



## Clinical trial results:

### A Phase 3, Open-label Trial to Evaluate the Safety, Tolerability, and Immunogenicity of 13-valent Pneumococcal Conjugate Vaccine Followed by 23-valent Pneumococcal Polysaccharide Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant Aged 2 Years and Older

#### Summary

|                          |                                     |
|--------------------------|-------------------------------------|
| EudraCT number           | 2009-012087-13                      |
| Trial protocol           | BE DE SE FR NL ES CZ Outside EU/EEA |
| Global end of trial date | 16 May 2013                         |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 29 June 2016   |
| First version publication date | 02 August 2015 |

#### Trial information

##### Trial identification

|                       |                           |
|-----------------------|---------------------------|
| Sponsor protocol code | B1851022 (6115A1-3003-WW) |
|-----------------------|---------------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00980655 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Pfizer Inc.  |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017   |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 15 October 2013 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 16 May 2013     |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the immune responses 1 month after 3 doses of 13-valent Pneumococcal Conjugate Vaccine (13vPnC) as measured by fold rises of serotype specific immunoglobulin G (IgG) geometric mean concentrations (GMCs) in subjects aged 2 Years and older.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 18 January 2010 |
| Long term follow-up planned                               | Yes             |
| Long term follow-up rationale                             | Safety          |
| Long term follow-up duration                              | 6 Months        |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Germany: 17       |
| Country: Number of subjects enrolled | Belgium: 81       |
| Country: Number of subjects enrolled | France: 46        |
| Country: Number of subjects enrolled | Netherlands: 1    |
| Country: Number of subjects enrolled | Spain: 26         |
| Country: Number of subjects enrolled | Sweden: 35        |
| Country: Number of subjects enrolled | Czech Republic: 7 |
| Country: Number of subjects enrolled | Poland: 13        |
| Country: Number of subjects enrolled | United States: 15 |
| Country: Number of subjects enrolled | Canada: 6         |
| Worldwide total number of subjects   | 247               |
| EEA total number of subjects         | 226               |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 34  |
| Adolescents (12-17 years)                 | 25  |
| Adults (18-64 years)                      | 168 |
| From 65 to 84 years                       | 20  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Total 61 and 190 subjects were enrolled in 13vPnC, 23vPS (Pediatric Subjects) and 13vPnC, 23vPS (Adult Subjects) respectively. Of these, 59 subjects in 13vPnC, 23vPS (Pediatric Subjects) and 188 subjects in 13vPnC, 23vPS (Adult Subjects) were treated.

### Period 1

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

### Arms

|                              |                                    |
|------------------------------|------------------------------------|
| Are arms mutually exclusive? | Yes                                |
| <b>Arm title</b>             | 13vPnC, 23vPS (Pediatric Subjects) |

Arm description:

Pediatric subjects aged 2 to 17 years received 4 single doses of 13vPnC followed by a single dose of 23-valent pneumococcal polysaccharide vaccine (23vPS). 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.

|  |                   |
|--|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | 23vPS             |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Single 0.5 milliliter (mL) dose of 23vPS intramuscular injection administered 1 month after 13vPnC Dose 4.

|  |                   |
|--|-------------------|
| Investigational medicinal product name | 13vPnC            |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Subjects received 4 single 0.5 mL doses of 13vPnC intramuscular injections. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | 13vPnC, 23vPS (Adult Subjects) |
|------------------|--------------------------------|

Arm description:

Adult subjects aged 18 years and above received 4 single doses of 13vPnC followed by single dose of 23vPS. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.

|  |                   |
|--|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | 23vPS             |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

Single 0.5 mL dose of 23vPS intramuscular injection administered 1 month after 13vPnC Dose 4.

|  |                   |
|--|-------------------|
| Investigational medicinal product name | 13vPnC            |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

4 single 0.5 mL doses of 13vPnC intramuscular injections. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3.

