |
| Any Swelling                | 116              | 99               | 103              | 133             |

| End point values            | INV_MMR Group        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3555                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| Any Pain                    | 919                  |  |  |  |
| Any Redness                 | 870                  |  |  |  |
| Any Swelling                | 318                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of subjects with any solicited general AEs**

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

End point description:

Assessed solicited general AEs were drowsiness, irritability and loss of appetite. Any = Occurrence of the symptom regardless of intensity grade or relation to vaccination.

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

End point timeframe:

During the 15-days (Days 0-14) post-vaccination period

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| End point values            | INV_MMR_L1<br>Group | INV_MMR_L2<br>Group | INV_MMR_L3<br>Group | COM_MMR<br>Group |
|-----------------------------|---------------------|---------------------|---------------------|------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group  |
| Number of subjects analysed | 1190                | 1176                | 1200                | 1243             |
| Units: Participants         |                     |                     |                     |                  |
| Any Drowsiness              | 533                 | 535                 | 533                 | 586              |
| Any Irritability/fussiness  | 764                 | 729                 | 765                 | 819              |
| Any Loss of appetite        | 546                 | 536                 | 526                 | 548              |

| End point values            | INV_MMR<br>Group     |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3566                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| Any Drowsiness              | 1601                 |  |  |  |
| Any Irritability/fussiness  | 2258                 |  |  |  |
| Any Loss of appetite        | 1608                 |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of subjects reporting any fever**

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|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting any fever |
|-----------------|--|

End point description:

Any fever = Fever  $\geq$  38°C.

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

End point timeframe:

During the 43-days (Days 0-42) post-vaccination period

---

| End point values            | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|-----------------------------|------------------|------------------|------------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed | 1190             | 1176             | 1200             | 1243            |
| Units: Participants         |                  |                  |                  |                 |
| Participants                | 404              | 422              | 418              | 412             |

| End point values            | INV_MMR Group        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3566                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| Participants                | 1244                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any rash

|   |                                       |
|---|---------------------------------------|
| End point title   | Number of subjects reporting any rash |
| End point description:  |                                       |
| Assessed were any localized or generalized rash, rash with fever, varicella-like rash, measles/rubella-like rash. Any = Occurrence of the symptom regardless of intensity grade or relation to vaccination. |                                       |
| End point type  | Secondary                             |
| End point timeframe:  |                                       |
| During the 43-days (Days 0-42) post-vaccination period  |                                       |

| End point values             | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|------------------------------|------------------|------------------|------------------|-----------------|
| Subject group type           | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed  | 1190             | 1176             | 1200             | 1243            |
| Units: Participants          |                  |                  |                  |                 |
| Any Localized or Generalized | 352              | 331              | 360              | 378             |
| Any with fever               | 106              | 123              | 118              | 104             |
| Any Varicella like           | 87               | 78               | 85               | 85              |
| Any Measles/Rubella like     | 71               | 88               | 76               | 77              |

| End point values             | INV_MMR Group        |  |  |  |
|------------------------------|----------------------|--|--|--|
| Subject group type           | Subject analysis set |  |  |  |
| Number of subjects analysed  | 3566                 |  |  |  |
| Units: Participants          |                      |  |  |  |
| Any Localized or Generalized | 1043                 |  |  |  |

|                          |     |  |  |  |
|--------------------------|-----|--|--|--|
| Any with fever           | 347 |  |  |  |
| Any Varicella like       | 250 |  |  |  |
| Any Measles/Rubella like | 235 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any MMR specific solicited AEs

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting any MMR specific solicited AEs |
|-----------------|---|

End point description:

Assessed MMR specific solicited AEs were any suspected signs of meningism including febrile convulsions and parotid/salivary gland swelling. Any = Occurrence of the symptom regardless of intensity grade or relation to vaccination.

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

End point timeframe:

During the 43-days (Days 0-42) post-vaccination period

| End point values                    | INV_MMR_L1<br>Group | INV_MMR_L2<br>Group | INV_MMR_L3<br>Group | COM_MMR<br>Group |
|-------------------------------------|---------------------|---------------------|---------------------|------------------|
| Subject group type                  | Reporting group     | Reporting group     | Reporting group     | Reporting group  |
| Number of subjects analysed         | 1190                | 1176                | 1200                | 1243             |
| Units: Participants                 |                     |                     |                     |                  |
| Any febrile convulsion              | 4                   | 1                   | 5                   | 3                |
| Any parotid/salivary gland swelling | 0                   | 0                   | 0                   | 0                |

| End point values                    | INV_MMR<br>Group     |  |  |  |
|-------------------------------------|----------------------|--|--|--|
| Subject group type                  | Subject analysis set |  |  |  |
| Number of subjects analysed         | 3566                 |  |  |  |
| Units: Participants                 |                      |  |  |  |
| Any febrile convulsion              | 10                   |  |  |  |
| Any parotid/salivary gland swelling | 0                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any unsolicited AEs

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting any unsolicited AEs |
|-----------------|--|

End point description:

Unsolicited adverse event (AE) was defined as any adverse event reported in addition to those solicited during the clinical study and also any solicited symptom with onset outside the specified period of

follow-up for solicited symptoms. Any = Occurrence of the symptom regardless of intensity grade or relation to vaccination.

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

End point timeframe:

During the 43-days (Days 0-42) post-vaccination period

| End point values            | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|-----------------------------|------------------|------------------|------------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed | 1239             | 1232             | 1243             | 1289            |
| Units: Participants         |                  |                  |                  |                 |
| Participants                | 615              | 633              | 609              | 618             |

| End point values            | INV_MMR Group        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3714                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| Participants                | 1857                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting AEs of specific interest

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting AEs of specific interest |
|-----------------|---|

End point description:

AEs of specific interest included new onset chronic disease (NOCD) (e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visits.

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

End point timeframe:

From Day 0 through the end of study (Day 180)

| End point values            | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|-----------------------------|------------------|------------------|------------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed | 1239             | 1232             | 1243             | 1289            |
| Units: Participants         |                  |                  |                  |                 |
| NOCDs                       | 40               | 39               | 49               | 48              |
| AEs prompting ER visits     | 123              | 116              | 136              | 134             |

| End point values            | INV_MMR Group        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3714                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| NOCDs                       | 128                  |  |  |  |
| AEs prompting ER visits     | 375                  |  |  |  |

## 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:  |  |
| SAEs assessed include medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity. Any SAE = Occurrence of SAE regardless of intensity grade or relation to vaccination. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| From Day 0 through the end of study (Day 180)   |  |

| End point values            | INV_MMR_L1 Group | INV_MMR_L2 Group | INV_MMR_L3 Group | COM_MMR Group   |
|-----------------------------|------------------|------------------|------------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group |
| Number of subjects analysed | 1239             | 1232             | 1243             | 1289            |
| Units: Participants         |                  |                  |                  |                 |
| Participants                | 21               | 28               | 28               | 25              |

| End point values            | INV_MMR Group        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 3714                 |  |  |  |
| Units: Participants         |                      |  |  |  |
| Participants                | 77                   |  |  |  |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs: From Day 0 through the end of study (Day-180); Solicited local and general symptoms: During the 4-day (Day 0-3) and 15-days (Day 0-14) post-vaccination period; Unsolicited adverse events: During the 43-days (Day 0-42) post-vaccination period.

Adverse event reporting additional description:

The analysis of the solicited symptoms was based on the Total Vaccinated cohort which included only children/doses with documented safety data (i.e., symptom screen/sheet completed).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | INV_MMR_L1 Group |
|-----------------------|------------------|

Reporting group description:

Subjects received 1 dose of INV\_MMR\_L1 vaccine co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | INV_MMR_L2 Group |
|-----------------------|------------------|

Reporting group description:

Subjects received 1 dose of INV\_MMR\_L2 vaccine co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | INV_MMR_L3 Group |
|-----------------------|------------------|

Reporting group description:

Subjects received 1 dose of INV\_MMR\_L3 vaccine co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

|                       |               |
|-----------------------|---------------|
| Reporting group title | INV_MMR Group |
|-----------------------|---------------|

Reporting group description:

This group included subjects from INV\_MMR\_L1, INV\_MMR\_L2 and INV\_MMR\_L3 groups for whom pooled analysis was conducted in addition to lot-to-lot consistency.

|                       |               |
|-----------------------|---------------|
| Reporting group title | COM_MMR Group |
|-----------------------|---------------|

Reporting group description:

Subjects received 1 dose of COM\_MMR Lot 1 and Lot 2 co-administered with VV and HAV vaccines at Visit 1 (Day 0). All US subjects were also given PCV-13 vaccine. The MMR vaccine was administered subcutaneously in the triceps region of the left arm while the VV vaccine was administered subcutaneously in the triceps region of the right arm. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively. Pooled analysis was conducted for this group.

| Serious adverse events                            | INV_MMR_L1 Group  | INV_MMR_L2 Group  | INV_MMR_L3 Group  |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events |                   |                   |                   |
| subjects affected / exposed                       | 21 / 1239 (1.69%) | 28 / 1232 (2.27%) | 28 / 1243 (2.25%) |
| number of deaths (all causes)                     | 0                 | 0                 | 0                 |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| number of deaths resulting from adverse events  | 0                | 0                | 0                |
| Injury, poisoning and procedural complications  |                  |                  |                  |
| Burns second degree                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Concussion                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Femur fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Foot fracture                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Head injury                                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 1239 (0.16%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Surgical and medical procedures                 |                  |                  |                  |
| Finger amputation                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nervous system disorders                        |                  |                  |                  |
| Epilepsy  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Febrile convulsion                              |                  |                  |                  |

|  |                  |                  |                  |
|--|------------------|------------------|------------------|
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Loss of consciousness                                |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Seizure  |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 2 / 1243 (0.16%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood and lymphatic system disorders                 |                  |                  |                  |
| Leukocytosis   |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| General disorders and administration site conditions |                  |                  |                  |
| Pyrexia  |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Immune system disorders                              |                  |                  |                  |
| Milk allergy   |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (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                           |                  |                  |                  |
| Diarrhoea  |                  |                  |                  |
| subjects affected / exposed                          | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Enterocolitis  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastritis                                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Respiratory, thoracic and mediastinal disorders |                  |                  |                  |
| Asthma  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 1239 (0.16%) | 2 / 1232 (0.16%) | 0 / 1243 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchial hyperreactivity                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 3 / 1232 (0.24%) | 0 / 1243 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoxia   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Skin and subcutaneous tissue disorders          |                  |                  |                  |
| Urticaria                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Infections and infestations                     |                  |                  |                  |
| Abscess   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchiolitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 2 / 1232 (0.16%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| Bronchitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 3 / 1239 (0.24%) | 2 / 1232 (0.16%) | 3 / 1243 (0.24%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cellulitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 2 / 1243 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Conjunctivitis                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Croup infectious                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Escherichia urinary tract infection             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Gastroenteritis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 2 / 1243 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroenteritis adenovirus                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| 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 rotavirus                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Gastroenteritis viral                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Herpangina                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Laryngitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Mycoplasma infection                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Neutropenic infection                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Otitis media                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 4 / 1243 (0.32%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otitis media acute                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Pharyngitis                                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumococcal sepsis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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                     | 2 / 1239 (0.16%) | 1 / 1232 (0.08%) | 3 / 1243 (0.24%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia bacterial                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia respiratory syncytial viral           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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 viral                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 2 / 1232 (0.16%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyelonephritis acute                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Respiratory syncytial virus bronchiolitis       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Respiratory tract infection viral               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Rotavirus infection                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Subcutaneous abscess                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Tonsillitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| 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                     | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Viral infection                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 2 / 1243 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Viral pharyngitis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |
| Viral upper respiratory tract infection         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Metabolism and nutrition disorders              |                  |                  |                  |
| Dehydration                                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 2 / 1232 (0.16%) | 3 / 1243 (0.24%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoglycaemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (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            |
| Type 1 diabetes mellitus                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (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            |

| <b>Serious adverse events</b>                     | INV_MMR Group     | COM_MMR Group     |  |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events |                   |                   |  |
| subjects affected / exposed                       | 77 / 3714 (2.07%) | 25 / 1289 (1.94%) |  |
| number of deaths (all causes)                     | 0                 | 0                 |  |
| number of deaths resulting from adverse events    | 0                 | 0                 |  |
| Injury, poisoning and procedural complications    |                   |                   |  |
| Burns second degree                               |                   |                   |  |
| subjects affected / exposed                       | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Concussion  |                   |                   |  |
| subjects affected / exposed                       | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Femur fracture                                    |                   |                   |  |
| subjects affected / exposed                       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Foot fracture                                     |                   |                   |  |
| subjects affected / exposed                       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| Head injury  |                  |                  |  |
| subjects affected / exposed                          | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Surgical and medical procedures                      |                  |                  |  |
| Finger amputation                                    |                  |                  |  |
| subjects affected / exposed                          | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                             |                  |                  |  |
| Epilepsy   |                  |                  |  |
| subjects affected / exposed                          | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Febrile convulsion                                   |                  |                  |  |
| subjects affected / exposed                          | 1 / 3714 (0.03%) | 5 / 1289 (0.39%) |  |
| occurrences causally related to treatment / all      | 1 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Loss of consciousness                                |                  |                  |  |
| subjects affected / exposed                          | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Seizure  |                  |                  |  |
| subjects affected / exposed                          | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Blood and lymphatic system disorders                 |                  |                  |  |
| Leukocytosis   |                  |                  |  |
| subjects affected / exposed                          | 1 / 3714 (0.03%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| General disorders and administration site conditions |                  |                  |  |
| Pyrexia  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immune system disorders                         |                  |                  |  |
| Milk allergy                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal disorders                      |                  |                  |  |
| Diarrhoea                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory, thoracic and mediastinal disorders |                  |                  |  |
| Asthma  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3714 (0.11%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchial hyperreactivity                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3714 (0.08%) | 3 / 1289 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxia   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Urticaria                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3714 (0.00%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Abscess   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchiolitis                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 3714 (0.11%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchitis                                      |                  |                  |  |
| subjects affected / exposed                     | 8 / 3714 (0.22%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cellulitis                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 3714 (0.08%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Conjunctivitis                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3714 (0.05%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Croup infectious                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia urinary tract infection             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Gastroenteritis                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 3714 (0.11%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis adenovirus                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis rotavirus                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis viral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpangina                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngitis                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mycoplasma infection                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasopharyngitis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neutropenic infection                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media                                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 3714 (0.11%) | 2 / 1289 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media acute                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pharyngitis                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumococcal sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia                                       |                  |                  |  |
| subjects affected / exposed                     | 6 / 3714 (0.16%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia bacterial                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia respiratory syncytial viral           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia viral                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 3714 (0.11%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis acute                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory syncytial virus bronchiolitis       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3714 (0.08%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory tract infection viral               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rotavirus infection                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous abscess                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tonsillitis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper respiratory tract infection               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral infection                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3714 (0.05%) | 3 / 1289 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral pharyngitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral upper respiratory tract infection         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolism and nutrition disorders              |                  |                  |  |
| Dehydration                                     |                  |                  |  |
| subjects affected / exposed                     | 5 / 3714 (0.13%) | 3 / 1289 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 1 diabetes mellitus                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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

| Non-serious adverse events  | INV_MMR_L1 Group        | INV_MMR_L2 Group        | INV_MMR_L3 Group        |
|---|-------------------------|-------------------------|-------------------------|
| Total subjects affected by non-serious adverse events               |                         |                         |                         |
| subjects affected / exposed   | 1089 / 1239<br>(87.89%) | 1053 / 1232<br>(85.47%) | 1090 / 1243<br>(87.69%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |                         |                         |
| Seborrhoeic keratosis   |                         |                         |                         |

|  |                       |                       |                       |
|--|-----------------------|-----------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all)     | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Vascular disorders                                   |                       |                       |                       |
| Haematoma  |                       |                       |                       |
| subjects affected / exposed                          | 0 / 1239 (0.00%)      | 1 / 1232 (0.08%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 0                     | 1                     | 0                     |
| Pallor   |                       |                       |                       |
| subjects affected / exposed                          | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                    | 0                     | 0                     | 1                     |
| Pregnancy, puerperium and perinatal conditions       |                       |                       |                       |
| Cephalhaematoma                                      |                       |                       |                       |
| subjects affected / exposed                          | 1 / 1239 (0.08%)      | 0 / 1232 (0.00%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 1                     | 0                     | 0                     |
| General disorders and administration site conditions |                       |                       |                       |
| Crying   |                       |                       |                       |
| subjects affected / exposed                          | 4 / 1239 (0.32%)      | 5 / 1232 (0.41%)      | 2 / 1243 (0.16%)      |
| occurrences (all)                                    | 4                     | 7                     | 2                     |
| Cyst   |                       |                       |                       |
| subjects affected / exposed                          | 1 / 1239 (0.08%)      | 0 / 1232 (0.00%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 2                     | 0                     | 0                     |
| Discomfort   |                       |                       |                       |
| subjects affected / exposed                          | 0 / 1239 (0.00%)      | 1 / 1232 (0.08%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 0                     | 1                     | 0                     |
| Feeling hot  |                       |                       |                       |
| subjects affected / exposed                          | 0 / 1239 (0.00%)      | 1 / 1232 (0.08%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 0                     | 1                     | 0                     |
| Influenza like illness                               |                       |                       |                       |
| subjects affected / exposed                          | 1 / 1239 (0.08%)      | 0 / 1232 (0.00%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                    | 1                     | 0                     | 0                     |
| Injection site bruising                              |                       |                       |                       |
| subjects affected / exposed                          | 4 / 1239 (0.32%)      | 5 / 1232 (0.41%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                    | 4                     | 5                     | 1                     |
| Injection site erosion                               |                       |                       |                       |
| subjects affected / exposed                          | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                    | 0                     | 0                     | 1                     |
| Injection site erythema                              |                       |                       |                       |



|                             |                        |                        |                        |
|-----------------------------|------------------------|------------------------|------------------------|
| subjects affected / exposed | 321 / 1239<br>(25.91%) | 294 / 1232<br>(23.86%) | 328 / 1243<br>(26.39%) |
| occurrences (all)           | 331                    | 303                    | 334                    |
| Injection site haematoma    |                        |                        |                        |
| subjects affected / exposed | 5 / 1239 (0.40%)       | 1 / 1232 (0.08%)       | 3 / 1243 (0.24%)       |
| occurrences (all)           | 6                      | 1                      | 3                      |
| Injection site haemorrhage  |                        |                        |                        |
| subjects affected / exposed | 0 / 1239 (0.00%)       | 1 / 1232 (0.08%)       | 1 / 1243 (0.08%)       |
| occurrences (all)           | 0                      | 1                      | 1                      |
| Injection site induration   |                        |                        |                        |
| subjects affected / exposed | 3 / 1239 (0.24%)       | 3 / 1232 (0.24%)       | 2 / 1243 (0.16%)       |
| occurrences (all)           | 3                      | 3                      | 2                      |
| Injection site mass         |                        |                        |                        |
| subjects affected / exposed | 0 / 1239 (0.00%)       | 2 / 1232 (0.16%)       | 1 / 1243 (0.08%)       |
| occurrences (all)           | 0                      | 2                      | 1                      |
| Injection site nodule       |                        |                        |                        |
| subjects affected / exposed | 0 / 1239 (0.00%)       | 0 / 1232 (0.00%)       | 0 / 1243 (0.00%)       |
| occurrences (all)           | 0                      | 0                      | 0                      |
| Injection site pain         |                        |                        |                        |
| subjects affected / exposed | 335 / 1239<br>(27.04%) | 316 / 1232<br>(25.65%) | 275 / 1243<br>(22.12%) |
| occurrences (all)           | 336                    | 317                    | 277                    |
| Injection site papule       |                        |                        |                        |
| subjects affected / exposed | 2 / 1239 (0.16%)       | 2 / 1232 (0.16%)       | 1 / 1243 (0.08%)       |
| occurrences (all)           | 2                      | 2                      | 1                      |
| Injection site swelling     |                        |                        |                        |
| subjects affected / exposed | 127 / 1239<br>(10.25%) | 106 / 1232 (8.60%)     | 113 / 1243 (9.09%)     |
| occurrences (all)           | 128                    | 107                    | 115                    |
| Injection site vesicles     |                        |                        |                        |
| subjects affected / exposed | 0 / 1239 (0.00%)       | 1 / 1232 (0.08%)       | 0 / 1243 (0.00%)       |
| occurrences (all)           | 0                      | 1                      | 0                      |
| Oedema peripheral           |                        |                        |                        |
| subjects affected / exposed | 0 / 1239 (0.00%)       | 1 / 1232 (0.08%)       | 0 / 1243 (0.00%)       |
| occurrences (all)           | 0                      | 1                      | 0                      |
| Pain                        |                        |                        |                        |
| subjects affected / exposed | 1 / 1239 (0.08%)       | 0 / 1232 (0.00%)       | 1 / 1243 (0.08%)       |
| occurrences (all)           | 1                      | 0                      | 1                      |

|  |                               |                               |                               |
|--|-------------------------------|-------------------------------|-------------------------------|
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                        | 405 / 1239<br>(32.69%)<br>406 | 422 / 1232<br>(34.25%)<br>423 | 419 / 1243<br>(33.71%)<br>419 |
| Secretion discharge<br>subjects affected / exposed<br>occurrences (all)            | 0 / 1239 (0.00%)<br>0         | 1 / 1232 (0.08%)<br>1         | 0 / 1243 (0.00%)<br>0         |
| Swelling<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 1239 (0.00%)<br>0         | 1 / 1232 (0.08%)<br>1         | 0 / 1243 (0.00%)<br>0         |
| Vessel puncture site haematoma<br>subjects affected / exposed<br>occurrences (all) | 0 / 1239 (0.00%)<br>0         | 1 / 1232 (0.08%)<br>1         | 1 / 1243 (0.08%)<br>1         |
| Immune system disorders  |                               |                               |                               |
| Allergy to arthropod bite<br>subjects affected / exposed<br>occurrences (all)      | 1 / 1239 (0.08%)<br>1         | 1 / 1232 (0.08%)<br>1         | 0 / 1243 (0.00%)<br>0         |
| Drug hypersensitivity<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 2 / 1243 (0.16%)<br>2         |
| Food allergy<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 1239 (0.16%)<br>2         | 2 / 1232 (0.16%)<br>2         | 5 / 1243 (0.40%)<br>6         |
| Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)               | 2 / 1239 (0.16%)<br>2         | 1 / 1232 (0.08%)<br>1         | 1 / 1243 (0.08%)<br>1         |
| Immunisation reaction<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Milk allergy<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 1 / 1243 (0.08%)<br>1         |
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)               | 2 / 1239 (0.16%)<br>2         | 2 / 1232 (0.16%)<br>2         | 0 / 1243 (0.00%)<br>0         |
| Social circumstances   |                               |                               |                               |

|  |                         |                         |                         |
|--|-------------------------|-------------------------|-------------------------|
| Diet noncompliance<br>subjects affected / exposed<br>occurrences (all)         | 0 / 1239 (0.00%)<br>0   | 0 / 1232 (0.00%)<br>0   | 1 / 1243 (0.08%)<br>1   |
| Reproductive system and breast disorders                                       |                         |                         |                         |
| Acquired phimosis<br>subjects affected / exposed<br>occurrences (all)          | 1 / 1239 (0.08%)<br>1   | 0 / 1232 (0.00%)<br>0   | 0 / 1243 (0.00%)<br>0   |
| Balanoposthitis<br>subjects affected / exposed<br>occurrences (all)            | 1 / 1239 (0.08%)<br>1   | 0 / 1232 (0.00%)<br>0   | 2 / 1243 (0.16%)<br>2   |
| Bilateral breast buds<br>subjects affected / exposed<br>occurrences (all)      | 0 / 1239 (0.00%)<br>0   | 1 / 1232 (0.08%)<br>1   | 0 / 1243 (0.00%)<br>0   |
| Genital labial adhesions<br>subjects affected / exposed<br>occurrences (all)   | 2 / 1239 (0.16%)<br>2   | 0 / 1232 (0.00%)<br>0   | 0 / 1243 (0.00%)<br>0   |
| Vaginal mucosal blistering<br>subjects affected / exposed<br>occurrences (all) | 0 / 1239 (0.00%)<br>0   | 0 / 1232 (0.00%)<br>0   | 1 / 1243 (0.08%)<br>1   |
| Respiratory, thoracic and mediastinal disorders                                |                         |                         |                         |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 1239 (0.08%)<br>1   | 0 / 1232 (0.00%)<br>0   | 2 / 1243 (0.16%)<br>2   |
| Bronchial hyperreactivity<br>subjects affected / exposed<br>occurrences (all)  | 1 / 1239 (0.08%)<br>1   | 0 / 1232 (0.00%)<br>0   | 2 / 1243 (0.16%)<br>2   |
| Bronchospasm<br>subjects affected / exposed<br>occurrences (all)               | 1 / 1239 (0.08%)<br>1   | 3 / 1232 (0.24%)<br>3   | 3 / 1243 (0.24%)<br>3   |
| Catarrh<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 1239 (0.16%)<br>2   | 1 / 1232 (0.08%)<br>1   | 0 / 1243 (0.00%)<br>0   |
| Cough<br>subjects affected / exposed<br>occurrences (all)                      | 33 / 1239 (2.66%)<br>36 | 42 / 1232 (3.41%)<br>42 | 38 / 1243 (3.06%)<br>38 |
| Dyspnoea   |                         |                         |                         |