| <b>Number of subjects in period 1</b> | 13vPnC, 23vPS<br>(Pediatric Subjects) | 13vPnC, 23vPS<br>(Adult Subjects) |
|---------------------------------------|---------------------------------------|-----------------------------------|
| Started                               | 59                                    | 188                               |
| Vaccinated 13vPnC Dose 1              | 59                                    | 188                               |
| Vaccinated 23vPS Dose                 | 45                                    | 140                               |
| Vaccinated 13vPnC Dose 4              | 46                                    | 146                               |
| Vaccinated 13vPnC Dose 2              | 55                                    | 176                               |
| Vaccinated 13vPnC Dose 3              | 54                                    | 167                               |
| Completed                             | 45                                    | 139                               |
| Not completed                         | 14                                    | 49                                |
| Adverse Event                         | 13                                    | 31                                |
| Death                                 | -                                     | 7                                 |
| Withdrawal by Subject                 | -                                     | 3                                 |
| Protocol Violation                    | 1                                     | 6                                 |
| Unspecified                           | -                                     | 1                                 |
| Lost to follow-up                     | -                                     | 1                                 |

## Baseline characteristics

### Reporting groups

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 13vPnC, 23vPS (Pediatric Subjects) |
|-----------------------|------------------------------------|

Reporting group description:

Pediatric subjects aged 2 to 17 years received 4 single doses of 13vPnC followed by a single dose of 23-valent pneumococcal polysaccharide vaccine (23vPS). 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | 13vPnC, 23vPS (Adult Subjects) |
|-----------------------|--------------------------------|

Reporting group description:

Adult subjects aged 18 years and above received 4 single doses of 13vPnC followed by single dose of 23vPS. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.

| Reporting group values             | 13vPnC, 23vPS<br>(Pediatric Subjects) | 13vPnC, 23vPS<br>(Adult Subjects) | Total |
|------------------------------------|---------------------------------------|-----------------------------------|-------|
| Number of subjects                 | 59                                    | 188                               | 247   |
| Age categorical<br>Units: Subjects |                                       |                                   |       |

|   |                |                 |     |
|---|----------------|-----------------|-----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 10.3<br>± 4.41 | 47.3<br>± 12.39 | -   |
| Gender categorical<br>Units: Subjects                                   |                |                 |     |
| Female  | 26             | 74              | 100 |
| Male  | 33             | 114             | 147 |

## End points

### End points reporting groups

|   |                                    |
|---|------------------------------------|
| Reporting group title   | 13vPnC, 23vPS (Pediatric Subjects) |
| Reporting group description:<br>Pediatric subjects aged 2 to 17 years received 4 single doses of 13vPnC followed by a single dose of 23-valent pneumococcal polysaccharide vaccine (23vPS). 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.                 |                                    |
| Reporting group title   | 13vPnC, 23vPS (Adult Subjects)     |
| Reporting group description:<br>Adult subjects aged 18 years and above received 4 single doses of 13vPnC followed by single dose of 23vPS. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4.  |                                    |
| Subject analysis set title  | 13vPnC, 23vPS (All Subjects)       |
| Subject analysis set type   | Full analysis                      |
| Subject analysis set description:<br>All subjects aged 2 years and above received 4 single 0.5 mL doses of 13vPnC intramuscular injections followed by single 0.5 mL dose of 23vPS intramuscular injection. 13vPnC Doses 1 to 3 were administered at 1-month intervals, 13vPnC Dose 4 was administered at 6 months after 13vPnC Dose 3, and 23vPS was administered 1 month after 13vPnC Dose 4. |                                    |