|                              |                   |                   |                   |
|------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 2 / 1243 (0.16%)  |
| occurrences (all)            | 0                 | 1                 | 2                 |
| Epistaxis                    |                   |                   |                   |
| subjects affected / exposed  | 2 / 1239 (0.16%)  | 4 / 1232 (0.32%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 2                 | 4                 | 1                 |
| Nasal congestion             |                   |                   |                   |
| subjects affected / exposed  | 10 / 1239 (0.81%) | 11 / 1232 (0.89%) | 5 / 1243 (0.40%)  |
| occurrences (all)            | 10                | 12                | 5                 |
| Nasal discomfort             |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 0                 | 0                 | 0                 |
| Oropharyngeal pain           |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 1                 | 1                 | 0                 |
| Rales                        |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 0                 | 0                 | 0                 |
| Respiratory disorder         |                   |                   |                   |
| subjects affected / exposed  | 2 / 1239 (0.16%)  | 0 / 1232 (0.00%)  | 4 / 1243 (0.32%)  |
| occurrences (all)            | 2                 | 0                 | 4                 |
| Respiratory distress         |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 0                 | 0                 | 0                 |
| Respiratory tract congestion |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 1                 | 0                 | 1                 |
| Rhinitis allergic            |                   |                   |                   |
| subjects affected / exposed  | 3 / 1239 (0.24%)  | 2 / 1232 (0.16%)  | 3 / 1243 (0.24%)  |
| occurrences (all)            | 3                 | 2                 | 3                 |
| Rhinorrhoea                  |                   |                   |                   |
| subjects affected / exposed  | 22 / 1239 (1.78%) | 23 / 1232 (1.87%) | 20 / 1243 (1.61%) |
| occurrences (all)            | 23                | 26                | 21                |
| Sinus congestion             |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 1                 | 0                 | 2                 |
| Sneezing                     |                   |                   |                   |

|  |                               |                               |                               |
|--|-------------------------------|-------------------------------|-------------------------------|
| subjects affected / exposed<br>occurrences (all)                                       | 1 / 1239 (0.08%)<br>1         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Tonsillar hypertrophy<br>subjects affected / exposed<br>occurrences (all)              | 0 / 1239 (0.00%)<br>0         | 1 / 1232 (0.08%)<br>1         | 0 / 1243 (0.00%)<br>0         |
| Upper respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all) | 1 / 1239 (0.08%)<br>1         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 1239 (0.16%)<br>3         | 6 / 1232 (0.49%)<br>6         | 6 / 1243 (0.48%)<br>6         |
| Psychiatric disorders  |                               |                               |                               |
| Aggression<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Depressed mood<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 1 / 1243 (0.08%)<br>1         |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 1239 (0.16%)<br>2         | 1 / 1232 (0.08%)<br>1         | 1 / 1243 (0.08%)<br>1         |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                       | 765 / 1239<br>(61.74%)<br>775 | 730 / 1232<br>(59.25%)<br>741 | 768 / 1243<br>(61.79%)<br>775 |
| Middle insomnia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 1239 (0.00%)<br>0         | 0 / 1232 (0.00%)<br>0         | 1 / 1243 (0.08%)<br>1         |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 1239 (0.24%)<br>3         | 0 / 1232 (0.00%)<br>0         | 0 / 1243 (0.00%)<br>0         |
| Sleep terror   |                               |                               |                               |

|  |                       |                       |                       |
|--|-----------------------|-----------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Tearfulness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 1 / 1232 (0.08%)<br>2 | 0 / 1243 (0.00%)<br>0 |
| Terminal insomnia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Investigations<br>Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1239 (0.00%)<br>0 | 1 / 1232 (0.08%)<br>1 | 0 / 1243 (0.00%)<br>0 |
| Cold agglutinins positive<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Otic examination normal<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>Accidental exposure to product<br>subjects affected / exposed<br>occurrences (all) | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Animal bite<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 2 / 1243 (0.16%)<br>2 |
| Arthropod bite<br>subjects affected / exposed<br>occurrences (all)   | 7 / 1239 (0.56%)<br>7 | 7 / 1232 (0.57%)<br>7 | 5 / 1243 (0.40%)<br>5 |
| Arthropod sting<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 2 / 1243 (0.16%)<br>3 |
| Bite   |                       |                       |                       |

|  |                  |                  |                  |
|--|------------------|------------------|------------------|
| subjects affected / exposed            | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 1                | 0                | 0                |
| Chemical poisoning                     |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 0                | 0                | 0                |
| Clavicle fracture                      |                  |                  |                  |
| subjects affected / exposed            | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 1                | 0                | 0                |
| Concussion                             |                  |                  |                  |
| subjects affected / exposed            | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 1                | 0                | 0                |
| Contusion                              |                  |                  |                  |
| subjects affected / exposed            | 4 / 1239 (0.32%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                      | 4                | 0                | 1                |
| Corneal abrasion                       |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                      | 0                | 0                | 1                |
| Craniocerebral injury                  |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                      | 0                | 0                | 1                |
| Ear canal injury                       |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                      | 0                | 0                | 1                |
| Ear injury                             |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                      | 0                | 0                | 1                |
| Eye contusion                          |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 0                | 1                | 0                |
| Face injury                            |                  |                  |                  |
| subjects affected / exposed            | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 1                | 0                | 0                |
| Fall                                   |                  |                  |                  |
| subjects affected / exposed            | 0 / 1239 (0.00%) | 2 / 1232 (0.16%) | 0 / 1243 (0.00%) |
| occurrences (all)                      | 0                | 2                | 0                |
| Foreign body in gastrointestinal tract |                  |                  |                  |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 2 / 1243 (0.16%) |
| occurrences (all)           | 0                | 0                | 2                |
| Gingival injury             |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Hand fracture               |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 1                | 0                |
| Head injury                 |                  |                  |                  |
| subjects affected / exposed | 5 / 1239 (0.40%) | 6 / 1232 (0.49%) | 6 / 1243 (0.48%) |
| occurrences (all)           | 5                | 6                | 6                |
| Heat stroke                 |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Laceration                  |                  |                  |                  |
| subjects affected / exposed | 5 / 1239 (0.40%) | 0 / 1232 (0.00%) | 2 / 1243 (0.16%) |
| occurrences (all)           | 5                | 0                | 2                |
| Limb injury                 |                  |                  |                  |
| subjects affected / exposed | 3 / 1239 (0.24%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 3                | 1                | 0                |
| Lip injury                  |                  |                  |                  |
| subjects affected / exposed | 2 / 1239 (0.16%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 2                | 1                | 0                |
| Nail avulsion               |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Radial head dislocation     |                  |                  |                  |
| subjects affected / exposed | 2 / 1239 (0.16%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 2                | 0                | 0                |
| Road traffic accident       |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Scratch                     |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Skin abrasion               |                  |                  |                  |



|                              |                  |                  |                  |
|------------------------------|------------------|------------------|------------------|
| subjects affected / exposed  | 0 / 1239 (0.00%) | 2 / 1232 (0.16%) | 1 / 1243 (0.08%) |
| occurrences (all)            | 0                | 2                | 1                |
| Superficial injury of eye    |                  |                  |                  |
| subjects affected / exposed  | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 0                | 0                | 0                |
| Thermal burn                 |                  |                  |                  |
| subjects affected / exposed  | 0 / 1239 (0.00%) | 3 / 1232 (0.24%) | 1 / 1243 (0.08%) |
| occurrences (all)            | 0                | 3                | 1                |
| Tibia fracture               |                  |                  |                  |
| subjects affected / exposed  | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)            | 0                | 0                | 1                |
| Tongue injury                |                  |                  |                  |
| subjects affected / exposed  | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 1                | 1                | 0                |
| Upper limb fracture          |                  |                  |                  |
| subjects affected / exposed  | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 0                | 0                | 0                |
| Wound                        |                  |                  |                  |
| subjects affected / exposed  | 1 / 1239 (0.08%) | 3 / 1232 (0.24%) | 1 / 1243 (0.08%) |
| occurrences (all)            | 1                | 3                | 1                |
| Nervous system disorders     |                  |                  |                  |
| Drooling                     |                  |                  |                  |
| subjects affected / exposed  | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 1                | 0                | 0                |
| Exaggerated startle response |                  |                  |                  |
| subjects affected / exposed  | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 1                | 0                | 0                |
| Febrile convulsion           |                  |                  |                  |
| subjects affected / exposed  | 4 / 1239 (0.32%) | 1 / 1232 (0.08%) | 5 / 1243 (0.40%) |
| occurrences (all)            | 4                | 1                | 5                |
| Gross motor delay            |                  |                  |                  |
| subjects affected / exposed  | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)            | 1                | 0                | 0                |
| Headache                     |                  |                  |                  |
| subjects affected / exposed  | 4 / 1239 (0.32%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)            | 4                | 0                | 1                |

|                                      |                     |                     |                     |
|--------------------------------------|---------------------|---------------------|---------------------|
| Lethargy                             |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 1 / 1232 (0.08%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 0                   | 1                   | 0                   |
| Nystagmus                            |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)                    | 0                   | 0                   | 1                   |
| Poor quality sleep                   |                     |                     |                     |
| subjects affected / exposed          | 4 / 1239 (0.32%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)                    | 5                   | 0                   | 1                   |
| Post-traumatic headache              |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 0                   | 0                   | 0                   |
| Somnolence                           |                     |                     |                     |
| subjects affected / exposed          | 534 / 1239 (43.10%) | 535 / 1232 (43.43%) | 533 / 1243 (42.88%) |
| occurrences (all)                    | 534                 | 535                 | 533                 |
| Speech disorder developmental        |                     |                     |                     |
| subjects affected / exposed          | 1 / 1239 (0.08%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 1                   | 0                   | 0                   |
| Tremor                               |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)                    | 0                   | 0                   | 1                   |
| Blood and lymphatic system disorders |                     |                     |                     |
| Anaemia                              |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 2 / 1232 (0.16%)    | 4 / 1243 (0.32%)    |
| occurrences (all)                    | 0                   | 2                   | 4                   |
| Iron deficiency anaemia              |                     |                     |                     |
| subjects affected / exposed          | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 0                   | 0                   | 0                   |
| Leukopenia                           |                     |                     |                     |
| subjects affected / exposed          | 1 / 1239 (0.08%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 1                   | 0                   | 0                   |
| Lymphadenitis                        |                     |                     |                     |
| subjects affected / exposed          | 1 / 1239 (0.08%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)                    | 1                   | 0                   | 0                   |
| Lymphadenopathy                      |                     |                     |                     |

|  |                       |                       |                       |
|--|-----------------------|-----------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all) | 5 / 1239 (0.40%)<br>5 | 5 / 1232 (0.41%)<br>5 | 2 / 1243 (0.16%)<br>2 |
| Ear and labyrinth disorders                      |                       |                       |                       |
| Cerumen impaction                                |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 0                     | 0                     | 1                     |
| Deafness   |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 0                     | 0                     | 1                     |
| Ear pain   |                       |                       |                       |
| subjects affected / exposed                      | 3 / 1239 (0.24%)      | 3 / 1232 (0.24%)      | 4 / 1243 (0.32%)      |
| occurrences (all)                                | 3                     | 3                     | 4                     |
| Ear swelling                                     |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 0                     | 0                     | 1                     |
| Eustachian tube dysfunction                      |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 0 / 1232 (0.00%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                | 0                     | 0                     | 0                     |
| Excessive cerumen production                     |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 1 / 1232 (0.08%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                | 0                     | 1                     | 0                     |
| Otorrhoea  |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 2 / 1232 (0.16%)      | 0 / 1243 (0.00%)      |
| occurrences (all)                                | 0                     | 2                     | 0                     |
| Eye disorders                                    |                       |                       |                       |
| Conjunctivitis allergic                          |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 1 / 1232 (0.08%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 0                     | 1                     | 1                     |
| Dacryostenosis acquired                          |                       |                       |                       |
| subjects affected / exposed                      | 1 / 1239 (0.08%)      | 1 / 1232 (0.08%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 1                     | 1                     | 1                     |
| Eye discharge                                    |                       |                       |                       |
| subjects affected / exposed                      | 0 / 1239 (0.00%)      | 2 / 1232 (0.16%)      | 1 / 1243 (0.08%)      |
| occurrences (all)                                | 0                     | 2                     | 1                     |
| Eye inflammation                                 |                       |                       |                       |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Eye irritation              |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 1                | 0                |
| Eye swelling                |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Eyelid oedema               |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 2                | 0                | 0                |
| Hypermetropia               |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Lacrimation increased       |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Lid sulcus deepened         |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Strabismus                  |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Gastrointestinal disorders  |                  |                  |                  |
| Abdominal discomfort        |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 1                | 0                |
| Abdominal pain              |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Abdominal pain upper        |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Anal fissure                |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 1                | 0                |