### Primary: Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 3 in All Subjects

|   |  |
|---|--|
| End point title   | Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 3 in All Subjects <sup>[1]</sup> |
| End point description:<br>GMFR for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) from before 13vPnC Dose 1 to 1 month after 13vPnC Dose 3 were computed using the logarithmically transformed assay results. Confidence interval (CI) for GMFR were back transformations of a CI based on the Student t distribution for the mean logarithm of the mean fold rise. GMFRs were calculated using all subjects with available data from both before 13vPnC Dose 1 and after 13vPnC Dose 3 blood draws. Evaluable immunogenicity population: eligible subjects who received vaccination as assigned; had blood drawn within pre-specified time-frames; had at least 1 valid, determinate assay result; had no major protocol violation, n = subjects evaluable for specified serotype. |  |
| End point type  | Primary  |
| End point timeframe:<br>Before 13vPnC Dose 1 (pre-vaccination), 1 month after 13vPnC Dose 3   |  |

Notes:

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

Justification: Only descriptive data was planned to be reported for this end point.

| End point values                         | 13vPnC, 23vPS (All Subjects) |  |  |  |
|--|------------------------------|--|--|--|
| Subject group type                       | Subject analysis set         |  |  |  |
| Number of subjects analysed              | 247 <sup>[2]</sup>           |  |  |  |
| Units: Fold rise                         |                              |  |  |  |
| geometric mean (confidence interval 95%) |                              |  |  |  |
| Serotype 1 (n=191)                       | 17.96 (13.63 to 23.66)       |  |  |  |
| Serotype 3 (n=192)                       | 5.07 (3.98 to 6.46)          |  |  |  |

|                      |                       |  |  |  |
|----------------------|-----------------------|--|--|--|
| Serotype 4 (n=193)   | 23.85 (17.61 to 32.3) |  |  |  |
| Serotype 5 (n=194)   | 2.99 (2.46 to 3.63)   |  |  |  |
| Serotype 6A (n=195)  | 5.35 (4.18 to 6.85)   |  |  |  |
| Serotype 6B (n=192)  | 5.18 (3.99 to 6.74)   |  |  |  |
| Serotype 7F (n=195)  | 10.28 (8.15 to 12.96) |  |  |  |
| Serotype 9V (n=196)  | 5.76 (4.63 to 7.17)   |  |  |  |
| Serotype 14 (n=197)  | 4.95 (3.72 to 6.58)   |  |  |  |
| Serotype 18C (n=196) | 8.22 (6.36 to 10.62)  |  |  |  |
| Serotype 19A (n=196) | 3.9 (3.1 to 4.89)     |  |  |  |
| Serotype 19F (n=195) | 6.73 (5.15 to 8.78)   |  |  |  |
| Serotype 23F (n=197) | 8.01 (6.11 to 10.51)  |  |  |  |

Notes:

[2] - N (number of subjects analyzed)=subjects evaluable for this measure.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After 13vPnC Dose 3 in Pediatric, Adult and All Subjects

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After 13vPnC Dose 3 in Pediatric, Adult and All Subjects |
|-----------------|--|

End point description:

Antibody GMC for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) for pediatric, adult and all subjects are presented. GMC (13vPnC) and corresponding 2-sided 95 percent (%) CIs were evaluated. Geometric means were calculated using all subjects with available data for 1 month after 13vPnC Dose 3 blood draw. CI for GMC are back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations. Evaluable immunogenicity population. Here, 'n' signifies all subjects who were evaluable for specified serotype for each treatment arm, respectively.

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

End point timeframe:

1 month after 13vPnC Dose 3

| End point values                         | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|--|--|--------------------------------------|---------------------------------|--|
| Subject group type                       | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed              | 49 <sup>[3]</sup>                        | 149 <sup>[4]</sup>                   | 198 <sup>[5]</sup>              |  |
| Units: microgram per milliliter (mcg/mL) |  |                                      |                                 |  |
| geometric mean (confidence interval 95%) |  |                                      |                                 |  |