|                                  |                   |                   |                   |
|----------------------------------|-------------------|-------------------|-------------------|
| Aphthous ulcer                   |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 0                 | 0                 |
| Chapped lips                     |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 0                 | 0                 |
| Constipation                     |                   |                   |                   |
| subjects affected / exposed      | 5 / 1239 (0.40%)  | 2 / 1232 (0.16%)  | 9 / 1243 (0.72%)  |
| occurrences (all)                | 5                 | 2                 | 9                 |
| Diarrhoea                        |                   |                   |                   |
| subjects affected / exposed      | 64 / 1239 (5.17%) | 58 / 1232 (4.71%) | 49 / 1243 (3.94%) |
| occurrences (all)                | 71                | 63                | 55                |
| Dyspepsia                        |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 0                 | 0                 |
| Dysphagia                        |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 1                 | 0                 |
| Faeces soft                      |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                | 0                 | 1                 | 1                 |
| Flatulence                       |                   |                   |                   |
| subjects affected / exposed      | 2 / 1239 (0.16%)  | 2 / 1232 (0.16%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                | 2                 | 2                 | 1                 |
| Gastrooesophageal reflux disease |                   |                   |                   |
| subjects affected / exposed      | 1 / 1239 (0.08%)  | 3 / 1232 (0.24%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 1                 | 3                 | 0                 |
| Gingival hypertrophy             |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 1                 | 0                 |
| Gingival pain                    |                   |                   |                   |
| subjects affected / exposed      | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                | 1                 | 0                 | 1                 |
| Gingival swelling                |                   |                   |                   |
| subjects affected / exposed      | 0 / 1239 (0.00%)  | 2 / 1232 (0.16%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                | 0                 | 2                 | 0                 |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| Haematochezia               |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Lip swelling                |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Nausea                      |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 1                | 1                | 1                |
| Oral contusion              |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Oral mucosal eruption       |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Post-tussive vomiting       |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Ranula                      |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Rectal haemorrhage          |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Regurgitation               |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Salivary gland enlargement  |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 1                | 1                |
| Salivary gland pain         |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Salivary hypersecretion     |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |

|  |                   |                   |                   |
|--|-------------------|-------------------|-------------------|
| Stomatitis                             |                   |                   |                   |
| subjects affected / exposed            | 0 / 1239 (0.00%)  | 4 / 1232 (0.32%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                      | 0                 | 4                 | 1                 |
| Teething                               |                   |                   |                   |
| subjects affected / exposed            | 91 / 1239 (7.34%) | 92 / 1232 (7.47%) | 77 / 1243 (6.19%) |
| occurrences (all)                      | 114               | 106               | 92                |
| Toothache                              |                   |                   |                   |
| subjects affected / exposed            | 4 / 1239 (0.32%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                      | 6                 | 0                 | 1                 |
| Vomiting                               |                   |                   |                   |
| subjects affected / exposed            | 38 / 1239 (3.07%) | 35 / 1232 (2.84%) | 34 / 1243 (2.74%) |
| occurrences (all)                      | 39                | 38                | 38                |
| Skin and subcutaneous tissue disorders |                   |                   |                   |
| Acne                                   |                   |                   |                   |
| subjects affected / exposed            | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                      | 0                 | 0                 | 1                 |
| Blister                                |                   |                   |                   |
| subjects affected / exposed            | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                      | 0                 | 0                 | 2                 |
| Dermatitis                             |                   |                   |                   |
| subjects affected / exposed            | 1 / 1239 (0.08%)  | 2 / 1232 (0.16%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                      | 1                 | 2                 | 1                 |
| Dermatitis allergic                    |                   |                   |                   |
| subjects affected / exposed            | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                      | 1                 | 0                 | 0                 |
| Dermatitis atopic                      |                   |                   |                   |
| subjects affected / exposed            | 2 / 1239 (0.16%)  | 3 / 1232 (0.24%)  | 4 / 1243 (0.32%)  |
| occurrences (all)                      | 2                 | 3                 | 4                 |
| Dermatitis contact                     |                   |                   |                   |
| subjects affected / exposed            | 1 / 1239 (0.08%)  | 2 / 1232 (0.16%)  | 2 / 1243 (0.16%)  |
| occurrences (all)                      | 1                 | 2                 | 2                 |
| Dermatitis diaper                      |                   |                   |                   |
| subjects affected / exposed            | 3 / 1239 (0.24%)  | 4 / 1232 (0.32%)  | 3 / 1243 (0.24%)  |
| occurrences (all)                      | 4                 | 4                 | 4                 |
| Drug eruption                          |                   |                   |                   |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Dry skin                    |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Eczema                      |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 2 / 1232 (0.16%) | 2 / 1243 (0.16%) |
| occurrences (all)           | 0                | 2                | 2                |
| Eczema nummular             |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Erythema                    |                  |                  |                  |
| subjects affected / exposed | 2 / 1239 (0.16%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 2                | 1                | 1                |
| Hyperhidrosis               |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Hyperkeratosis              |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 1                | 0                |
| Ingrowing nail              |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Keratosis pilaris           |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)           | 0                | 0                | 1                |
| Macule                      |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 0                | 0                |
| Miliaria                    |                  |                  |                  |
| subjects affected / exposed | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 1                | 0                | 0                |
| Papule                      |                  |                  |                  |
| subjects affected / exposed | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)           | 0                | 1                | 0                |
| Prurigo                     |                  |                  |                  |



|                             |                     |                     |                     |
|-----------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed | 2 / 1239 (0.16%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)           | 2                   | 0                   | 0                   |
| Pruritus                    |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 0                   | 0                   | 1                   |
| Rash                        |                     |                     |                     |
| subjects affected / exposed | 352 / 1239 (28.41%) | 331 / 1232 (26.87%) | 360 / 1243 (28.96%) |
| occurrences (all)           | 352                 | 331                 | 360                 |
| Seborrhoea                  |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 1 / 1232 (0.08%)    | 0 / 1243 (0.00%)    |
| occurrences (all)           | 0                   | 1                   | 0                   |
| Skin irritation             |                     |                     |                     |
| subjects affected / exposed | 2 / 1239 (0.16%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)           | 2                   | 0                   | 0                   |
| Skin mass                   |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 0                   | 0                   | 1                   |
| Skin warm                   |                     |                     |                     |
| subjects affected / exposed | 1 / 1239 (0.08%)    | 1 / 1232 (0.08%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 1                   | 1                   | 1                   |
| Solar dermatitis            |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 0 / 1243 (0.00%)    |
| occurrences (all)           | 0                   | 0                   | 0                   |
| Swelling face               |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 1 / 1232 (0.08%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 0                   | 1                   | 1                   |
| Urticaria                   |                     |                     |                     |
| subjects affected / exposed | 2 / 1239 (0.16%)    | 1 / 1232 (0.08%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 4                   | 1                   | 1                   |
| Renal and urinary disorders |                     |                     |                     |
| Dysuria                     |                     |                     |                     |
| subjects affected / exposed | 0 / 1239 (0.00%)    | 0 / 1232 (0.00%)    | 1 / 1243 (0.08%)    |
| occurrences (all)           | 0                   | 0                   | 1                   |
| Polyuria                    |                     |                     |                     |

|   |                       |                       |                       |
|---|-----------------------|-----------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Urinary tract disorder<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 1239 (0.08%)<br>1 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders   |                       |                       |                       |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Elbow deformity<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 0 / 1243 (0.00%)<br>0 |
| Knee deformity<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 1239 (0.00%)<br>0 | 1 / 1232 (0.08%)<br>1 | 0 / 1243 (0.00%)<br>0 |
| Synovial cyst<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 1239 (0.00%)<br>0 | 1 / 1232 (0.08%)<br>1 | 0 / 1243 (0.00%)<br>0 |
| Infections and infestations   |                       |                       |                       |
| Abscess limb<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Acute sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 1239 (0.08%)<br>1 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Adenovirus infection<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 1239 (0.08%)<br>1 | 1 / 1232 (0.08%)<br>1 | 0 / 1243 (0.00%)<br>0 |
| Beta haemolytic streptococcal infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Body tinea<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 1239 (0.00%)<br>0 | 0 / 1232 (0.00%)<br>0 | 1 / 1243 (0.08%)<br>1 |
| Bronchiolitis   |                       |                       |                       |

|                                 |                   |                   |                   |
|---------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed     | 2 / 1239 (0.16%)  | 7 / 1232 (0.57%)  | 7 / 1243 (0.56%)  |
| occurrences (all)               | 2                 | 7                 | 7                 |
| Bronchitis                      |                   |                   |                   |
| subjects affected / exposed     | 10 / 1239 (0.81%) | 12 / 1232 (0.97%) | 10 / 1243 (0.80%) |
| occurrences (all)               | 10                | 13                | 11                |
| Bullous impetigo                |                   |                   |                   |
| subjects affected / exposed     | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)               | 0                 | 1                 | 0                 |
| Candida infection               |                   |                   |                   |
| subjects affected / exposed     | 1 / 1239 (0.08%)  | 2 / 1232 (0.16%)  | 1 / 1243 (0.08%)  |
| occurrences (all)               | 1                 | 3                 | 1                 |
| Candida nappy rash              |                   |                   |                   |
| subjects affected / exposed     | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)               | 1                 | 0                 | 0                 |
| Cellulitis                      |                   |                   |                   |
| subjects affected / exposed     | 2 / 1239 (0.16%)  | 0 / 1232 (0.00%)  | 3 / 1243 (0.24%)  |
| occurrences (all)               | 2                 | 0                 | 3                 |
| Clostridium difficile infection |                   |                   |                   |
| subjects affected / exposed     | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)               | 1                 | 0                 | 0                 |
| Conjunctivitis                  |                   |                   |                   |
| subjects affected / exposed     | 26 / 1239 (2.10%) | 21 / 1232 (1.70%) | 39 / 1243 (3.14%) |
| occurrences (all)               | 26                | 21                | 41                |
| Conjunctivitis bacterial        |                   |                   |                   |
| subjects affected / exposed     | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)               | 0                 | 1                 | 1                 |
| Coxsackie viral infection       |                   |                   |                   |
| subjects affected / exposed     | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)               | 0                 | 0                 | 0                 |
| Croup infectious                |                   |                   |                   |
| subjects affected / exposed     | 4 / 1239 (0.32%)  | 11 / 1232 (0.89%) | 8 / 1243 (0.64%)  |
| occurrences (all)               | 4                 | 11                | 8                 |
| Ear infection                   |                   |                   |                   |
| subjects affected / exposed     | 9 / 1239 (0.73%)  | 14 / 1232 (1.14%) | 4 / 1243 (0.32%)  |
| occurrences (all)               | 9                 | 14                | 4                 |
| Enterovirus infection           |                   |                   |                   |

|                              |                   |                   |                   |
|------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 2 / 1232 (0.16%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 1                 | 2                 | 0                 |
| Epstein-barr virus infection |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 0                 | 0                 | 1                 |
| Exanthema subitum            |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 0                 | 0                 | 0                 |
| Eye infection                |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 3 / 1232 (0.24%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 1                 | 3                 | 1                 |
| Folliculitis                 |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 3 / 1232 (0.24%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 0                 | 3                 | 1                 |
| Fungal infection             |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 0                 | 0                 | 1                 |
| Gastroenteritis              |                   |                   |                   |
| subjects affected / exposed  | 27 / 1239 (2.18%) | 21 / 1232 (1.70%) | 35 / 1243 (2.82%) |
| occurrences (all)            | 28                | 21                | 38                |
| Gastroenteritis norovirus    |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 0                 | 0                 | 1                 |
| Gastroenteritis rotavirus    |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 1                 | 0                 | 0                 |
| Gastroenteritis viral        |                   |                   |                   |
| subjects affected / exposed  | 3 / 1239 (0.24%)  | 6 / 1232 (0.49%)  | 6 / 1243 (0.48%)  |
| occurrences (all)            | 3                 | 6                 | 6                 |
| Gastrointestinal infection   |                   |                   |                   |
| subjects affected / exposed  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)            | 0                 | 0                 | 0                 |
| Gingivitis                   |                   |                   |                   |
| subjects affected / exposed  | 1 / 1239 (0.08%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)            | 1                 | 1                 | 1                 |
| Hand-foot-and-mouth disease  |                   |                   |                   |

|                                   |                  |                  |                  |
|-----------------------------------|------------------|------------------|------------------|
| subjects affected / exposed       | 2 / 1239 (0.16%) | 3 / 1232 (0.24%) | 9 / 1243 (0.72%) |
| occurrences (all)                 | 2                | 3                | 9                |
| Herpangina                        |                  |                  |                  |
| subjects affected / exposed       | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 0                | 1                | 1                |
| Herpes simplex                    |                  |                  |                  |
| subjects affected / exposed       | 0 / 1239 (0.00%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)                 | 0                | 1                | 0                |
| Hordeolum                         |                  |                  |                  |
| subjects affected / exposed       | 1 / 1239 (0.08%) | 1 / 1232 (0.08%) | 0 / 1243 (0.00%) |
| occurrences (all)                 | 1                | 1                | 0                |
| Impetigo                          |                  |                  |                  |
| subjects affected / exposed       | 4 / 1239 (0.32%) | 1 / 1232 (0.08%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 4                | 1                | 1                |
| Infected bite                     |                  |                  |                  |
| subjects affected / exposed       | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 0                | 0                | 1                |
| Influenza                         |                  |                  |                  |
| subjects affected / exposed       | 2 / 1239 (0.16%) | 5 / 1232 (0.41%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 2                | 5                | 1                |
| Injection site abscess            |                  |                  |                  |
| subjects affected / exposed       | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 0 / 1243 (0.00%) |
| occurrences (all)                 | 1                | 0                | 0                |
| Laryngitis                        |                  |                  |                  |
| subjects affected / exposed       | 1 / 1239 (0.08%) | 7 / 1232 (0.57%) | 2 / 1243 (0.16%) |
| occurrences (all)                 | 1                | 9                | 2                |
| Lice infestation                  |                  |                  |                  |
| subjects affected / exposed       | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 0                | 0                | 1                |
| Localised infection               |                  |                  |                  |
| subjects affected / exposed       | 0 / 1239 (0.00%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 0                | 0                | 1                |
| Lower respiratory tract infection |                  |                  |                  |
| subjects affected / exposed       | 1 / 1239 (0.08%) | 0 / 1232 (0.00%) | 1 / 1243 (0.08%) |
| occurrences (all)                 | 1                | 0                | 1                |
| Molluscum contagiosum             |                  |                  |                  |

|                             |                   |                   |                   |
|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1239 (0.08%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)           | 1                 | 1                 | 1                 |
| Nasopharyngitis             |                   |                   |                   |
| subjects affected / exposed | 74 / 1239 (5.97%) | 75 / 1232 (6.09%) | 74 / 1243 (5.95%) |
| occurrences (all)           | 83                | 82                | 82                |
| Oral candidiasis            |                   |                   |                   |
| subjects affected / exposed | 2 / 1239 (0.16%)  | 2 / 1232 (0.16%)  | 1 / 1243 (0.08%)  |
| occurrences (all)           | 2                 | 2                 | 1                 |
| Oral herpes                 |                   |                   |                   |
| subjects affected / exposed | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)           | 0                 | 1                 | 1                 |
| Oral infection              |                   |                   |                   |
| subjects affected / exposed | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)           | 0                 | 0                 | 0                 |
| Otitis externa              |                   |                   |                   |
| subjects affected / exposed | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)           | 0                 | 0                 | 1                 |
| Otitis media                |                   |                   |                   |
| subjects affected / exposed | 80 / 1239 (6.46%) | 75 / 1232 (6.09%) | 62 / 1243 (4.99%) |
| occurrences (all)           | 86                | 79                | 67                |
| Otitis media acute          |                   |                   |                   |
| subjects affected / exposed | 8 / 1239 (0.65%)  | 7 / 1232 (0.57%)  | 13 / 1243 (1.05%) |
| occurrences (all)           | 10                | 7                 | 14                |
| Otitis media chronic        |                   |                   |                   |
| subjects affected / exposed | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)           | 0                 | 0                 | 1                 |
| Paronychia                  |                   |                   |                   |
| subjects affected / exposed | 0 / 1239 (0.00%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)           | 0                 | 1                 | 0                 |
| Periorbital cellulitis      |                   |                   |                   |
| subjects affected / exposed | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)           | 1                 | 0                 | 0                 |
| Pharyngitis                 |                   |                   |                   |
| subjects affected / exposed | 20 / 1239 (1.61%) | 30 / 1232 (2.44%) | 14 / 1243 (1.13%) |
| occurrences (all)           | 20                | 30                | 14                |
| Pharyngitis streptococcal   |                   |                   |                   |

|  |                   |                   |                   |
|--|-------------------|-------------------|-------------------|
| subjects affected / exposed                  | 0 / 1239 (0.00%)  | 3 / 1232 (0.24%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                            | 0                 | 3                 | 1                 |
| Pharyngotonsillitis                          |                   |                   |                   |
| subjects affected / exposed                  | 2 / 1239 (0.16%)  | 1 / 1232 (0.08%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                            | 2                 | 1                 | 1                 |
| Pneumonia                                    |                   |                   |                   |
| subjects affected / exposed                  | 1 / 1239 (0.08%)  | 1 / 1232 (0.08%)  | 5 / 1243 (0.40%)  |
| occurrences (all)                            | 1                 | 1                 | 5                 |
| Respiratory syncytial virus<br>bronchiolitis |                   |                   |                   |
| subjects affected / exposed                  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                            | 0                 | 0                 | 0                 |
| Respiratory syncytial virus infection        |                   |                   |                   |
| subjects affected / exposed                  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                            | 0                 | 0                 | 0                 |
| Respiratory tract infection                  |                   |                   |                   |
| subjects affected / exposed                  | 8 / 1239 (0.65%)  | 11 / 1232 (0.89%) | 9 / 1243 (0.72%)  |
| occurrences (all)                            | 8                 | 12                | 11                |
| Respiratory tract infection viral            |                   |                   |                   |
| subjects affected / exposed                  | 3 / 1239 (0.24%)  | 1 / 1232 (0.08%)  | 0 / 1243 (0.00%)  |
| occurrences (all)                            | 3                 | 1                 | 0                 |
| Rhinitis                                     |                   |                   |                   |
| subjects affected / exposed                  | 46 / 1239 (3.71%) | 49 / 1232 (3.98%) | 38 / 1243 (3.06%) |
| occurrences (all)                            | 50                | 55                | 42                |
| Roseola                                      |                   |                   |                   |
| subjects affected / exposed                  | 1 / 1239 (0.08%)  | 2 / 1232 (0.16%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                            | 1                 | 2                 | 1                 |
| Salmonellosis                                |                   |                   |                   |
| subjects affected / exposed                  | 0 / 1239 (0.00%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                            | 0                 | 0                 | 1                 |
| Scarlet fever                                |                   |                   |                   |
| subjects affected / exposed                  | 1 / 1239 (0.08%)  | 0 / 1232 (0.00%)  | 1 / 1243 (0.08%)  |
| occurrences (all)                            | 1                 | 0                 | 1                 |
| Sinusitis                                    |                   |                   |                   |
| subjects affected / exposed                  | 9 / 1239 (0.73%)  | 3 / 1232 (0.24%)  | 4 / 1243 (0.32%)  |
| occurrences (all)                            | 10                | 3                 | 4                 |

|   |                           |                            |                           |
|---|---------------------------|----------------------------|---------------------------|
| Skin bacterial infection<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1239 (0.00%)<br>0     | 0 / 1232 (0.00%)<br>0      | 1 / 1243 (0.08%)<br>1     |
| Skin candida<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 1239 (0.08%)<br>1     | 0 / 1232 (0.00%)<br>0      | 1 / 1243 (0.08%)<br>1     |
| Staphylococcal infection<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1239 (0.00%)<br>0     | 0 / 1232 (0.00%)<br>0      | 0 / 1243 (0.00%)<br>0     |
| Streptococcal infection<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1239 (0.00%)<br>0     | 2 / 1232 (0.16%)<br>2      | 3 / 1243 (0.24%)<br>3     |
| Subcutaneous abscess<br>subjects affected / exposed<br>occurrences (all)              | 1 / 1239 (0.08%)<br>1     | 0 / 1232 (0.00%)<br>0      | 0 / 1243 (0.00%)<br>0     |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)                       | 21 / 1239 (1.69%)<br>22   | 9 / 1232 (0.73%)<br>10     | 9 / 1243 (0.72%)<br>11    |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1239 (0.00%)<br>0     | 1 / 1232 (0.08%)<br>1      | 0 / 1243 (0.00%)<br>0     |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 106 / 1239 (8.56%)<br>117 | 124 / 1232 (10.06%)<br>132 | 122 / 1243 (9.81%)<br>132 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 1239 (0.08%)<br>2     | 1 / 1232 (0.08%)<br>1      | 1 / 1243 (0.08%)<br>1     |
| Viral diarrhoea<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 1239 (0.08%)<br>1     | 0 / 1232 (0.00%)<br>0      | 1 / 1243 (0.08%)<br>1     |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                   | 15 / 1239 (1.21%)<br>15   | 21 / 1232 (1.70%)<br>22    | 23 / 1243 (1.85%)<br>26   |
| Viral pharyngitis   |                           |                            |                           |



|  |                            |                            |                            |
|--|----------------------------|----------------------------|----------------------------|
| subjects affected / exposed<br>occurrences (all)   | 2 / 1239 (0.16%)<br>2      | 2 / 1232 (0.16%)<br>2      | 0 / 1243 (0.00%)<br>0      |
| Viral rash<br>subjects affected / exposed<br>occurrences (all)   | 1 / 1239 (0.08%)<br>1      | 0 / 1232 (0.00%)<br>0      | 0 / 1243 (0.00%)<br>0      |
| Viral tonsillitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0      | 0 / 1232 (0.00%)<br>0      | 0 / 1243 (0.00%)<br>0      |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 1239 (0.24%)<br>3      | 3 / 1232 (0.24%)<br>3      | 4 / 1243 (0.32%)<br>4      |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 547 / 1239 (44.15%)<br>548 | 537 / 1232 (43.59%)<br>538 | 526 / 1243 (42.32%)<br>528 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1239 (0.00%)<br>0      | 0 / 1232 (0.00%)<br>0      | 0 / 1243 (0.00%)<br>0      |
| Lactose intolerance<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 1239 (0.08%)<br>1      | 1 / 1232 (0.08%)<br>1      | 0 / 1243 (0.00%)<br>0      |
| Polydipsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1239 (0.00%)<br>0      | 0 / 1232 (0.00%)<br>0      | 1 / 1243 (0.08%)<br>1      |

| <b>Non-serious adverse events</b>  | INV_MMR Group         | COM_MMR Group         |  |
|--|-----------------------|-----------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 3232 / 3714 (87.02%)  | 1138 / 1289 (88.29%)  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Seborrhoeic keratosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 3714 (0.00%)<br>0 | 1 / 1289 (0.08%)<br>1 |  |
| Vascular disorders<br>Haematoma<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>1 | 0 / 1289 (0.00%)<br>0 |  |

|   |                               |                               |  |
|---|-------------------------------|-------------------------------|--|
| Pallor<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>1         | 0 / 1289 (0.00%)<br>0         |  |
| Pregnancy, puerperium and perinatal conditions<br>Cephalhaematoma<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1         | 0 / 1289 (0.00%)<br>0         |  |
| General disorders and administration site conditions<br>Crying<br>subjects affected / exposed<br>occurrences (all)    | 11 / 3714 (0.30%)<br>13       | 4 / 1289 (0.31%)<br>5         |  |
| Cyst<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>2         | 0 / 1289 (0.00%)<br>0         |  |
| Discomfort<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>1         | 0 / 1289 (0.00%)<br>0         |  |
| Feeling hot<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3714 (0.03%)<br>1         | 1 / 1289 (0.08%)<br>1         |  |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>1         | 0 / 1289 (0.00%)<br>0         |  |
| Injection site bruising<br>subjects affected / exposed<br>occurrences (all)   | 10 / 3714 (0.27%)<br>10       | 2 / 1289 (0.16%)<br>2         |  |
| Injection site erosion<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3714 (0.03%)<br>1         | 1 / 1289 (0.08%)<br>1         |  |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)   | 943 / 3714<br>(25.39%)<br>968 | 335 / 1289<br>(25.99%)<br>341 |  |
| Injection site haematoma<br>subjects affected / exposed<br>occurrences (all)  | 9 / 3714 (0.24%)<br>10        | 0 / 1289 (0.00%)<br>0         |  |

|  |                                 |                               |  |
|--|---------------------------------|-------------------------------|--|
| Injection site haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 2 / 3714 (0.05%)<br>2           | 2 / 1289 (0.16%)<br>2         |  |
| Injection site induration<br>subjects affected / exposed<br>occurrences (all)  | 8 / 3714 (0.22%)<br>8           | 3 / 1289 (0.23%)<br>3         |  |
| Injection site mass<br>subjects affected / exposed<br>occurrences (all)        | 3 / 3714 (0.08%)<br>3           | 0 / 1289 (0.00%)<br>0         |  |
| Injection site nodule<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)        | 926 / 3714<br>(24.93%)<br>930   | 352 / 1289<br>(27.31%)<br>352 |  |
| Injection site papule<br>subjects affected / exposed<br>occurrences (all)      | 5 / 3714 (0.13%)<br>5           | 5 / 1289 (0.39%)<br>5         |  |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)    | 346 / 3714 (9.32%)<br>350       | 139 / 1289<br>(10.78%)<br>142 |  |
| Injection site vesicles<br>subjects affected / exposed<br>occurrences (all)    | 1 / 3714 (0.03%)<br>1           | 1 / 1289 (0.08%)<br>1         |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)          | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 3714 (0.05%)<br>2           | 2 / 1289 (0.16%)<br>2         |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                    | 1246 / 3714<br>(33.55%)<br>1248 | 412 / 1289<br>(31.96%)<br>412 |  |
| Secretion discharge  |                                 |                               |  |

|  |                        |                       |  |
|--|------------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 3714 (0.03%)<br>1  | 0 / 1289 (0.00%)<br>0 |  |
| Swelling<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3714 (0.03%)<br>1  | 0 / 1289 (0.00%)<br>0 |  |
| Vessel puncture site haematoma<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 3714 (0.05%)<br>2  | 0 / 1289 (0.00%)<br>0 |  |
| Immune system disorders<br>Allergy to arthropod bite<br>subjects affected / exposed<br>occurrences (all) | 2 / 3714 (0.05%)<br>2  | 0 / 1289 (0.00%)<br>0 |  |
| Drug hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                | 2 / 3714 (0.05%)<br>2  | 1 / 1289 (0.08%)<br>1 |  |
| Food allergy<br>subjects affected / exposed<br>occurrences (all)   | 9 / 3714 (0.24%)<br>10 | 4 / 1289 (0.31%)<br>4 |  |
| Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                     | 4 / 3714 (0.11%)<br>4  | 2 / 1289 (0.16%)<br>2 |  |
| Immunisation reaction<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 3714 (0.00%)<br>0  | 1 / 1289 (0.08%)<br>1 |  |
| Milk allergy<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3714 (0.03%)<br>1  | 0 / 1289 (0.00%)<br>0 |  |
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)                                     | 4 / 3714 (0.11%)<br>4  | 1 / 1289 (0.08%)<br>1 |  |
| Social circumstances<br>Diet noncompliance<br>subjects affected / exposed<br>occurrences (all)           | 1 / 3714 (0.03%)<br>1  | 1 / 1289 (0.08%)<br>1 |  |
| Reproductive system and breast disorders   |                        |                       |  |

|  |                           |                         |  |
|--|---------------------------|-------------------------|--|
| Acquired phimosis<br>subjects affected / exposed<br>occurrences (all)          | 1 / 3714 (0.03%)<br>1     | 0 / 1289 (0.00%)<br>0   |  |
| Balanoposthitis<br>subjects affected / exposed<br>occurrences (all)            | 3 / 3714 (0.08%)<br>3     | 1 / 1289 (0.08%)<br>1   |  |
| Bilateral breast buds<br>subjects affected / exposed<br>occurrences (all)      | 1 / 3714 (0.03%)<br>1     | 0 / 1289 (0.00%)<br>0   |  |
| Genital labial adhesions<br>subjects affected / exposed<br>occurrences (all)   | 2 / 3714 (0.05%)<br>2     | 0 / 1289 (0.00%)<br>0   |  |
| Vaginal mucosal blistering<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1     | 0 / 1289 (0.00%)<br>0   |  |
| Respiratory, thoracic and mediastinal disorders                                |                           |                         |  |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 3714 (0.08%)<br>3     | 4 / 1289 (0.31%)<br>5   |  |
| Bronchial hyperreactivity<br>subjects affected / exposed<br>occurrences (all)  | 3 / 3714 (0.08%)<br>3     | 2 / 1289 (0.16%)<br>2   |  |
| Bronchospasm<br>subjects affected / exposed<br>occurrences (all)               | 7 / 3714 (0.19%)<br>7     | 2 / 1289 (0.16%)<br>2   |  |
| Catarrh<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 3714 (0.08%)<br>3     | 2 / 1289 (0.16%)<br>2   |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                      | 113 / 3714 (3.04%)<br>116 | 36 / 1289 (2.79%)<br>38 |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                   | 3 / 3714 (0.08%)<br>3     | 2 / 1289 (0.16%)<br>2   |  |
| Epistaxis  |                           |                         |  |

|                              |                   |                   |
|------------------------------|-------------------|-------------------|
| subjects affected / exposed  | 7 / 3714 (0.19%)  | 2 / 1289 (0.16%)  |
| occurrences (all)            | 7                 | 2                 |
| Nasal congestion             |                   |                   |
| subjects affected / exposed  | 26 / 3714 (0.70%) | 11 / 1289 (0.85%) |
| occurrences (all)            | 27                | 11                |
| Nasal discomfort             |                   |                   |
| subjects affected / exposed  | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 0                 | 1                 |
| Oropharyngeal pain           |                   |                   |
| subjects affected / exposed  | 2 / 3714 (0.05%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 2                 | 1                 |
| Rales                        |                   |                   |
| subjects affected / exposed  | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 0                 | 1                 |
| Respiratory disorder         |                   |                   |
| subjects affected / exposed  | 6 / 3714 (0.16%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 6                 | 1                 |
| Respiratory distress         |                   |                   |
| subjects affected / exposed  | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 0                 | 1                 |
| Respiratory tract congestion |                   |                   |
| subjects affected / exposed  | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%)  |
| occurrences (all)            | 2                 | 0                 |
| Rhinitis allergic            |                   |                   |
| subjects affected / exposed  | 8 / 3714 (0.22%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 8                 | 1                 |
| Rhinorrhoea                  |                   |                   |
| subjects affected / exposed  | 65 / 3714 (1.75%) | 21 / 1289 (1.63%) |
| occurrences (all)            | 70                | 22                |
| Sinus congestion             |                   |                   |
| subjects affected / exposed  | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%)  |
| occurrences (all)            | 3                 | 0                 |
| Sneezing                     |                   |                   |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 1 / 1289 (0.08%)  |
| occurrences (all)            | 1                 | 1                 |
| Tonsillar hypertrophy        |                   |                   |

|  |                                 |                               |  |
|--|---------------------------------|-------------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                       | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Upper respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                           | 14 / 3714 (0.38%)<br>15         | 1 / 1289 (0.08%)<br>1         |  |
| Psychiatric disorders  |                                 |                               |  |
| Aggression<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Depressed mood<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                           | 4 / 3714 (0.11%)<br>4           | 1 / 1289 (0.08%)<br>1         |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                       | 2263 / 3714<br>(60.93%)<br>2291 | 822 / 1289<br>(63.77%)<br>838 |  |
| Middle insomnia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 3714 (0.03%)<br>1           | 2 / 1289 (0.16%)<br>2         |  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 3714 (0.08%)<br>3           | 0 / 1289 (0.00%)<br>0         |  |
| Sleep terror<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Tearfulness  |                                 |                               |  |

|  |                         |                       |  |
|--|-------------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                   | 1 / 3714 (0.03%)<br>2   | 0 / 1289 (0.00%)<br>0 |  |
| Terminal insomnia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 3714 (0.00%)<br>0   | 1 / 1289 (0.08%)<br>1 |  |
| Investigations   |                         |                       |  |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Cold agglutinins positive<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3714 (0.00%)<br>0   | 1 / 1289 (0.08%)<br>1 |  |
| Otic examination normal<br>subjects affected / exposed<br>occurrences (all)        | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 3714 (0.00%)<br>0   | 1 / 1289 (0.08%)<br>1 |  |
| Injury, poisoning and procedural complications                                     |                         |                       |  |
| Accidental exposure to product<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Animal bite<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 3714 (0.05%)<br>2   | 0 / 1289 (0.00%)<br>0 |  |
| Arthropod bite<br>subjects affected / exposed<br>occurrences (all)                 | 19 / 3714 (0.51%)<br>19 | 4 / 1289 (0.31%)<br>4 |  |
| Arthropod sting<br>subjects affected / exposed<br>occurrences (all)                | 2 / 3714 (0.05%)<br>3   | 0 / 1289 (0.00%)<br>0 |  |
| Bite<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Chemical poisoning   |                         |                       |  |



|  |                  |                  |
|--|------------------|------------------|
| subjects affected / exposed            | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)                      | 0                | 1                |
| Clavicle fracture                      |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Concussion                             |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Contusion                              |                  |                  |
| subjects affected / exposed            | 5 / 3714 (0.13%) | 4 / 1289 (0.31%) |
| occurrences (all)                      | 5                | 4                |
| Corneal abrasion                       |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Craniocerebral injury                  |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 2 / 1289 (0.16%) |
| occurrences (all)                      | 1                | 2                |
| Ear canal injury                       |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Ear injury                             |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Eye contusion                          |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Face injury                            |                  |                  |
| subjects affected / exposed            | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 1                | 0                |
| Fall                                   |                  |                  |
| subjects affected / exposed            | 2 / 3714 (0.05%) | 1 / 1289 (0.08%) |
| occurrences (all)                      | 2                | 1                |
| Foreign body in gastrointestinal tract |                  |                  |
| subjects affected / exposed            | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |
| occurrences (all)                      | 2                | 0                |
| Gingival injury                        |                  |                  |

|                             |                   |                  |
|-----------------------------|-------------------|------------------|
| subjects affected / exposed | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                 | 1                |
| Hand fracture               |                   |                  |
| subjects affected / exposed | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 2                 | 0                |
| Head injury                 |                   |                  |
| subjects affected / exposed | 17 / 3714 (0.46%) | 2 / 1289 (0.16%) |
| occurrences (all)           | 17                | 2                |
| Heat stroke                 |                   |                  |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                 | 0                |
| Laceration                  |                   |                  |
| subjects affected / exposed | 7 / 3714 (0.19%)  | 2 / 1289 (0.16%) |
| occurrences (all)           | 7                 | 2                |
| Limb injury                 |                   |                  |
| subjects affected / exposed | 4 / 3714 (0.11%)  | 2 / 1289 (0.16%) |
| occurrences (all)           | 4                 | 2                |
| Lip injury                  |                   |                  |
| subjects affected / exposed | 3 / 3714 (0.08%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 3                 | 0                |
| Nail avulsion               |                   |                  |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                 | 0                |
| Radial head dislocation     |                   |                  |
| subjects affected / exposed | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 2                 | 0                |
| Road traffic accident       |                   |                  |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 1 / 1289 (0.08%) |
| occurrences (all)           | 1                 | 1                |
| Scratch                     |                   |                  |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                 | 0                |
| Skin abrasion               |                   |                  |
| subjects affected / exposed | 3 / 3714 (0.08%)  | 0 / 1289 (0.00%) |
| occurrences (all)           | 3                 | 0                |
| Superficial injury of eye   |                   |                  |

|                              |                   |                  |  |
|------------------------------|-------------------|------------------|--|
| subjects affected / exposed  | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 0                 | 1                |  |
| Thermal burn                 |                   |                  |  |
| subjects affected / exposed  | 4 / 3714 (0.11%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 4                 | 1                |  |
| Tibia fracture               |                   |                  |  |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 1                 | 1                |  |
| Tongue injury                |                   |                  |  |
| subjects affected / exposed  | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%) |  |
| occurrences (all)            | 2                 | 0                |  |
| Upper limb fracture          |                   |                  |  |
| subjects affected / exposed  | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 0                 | 1                |  |
| Wound                        |                   |                  |  |
| subjects affected / exposed  | 5 / 3714 (0.13%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 5                 | 1                |  |
| Nervous system disorders     |                   |                  |  |
| Drooling                     |                   |                  |  |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |  |
| occurrences (all)            | 1                 | 0                |  |
| Exaggerated startle response |                   |                  |  |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |  |
| occurrences (all)            | 1                 | 0                |  |
| Febrile convulsion           |                   |                  |  |
| subjects affected / exposed  | 10 / 3714 (0.27%) | 3 / 1289 (0.23%) |  |
| occurrences (all)            | 10                | 3                |  |
| Gross motor delay            |                   |                  |  |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |  |
| occurrences (all)            | 1                 | 0                |  |
| Headache                     |                   |                  |  |
| subjects affected / exposed  | 5 / 3714 (0.13%)  | 1 / 1289 (0.08%) |  |
| occurrences (all)            | 5                 | 1                |  |
| Lethargy                     |                   |                  |  |
| subjects affected / exposed  | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%) |  |
| occurrences (all)            | 1                 | 0                |  |

|   |                                 |                               |  |
|---|---------------------------------|-------------------------------|--|
| Nystagmus<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Poor quality sleep<br>subjects affected / exposed<br>occurrences (all)            | 5 / 3714 (0.13%)<br>6           | 1 / 1289 (0.08%)<br>1         |  |
| Post-traumatic headache<br>subjects affected / exposed<br>occurrences (all)       | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                    | 1602 / 3714<br>(43.13%)<br>1602 | 586 / 1289<br>(45.46%)<br>586 |  |
| Speech disorder developmental<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Tremor<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Blood and lymphatic system disorders  |                                 |                               |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                       | 6 / 3714 (0.16%)<br>6           | 0 / 1289 (0.00%)<br>0         |  |
| Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Lymphadenitis<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 3714 (0.03%)<br>1           | 1 / 1289 (0.08%)<br>1         |  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)               | 12 / 3714 (0.32%)<br>12         | 4 / 1289 (0.31%)<br>4         |  |
| Ear and labyrinth disorders   |                                 |                               |  |

|  |                         |                       |  |
|--|-------------------------|-----------------------|--|
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)            | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Deafness<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                     | 10 / 3714 (0.27%)<br>10 | 4 / 1289 (0.31%)<br>4 |  |
| Ear swelling<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Eustachian tube dysfunction<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3714 (0.00%)<br>0   | 1 / 1289 (0.08%)<br>1 |  |
| Excessive cerumen production<br>subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1   | 0 / 1289 (0.00%)<br>0 |  |
| Otorrhoea<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 3714 (0.05%)<br>2   | 0 / 1289 (0.00%)<br>0 |  |
| Eye disorders  |                         |                       |  |
| Conjunctivitis allergic<br>subjects affected / exposed<br>occurrences (all)      | 2 / 3714 (0.05%)<br>2   | 0 / 1289 (0.00%)<br>0 |  |
| Dacryostenosis acquired<br>subjects affected / exposed<br>occurrences (all)      | 3 / 3714 (0.08%)<br>3   | 0 / 1289 (0.00%)<br>0 |  |
| Eye discharge<br>subjects affected / exposed<br>occurrences (all)                | 3 / 3714 (0.08%)<br>3   | 0 / 1289 (0.00%)<br>0 |  |
| Eye inflammation<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3714 (0.00%)<br>0   | 1 / 1289 (0.08%)<br>1 |  |
| Eye irritation   |                         |                       |  |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Eye swelling                |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Eyelid oedema               |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences (all)           | 2                | 1                |  |
| Hypermetropia               |                  |                  |  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |  |
| occurrences (all)           | 0                | 1                |  |
| Lacrimation increased       |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Lid sulcus deepened         |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Strabismus                  |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Gastrointestinal disorders  |                  |                  |  |
| Abdominal discomfort        |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences (all)           | 1                | 1                |  |
| Abdominal pain              |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |  |
| occurrences (all)           | 1                | 1                |  |
| Abdominal pain upper        |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 4 / 1289 (0.31%) |  |
| occurrences (all)           | 1                | 6                |  |
| Anal fissure                |                  |                  |  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |  |
| occurrences (all)           | 1                | 0                |  |
| Aphthous ulcer              |                  |                  |  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 2 / 1289 (0.16%) |  |
| occurrences (all)           | 0                | 2                |  |

|                                  |                    |                   |
|----------------------------------|--------------------|-------------------|
| Chapped lips                     |                    |                   |
| subjects affected / exposed      | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                | 0                  | 1                 |
| Constipation                     |                    |                   |
| subjects affected / exposed      | 16 / 3714 (0.43%)  | 8 / 1289 (0.62%)  |
| occurrences (all)                | 16                 | 8                 |
| Diarrhoea                        |                    |                   |
| subjects affected / exposed      | 171 / 3714 (4.60%) | 64 / 1289 (4.97%) |
| occurrences (all)                | 189                | 68                |
| Dyspepsia                        |                    |                   |
| subjects affected / exposed      | 0 / 3714 (0.00%)   | 2 / 1289 (0.16%)  |
| occurrences (all)                | 0                  | 2                 |
| Dysphagia                        |                    |                   |
| subjects affected / exposed      | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                | 1                  | 0                 |
| Faeces soft                      |                    |                   |
| subjects affected / exposed      | 2 / 3714 (0.05%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                | 2                  | 0                 |
| Flatulence                       |                    |                   |
| subjects affected / exposed      | 5 / 3714 (0.13%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                | 5                  | 1                 |
| Gastrooesophageal reflux disease |                    |                   |
| subjects affected / exposed      | 4 / 3714 (0.11%)   | 3 / 1289 (0.23%)  |
| occurrences (all)                | 4                  | 3                 |
| Gingival hypertrophy             |                    |                   |
| subjects affected / exposed      | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                | 1                  | 0                 |
| Gingival pain                    |                    |                   |
| subjects affected / exposed      | 2 / 3714 (0.05%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                | 2                  | 0                 |
| Gingival swelling                |                    |                   |
| subjects affected / exposed      | 2 / 3714 (0.05%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                | 2                  | 1                 |
| Haematochezia                    |                    |                   |
| subjects affected / exposed      | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                | 1                  | 0                 |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| Lip swelling                |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Nausea                      |                  |                  |
| subjects affected / exposed | 3 / 3714 (0.08%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 3                | 1                |
| Oral contusion              |                  |                  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 2 / 1289 (0.16%) |
| occurrences (all)           | 0                | 2                |
| Oral mucosal eruption       |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Post-tussive vomiting       |                  |                  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                | 1                |
| Ranula                      |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Rectal haemorrhage          |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Regurgitation               |                  |                  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                | 2                |
| Salivary gland enlargement  |                  |                  |
| subjects affected / exposed | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 2                | 0                |
| Salivary gland pain         |                  |                  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                | 1                |
| Salivary hypersecretion     |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 1                | 2                |
| Stomatitis                  |                  |                  |
| subjects affected / exposed | 5 / 3714 (0.13%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 5                | 1                |



|  |                    |                   |  |
|--|--------------------|-------------------|--|
| Teething                               |                    |                   |  |
| subjects affected / exposed            | 260 / 3714 (7.00%) | 95 / 1289 (7.37%) |  |
| occurrences (all)                      | 312                | 114               |  |
| Toothache                              |                    |                   |  |
| subjects affected / exposed            | 5 / 3714 (0.13%)   | 6 / 1289 (0.47%)  |  |
| occurrences (all)                      | 7                  | 7                 |  |
| Vomiting                               |                    |                   |  |
| subjects affected / exposed            | 107 / 3714 (2.88%) | 43 / 1289 (3.34%) |  |
| occurrences (all)                      | 115                | 46                |  |
| Skin and subcutaneous tissue disorders |                    |                   |  |
| Acne                                   |                    |                   |  |
| subjects affected / exposed            | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |  |
| occurrences (all)                      | 1                  | 0                 |  |
| Blister                                |                    |                   |  |
| subjects affected / exposed            | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |  |
| occurrences (all)                      | 2                  | 0                 |  |
| Dermatitis                             |                    |                   |  |
| subjects affected / exposed            | 4 / 3714 (0.11%)   | 2 / 1289 (0.16%)  |  |
| occurrences (all)                      | 4                  | 2                 |  |
| Dermatitis allergic                    |                    |                   |  |
| subjects affected / exposed            | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |  |
| occurrences (all)                      | 1                  | 0                 |  |
| Dermatitis atopic                      |                    |                   |  |
| subjects affected / exposed            | 9 / 3714 (0.24%)   | 3 / 1289 (0.23%)  |  |
| occurrences (all)                      | 9                  | 3                 |  |
| Dermatitis contact                     |                    |                   |  |
| subjects affected / exposed            | 5 / 3714 (0.13%)   | 0 / 1289 (0.00%)  |  |
| occurrences (all)                      | 5                  | 0                 |  |
| Dermatitis diaper                      |                    |                   |  |
| subjects affected / exposed            | 10 / 3714 (0.27%)  | 5 / 1289 (0.39%)  |  |
| occurrences (all)                      | 12                 | 5                 |  |
| Drug eruption                          |                    |                   |  |
| subjects affected / exposed            | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)  |  |
| occurrences (all)                      | 0                  | 1                 |  |
| Dry skin                               |                    |                   |  |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                | 1                |
| Eczema                      |                  |                  |
| subjects affected / exposed | 4 / 3714 (0.11%) | 5 / 1289 (0.39%) |
| occurrences (all)           | 4                | 5                |
| Eczema nummular             |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Erythema                    |                  |                  |
| subjects affected / exposed | 4 / 3714 (0.11%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 4                | 1                |
| Hyperhidrosis               |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Hyperkeratosis              |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Ingrowing nail              |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Keratosis pilaris           |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Macule                      |                  |                  |
| subjects affected / exposed | 0 / 3714 (0.00%) | 1 / 1289 (0.08%) |
| occurrences (all)           | 0                | 1                |
| Miliaria                    |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Papule                      |                  |                  |
| subjects affected / exposed | 1 / 3714 (0.03%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 1                | 0                |
| Prurigo                     |                  |                  |
| subjects affected / exposed | 2 / 3714 (0.05%) | 0 / 1289 (0.00%) |
| occurrences (all)           | 2                | 0                |
| Pruritus                    |                  |                  |

|  |                                 |                               |  |
|--|---------------------------------|-------------------------------|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Rash   |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 1043 / 3714<br>(28.08%)<br>1043 | 378 / 1289<br>(29.33%)<br>378 |  |
| Seborrhoea                                       |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Skin irritation                                  |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 2 / 3714 (0.05%)<br>2           | 2 / 1289 (0.16%)<br>2         |  |
| Skin mass  |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Skin warm  |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 3 / 3714 (0.08%)<br>3           | 1 / 1289 (0.08%)<br>1         |  |
| Solar dermatitis                                 |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Swelling face                                    |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 2 / 3714 (0.05%)<br>2           | 1 / 1289 (0.08%)<br>1         |  |
| Urticaria  |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 4 / 3714 (0.11%)<br>6           | 0 / 1289 (0.00%)<br>0         |  |
| Renal and urinary disorders                      |                                 |                               |  |
| Dysuria  |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Polyuria   |                                 |                               |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>0         |  |
| Urinary tract disorder                           |                                 |                               |  |

|  |                       |                       |  |
|--|-----------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 3714 (0.03%)<br>1 | 0 / 1289 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders  |                       |                       |  |
| Arthralgia                                       |                       |                       |  |
| subjects affected / exposed                      | 0 / 3714 (0.00%)      | 1 / 1289 (0.08%)      |  |
| occurrences (all)                                | 0                     | 1                     |  |
| Elbow deformity                                  |                       |                       |  |
| subjects affected / exposed                      | 0 / 3714 (0.00%)      | 1 / 1289 (0.08%)      |  |
| occurrences (all)                                | 0                     | 1                     |  |
| Knee deformity                                   |                       |                       |  |
| subjects affected / exposed                      | 1 / 3714 (0.03%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 1                     | 0                     |  |
| Synovial cyst                                    |                       |                       |  |
| subjects affected / exposed                      | 1 / 3714 (0.03%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 1                     | 0                     |  |
| Infections and infestations                      |                       |                       |  |
| Abscess limb                                     |                       |                       |  |
| subjects affected / exposed                      | 1 / 3714 (0.03%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 1                     | 0                     |  |
| Acute sinusitis                                  |                       |                       |  |
| subjects affected / exposed                      | 2 / 3714 (0.05%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 2                     | 0                     |  |
| Adenovirus infection                             |                       |                       |  |
| subjects affected / exposed                      | 2 / 3714 (0.05%)      | 1 / 1289 (0.08%)      |  |
| occurrences (all)                                | 2                     | 1                     |  |
| Beta haemolytic streptococcal infection          |                       |                       |  |
| subjects affected / exposed                      | 1 / 3714 (0.03%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 1                     | 0                     |  |
| Body tinea                                       |                       |                       |  |
| subjects affected / exposed                      | 1 / 3714 (0.03%)      | 0 / 1289 (0.00%)      |  |
| occurrences (all)                                | 1                     | 0                     |  |
| Bronchiolitis                                    |                       |                       |  |
| subjects affected / exposed                      | 16 / 3714 (0.43%)     | 6 / 1289 (0.47%)      |  |
| occurrences (all)                                | 16                    | 6                     |  |
| Bronchitis                                       |                       |                       |  |

|                                 |                   |                   |
|---------------------------------|-------------------|-------------------|
| subjects affected / exposed     | 32 / 3714 (0.86%) | 12 / 1289 (0.93%) |
| occurrences (all)               | 34                | 13                |
| Bullous impetigo                |                   |                   |
| subjects affected / exposed     | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)               | 1                 | 0                 |
| Candida infection               |                   |                   |
| subjects affected / exposed     | 4 / 3714 (0.11%)  | 2 / 1289 (0.16%)  |
| occurrences (all)               | 5                 | 2                 |
| Candida nappy rash              |                   |                   |
| subjects affected / exposed     | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)               | 1                 | 0                 |
| Cellulitis                      |                   |                   |
| subjects affected / exposed     | 5 / 3714 (0.13%)  | 0 / 1289 (0.00%)  |
| occurrences (all)               | 5                 | 0                 |
| Clostridium difficile infection |                   |                   |
| subjects affected / exposed     | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)               | 1                 | 0                 |
| Conjunctivitis                  |                   |                   |
| subjects affected / exposed     | 86 / 3714 (2.32%) | 32 / 1289 (2.48%) |
| occurrences (all)               | 88                | 33                |
| Conjunctivitis bacterial        |                   |                   |
| subjects affected / exposed     | 2 / 3714 (0.05%)  | 0 / 1289 (0.00%)  |
| occurrences (all)               | 2                 | 0                 |
| Coxsackie viral infection       |                   |                   |
| subjects affected / exposed     | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%)  |
| occurrences (all)               | 0                 | 1                 |
| Croup infectious                |                   |                   |
| subjects affected / exposed     | 23 / 3714 (0.62%) | 6 / 1289 (0.47%)  |
| occurrences (all)               | 23                | 6                 |
| Ear infection                   |                   |                   |
| subjects affected / exposed     | 27 / 3714 (0.73%) | 13 / 1289 (1.01%) |
| occurrences (all)               | 27                | 13                |
| Enterovirus infection           |                   |                   |
| subjects affected / exposed     | 3 / 3714 (0.08%)  | 2 / 1289 (0.16%)  |
| occurrences (all)               | 3                 | 2                 |
| Epstein-barr virus infection    |                   |                   |

|                             |                   |                   |
|-----------------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)           | 1                 | 0                 |
| Exanthema subitum           |                   |                   |
| subjects affected / exposed | 0 / 3714 (0.00%)  | 2 / 1289 (0.16%)  |
| occurrences (all)           | 0                 | 2                 |
| Eye infection               |                   |                   |
| subjects affected / exposed | 5 / 3714 (0.13%)  | 4 / 1289 (0.31%)  |
| occurrences (all)           | 5                 | 4                 |
| Folliculitis                |                   |                   |
| subjects affected / exposed | 4 / 3714 (0.11%)  | 0 / 1289 (0.00%)  |
| occurrences (all)           | 4                 | 0                 |
| Fungal infection            |                   |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 1 / 1289 (0.08%)  |
| occurrences (all)           | 1                 | 1                 |
| Gastroenteritis             |                   |                   |
| subjects affected / exposed | 83 / 3714 (2.23%) | 31 / 1289 (2.40%) |
| occurrences (all)           | 87                | 32                |
| Gastroenteritis norovirus   |                   |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 1 / 1289 (0.08%)  |
| occurrences (all)           | 1                 | 1                 |
| Gastroenteritis rotavirus   |                   |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)           | 1                 | 0                 |
| Gastroenteritis viral       |                   |                   |
| subjects affected / exposed | 15 / 3714 (0.40%) | 6 / 1289 (0.47%)  |
| occurrences (all)           | 15                | 6                 |
| Gastrointestinal infection  |                   |                   |
| subjects affected / exposed | 0 / 3714 (0.00%)  | 1 / 1289 (0.08%)  |
| occurrences (all)           | 0                 | 1                 |
| Gingivitis                  |                   |                   |
| subjects affected / exposed | 3 / 3714 (0.08%)  | 0 / 1289 (0.00%)  |
| occurrences (all)           | 3                 | 0                 |
| Hand-foot-and-mouth disease |                   |                   |
| subjects affected / exposed | 14 / 3714 (0.38%) | 5 / 1289 (0.39%)  |
| occurrences (all)           | 14                | 5                 |
| Herpangina                  |                   |                   |

|                                   |                   |                   |
|-----------------------------------|-------------------|-------------------|
| subjects affected / exposed       | 2 / 3714 (0.05%)  | 2 / 1289 (0.16%)  |
| occurrences (all)                 | 2                 | 2                 |
| Herpes simplex                    |                   |                   |
| subjects affected / exposed       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 1                 | 0                 |
| Hordeolum                         |                   |                   |
| subjects affected / exposed       | 2 / 3714 (0.05%)  | 1 / 1289 (0.08%)  |
| occurrences (all)                 | 2                 | 1                 |
| Impetigo                          |                   |                   |
| subjects affected / exposed       | 6 / 3714 (0.16%)  | 2 / 1289 (0.16%)  |
| occurrences (all)                 | 6                 | 2                 |
| Infected bite                     |                   |                   |
| subjects affected / exposed       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 1                 | 0                 |
| Influenza                         |                   |                   |
| subjects affected / exposed       | 8 / 3714 (0.22%)  | 10 / 1289 (0.78%) |
| occurrences (all)                 | 8                 | 12                |
| Injection site abscess            |                   |                   |
| subjects affected / exposed       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 1                 | 0                 |
| Laryngitis                        |                   |                   |
| subjects affected / exposed       | 10 / 3714 (0.27%) | 6 / 1289 (0.47%)  |
| occurrences (all)                 | 12                | 6                 |
| Lice infestation                  |                   |                   |
| subjects affected / exposed       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 1                 | 0                 |
| Localised infection               |                   |                   |
| subjects affected / exposed       | 1 / 3714 (0.03%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 1                 | 0                 |
| Lower respiratory tract infection |                   |                   |
| subjects affected / exposed       | 2 / 3714 (0.05%)  | 2 / 1289 (0.16%)  |
| occurrences (all)                 | 2                 | 2                 |
| Molluscum contagiosum             |                   |                   |
| subjects affected / exposed       | 3 / 3714 (0.08%)  | 0 / 1289 (0.00%)  |
| occurrences (all)                 | 3                 | 0                 |
| Nasopharyngitis                   |                   |                   |

|                             |                    |                   |
|-----------------------------|--------------------|-------------------|
| subjects affected / exposed | 223 / 3714 (6.00%) | 65 / 1289 (5.04%) |
| occurrences (all)           | 247                | 68                |
| Oral candidiasis            |                    |                   |
| subjects affected / exposed | 5 / 3714 (0.13%)   | 0 / 1289 (0.00%)  |
| occurrences (all)           | 5                  | 0                 |
| Oral herpes                 |                    |                   |
| subjects affected / exposed | 2 / 3714 (0.05%)   | 2 / 1289 (0.16%)  |
| occurrences (all)           | 2                  | 2                 |
| Oral infection              |                    |                   |
| subjects affected / exposed | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)  |
| occurrences (all)           | 0                  | 1                 |
| Otitis externa              |                    |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)   | 1 / 1289 (0.08%)  |
| occurrences (all)           | 1                  | 1                 |
| Otitis media                |                    |                   |
| subjects affected / exposed | 217 / 3714 (5.84%) | 86 / 1289 (6.67%) |
| occurrences (all)           | 232                | 89                |
| Otitis media acute          |                    |                   |
| subjects affected / exposed | 28 / 3714 (0.75%)  | 9 / 1289 (0.70%)  |
| occurrences (all)           | 31                 | 9                 |
| Otitis media chronic        |                    |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)           | 1                  | 0                 |
| Paronychia                  |                    |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)           | 1                  | 0                 |
| Periorbital cellulitis      |                    |                   |
| subjects affected / exposed | 1 / 3714 (0.03%)   | 1 / 1289 (0.08%)  |
| occurrences (all)           | 1                  | 1                 |
| Pharyngitis                 |                    |                   |
| subjects affected / exposed | 64 / 3714 (1.72%)  | 23 / 1289 (1.78%) |
| occurrences (all)           | 64                 | 24                |
| Pharyngitis streptococcal   |                    |                   |
| subjects affected / exposed | 4 / 3714 (0.11%)   | 0 / 1289 (0.00%)  |
| occurrences (all)           | 4                  | 0                 |
| Pharyngotonsillitis         |                    |                   |



|  |                    |                   |
|--|--------------------|-------------------|
| subjects affected / exposed                  | 4 / 3714 (0.11%)   | 2 / 1289 (0.16%)  |
| occurrences (all)                            | 4                  | 2                 |
| Pneumonia                                    |                    |                   |
| subjects affected / exposed                  | 7 / 3714 (0.19%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                            | 7                  | 1                 |
| Respiratory syncytial virus<br>bronchiolitis |                    |                   |
| subjects affected / exposed                  | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                            | 0                  | 1                 |
| Respiratory syncytial virus infection        |                    |                   |
| subjects affected / exposed                  | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)  |
| occurrences (all)                            | 0                  | 1                 |
| Respiratory tract infection                  |                    |                   |
| subjects affected / exposed                  | 28 / 3714 (0.75%)  | 7 / 1289 (0.54%)  |
| occurrences (all)                            | 31                 | 9                 |
| Respiratory tract infection viral            |                    |                   |
| subjects affected / exposed                  | 4 / 3714 (0.11%)   | 4 / 1289 (0.31%)  |
| occurrences (all)                            | 4                  | 4                 |
| Rhinitis                                     |                    |                   |
| subjects affected / exposed                  | 133 / 3714 (3.58%) | 41 / 1289 (3.18%) |
| occurrences (all)                            | 147                | 44                |
| Roseola                                      |                    |                   |
| subjects affected / exposed                  | 4 / 3714 (0.11%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                            | 4                  | 0                 |
| Salmonellosis                                |                    |                   |
| subjects affected / exposed                  | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                            | 1                  | 0                 |
| Scarlet fever                                |                    |                   |
| subjects affected / exposed                  | 2 / 3714 (0.05%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                            | 2                  | 0                 |
| Sinusitis                                    |                    |                   |
| subjects affected / exposed                  | 16 / 3714 (0.43%)  | 3 / 1289 (0.23%)  |
| occurrences (all)                            | 17                 | 3                 |
| Skin bacterial infection                     |                    |                   |
| subjects affected / exposed                  | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)  |
| occurrences (all)                            | 1                  | 0                 |

|                                   |                    |                    |
|-----------------------------------|--------------------|--------------------|
| Skin candida                      |                    |                    |
| subjects affected / exposed       | 2 / 3714 (0.05%)   | 0 / 1289 (0.00%)   |
| occurrences (all)                 | 2                  | 0                  |
| Staphylococcal infection          |                    |                    |
| subjects affected / exposed       | 0 / 3714 (0.00%)   | 1 / 1289 (0.08%)   |
| occurrences (all)                 | 0                  | 1                  |
| Streptococcal infection           |                    |                    |
| subjects affected / exposed       | 5 / 3714 (0.13%)   | 3 / 1289 (0.23%)   |
| occurrences (all)                 | 5                  | 3                  |
| Subcutaneous abscess              |                    |                    |
| subjects affected / exposed       | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)   |
| occurrences (all)                 | 1                  | 0                  |
| Tonsillitis                       |                    |                    |
| subjects affected / exposed       | 39 / 3714 (1.05%)  | 15 / 1289 (1.16%)  |
| occurrences (all)                 | 43                 | 16                 |
| Tooth abscess                     |                    |                    |
| subjects affected / exposed       | 1 / 3714 (0.03%)   | 0 / 1289 (0.00%)   |
| occurrences (all)                 | 1                  | 0                  |
| Upper respiratory tract infection |                    |                    |
| subjects affected / exposed       | 352 / 3714 (9.48%) | 122 / 1289 (9.46%) |
| occurrences (all)                 | 381                | 129                |
| Urinary tract infection           |                    |                    |
| subjects affected / exposed       | 3 / 3714 (0.08%)   | 2 / 1289 (0.16%)   |
| occurrences (all)                 | 4                  | 2                  |
| Viral diarrhoea                   |                    |                    |
| subjects affected / exposed       | 2 / 3714 (0.05%)   | 1 / 1289 (0.08%)   |
| occurrences (all)                 | 2                  | 1                  |
| Viral infection                   |                    |                    |
| subjects affected / exposed       | 59 / 3714 (1.59%)  | 15 / 1289 (1.16%)  |
| occurrences (all)                 | 63                 | 15                 |
| Viral pharyngitis                 |                    |                    |
| subjects affected / exposed       | 4 / 3714 (0.11%)   | 1 / 1289 (0.08%)   |
| occurrences (all)                 | 4                  | 1                  |
| Viral rash                        |                    |                    |
| subjects affected / exposed       | 1 / 3714 (0.03%)   | 1 / 1289 (0.08%)   |
| occurrences (all)                 | 1                  | 1                  |

|  |                                 |                               |  |
|--|---------------------------------|-------------------------------|--|
| Viral tonsillitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                  | 10 / 3714 (0.27%)<br>10         | 3 / 1289 (0.23%)<br>3         |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1610 / 3714<br>(43.35%)<br>1614 | 549 / 1289<br>(42.59%)<br>550 |  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3714 (0.00%)<br>0           | 1 / 1289 (0.08%)<br>1         |  |
| Lactose intolerance<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 3714 (0.05%)<br>2           | 0 / 1289 (0.00%)<br>0         |  |
| Polydipsia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3714 (0.03%)<br>1           | 0 / 1289 (0.00%)<br>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