|                               |                      |                     |                     |
|-------------------------------|----------------------|---------------------|---------------------|
| Serotype 1 (n=49, 147, 196)   | 3.52 (2.38 to 5.19)  | 2.05 (1.53 to 2.76) | 2.35 (1.84 to 2.99) |
| Serotype 3 (n=49, 147, 196)   | 1.6 (1.13 to 2.26)   | 0.62 (0.49 to 0.79) | 0.79 (0.64 to 0.97) |
| Serotype 4 (n=49, 147, 196)   | 4.13 (2.68 to 6.36)  | 1.78 (1.35 to 2.34) | 2.2 (1.73 to 2.78)  |
| Serotype 5 (n=48, 149, 197)   | 4.18 (2.95 to 5.91)  | 2 (1.6 to 2.51)     | 2.39 (1.97 to 2.91) |
| Serotype 6A (n=49, 148, 197)  | 7.61 (5.16 to 11.23) | 3.31 (2.53 to 4.33) | 4.07 (3.25 to 5.11) |
| Serotype 6B (n=48, 147, 195)  | 6.29 (3.88 to 10.19) | 3 (2.25 to 3.98)    | 3.6 (2.81 to 4.61)  |
| Serotype 7F (n=48, 149, 197)  | 7.34 (5.12 to 10.53) | 3.92 (3.08 to 5)    | 4.57 (3.72 to 5.61) |
| Serotype 9V (n=49, 149, 198)  | 4.17 (3.01 to 5.98)  | 2.44 (1.93 to 3.1)  | 2.79 (2.29 to 3.4)  |
| Serotype 14 (n=49, 149, 198)  | 6.22 (4.03 to 9.61)  | 5.99 (4.35 to 8.26) | 6.05 (4.65 to 7.86) |
| Serotype 18C (n=49, 148, 197) | 4.17 (2.9 to 5.98)   | 3.04 (2.37 to 3.91) | 3.29 (2.67 to 4.05) |
| Serotype 19A (n=49, 148, 197) | 8.26 (5.86 to 11.65) | 4.77 (3.77 to 6.04) | 5.47 (4.49 to 6.67) |
| Serotype 19F (n=49, 148, 197) | 5.8 (3.8 to 8.84)    | 3.48 (2.69 to 4.5)  | 3.95 (3.17 to 4.93) |
| Serotype 23F (n=49, 149, 198) | 6.74 (4.12 to 11.05) | 3.87 (2.85 to 5.26) | 4.44 (3.42 to 5.77) |

Notes:

[3] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[4] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[5] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After 13vPnC Dose 4 in Pediatric, Adult and All Subjects

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After 13vPnC Dose 4 in Pediatric, Adult and All Subjects |
|-----------------|--|

End point description:

Antibody GMC for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) for pediatric, adult and all subjects are presented. GMC (13vPnC) and corresponding 2-sided 95% CIs were evaluated. Geometric means were calculated using all subjects with available data for 1 month after 13vPnC Dose 4 blood draw. CI for GMC are back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations. Evaluable immunogenicity population. Here , 'n' signifies all subjects who were evaluable for specified serotype for each treatment arm, respectively.

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

End point timeframe:

1 month after 13vPnC Dose 4

| End point values                            | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---|--|--------------------------------------|---------------------------------|--|
| Subject group type                          | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                 | 38 <sup>[6]</sup>                        | 124 <sup>[7]</sup>                   | 162 <sup>[8]</sup>              |  |
| Units: mcg/mL                               |  |                                      |                                 |  |
| geometric mean (confidence interval<br>95%) |  |                                      |                                 |  |
| Serotype 1 (n=38, 123, 161)                 | 8.75 (5.64 to<br>13.59)                  | 4.67 (0.71 to<br>1.17)               | 5.41 (0.7 to<br>1.2)            |  |
| Serotype 3 (n=38, 123, 161)                 | 1.23 (0.89 to<br>1.7)                    | 0.91 (3.31 to<br>6.27)               | 0.97 (3.99 to<br>6.86)          |  |
| Serotype 4 (n=36, 124, 160)                 | 8.41 (5.15 to<br>13.72)                  | 4.56 (4.28 to<br>7.26)               | 5.23 (4.95 to<br>7.64)          |  |
| Serotype 5 (n=38, 122, 160)                 | 8.43 (6.07 to<br>11.7)                   | 5.57 (8.63 to<br>17)                 | 6.15 (9.99 to<br>17.13)         |  |
| Serotype 6A (n=37, 122, 159)                | 16.33 (10.59<br>to 25.16)                | 12.23 (8.81 to<br>16.98)             | 13.08 (10.04<br>to 17.7)        |  |
| Serotype 6B (n=38, 124, 162)                | 18.13 (11.15<br>to 29.47)                | 12.13 (3.37 to<br>6.47)              | 13.33 (7 to<br>10.83)           |  |
| Serotype 7F (n=38, 124, 162)                | 10.37 (7.36 to<br>14.61)                 | 8.26 (6.33 to<br>10.78)              | 8.71 (4.13 to<br>7.1)           |  |
| Serotype 9V (n=37, 124, 161)                | 7.78 (5.21 to<br>11.61)                  | 5.09 (3.93 to<br>6.59)               | 5.61 (4.5 to<br>6.98)           |  |
| Serotype 14 (n=37, 124, 161)                | 16.04 (10.04<br>to 25.63)                | 12.24 (9.09 to<br>16.47)             | 13.02 (10.13<br>to 16.74)       |  |
| Serotype 18C (n=38, 122, 160)               | 6.54 (4.04 to<br>10.59)                  | 6.69 (5.01 to<br>8.93)               | 6.65 (5.2 to<br>8.51)           |  |
| Serotype 19A (n=37, 124, 161)               | 16.94 (11.05<br>to 25.98)                | 12.99 (9.78 to<br>17.26)             | 13.81 (10.88<br>to 17.52)       |  |
| Serotype 19F (n=38, 123, 161)               | 19.96 (12.19<br>to 32.68)                | 13.69 (9.93 to<br>18.88)             | 14.96 (11.42<br>to 19.61)       |  |
| Serotype 23F (n=38, 123, 161)               | 16.65 (10.73<br>to 25.82)                | 12.68 (8.82 to<br>18.22)             | 13.52 (10.07<br>to 18.15)       |  |

Notes:

[6] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[7] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[8] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 3 in Pediatric and Adult Subjects

|                 |   |
|-----------------|---|
| End point title | Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 3 in Pediatric and Adult Subjects |
|-----------------|---|

End point description:

GMFR for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) from before 13vPnC Dose 1 to 1 month after 13vPnC Dose 3 were computed using the logarithmically transformed assay results. CI for GMFR were back transformations of a CI based on the Student t distribution for the mean logarithm of the mean fold rise. GMFRs were calculated using all students with available data from both before 13vPnC Dose 1 and after 13vPnC Dose 3 blood draws. Evaluable immunogenicity population. Here, 'n' signifies all subjects who were evaluable for specified serotype for each treatment arm, respectively.

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

End point timeframe:

Before 13vPnC Dose 1 (pre-vaccination), 1 month after 13vPnC Dose 3

| End point values                            | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) |  |  |
|---|--|--------------------------------------|--|--|
| Subject group type                          | Reporting group                          | Reporting group                      |  |  |
| Number of subjects analysed                 | 49 <sup>[9]</sup>                        | 148 <sup>[10]</sup>                  |  |  |
| Units: Fold rise                            |  |                                      |  |  |
| geometric mean (confidence interval<br>95%) |  |                                      |  |  |
| Serotype 1 (n=48, 143)                      | 27.64 (16.75<br>to 45.62)                | 15.54 (11.2 to<br>21.56)             |  |  |
| Serotype 3 (n=48, 144)                      | 7.58 (4.74 to<br>12.13)                  | 4.43 (3.35 to<br>5.88)               |  |  |
| Serotype 4 (n=49, 144)                      | 40.83 (23.84<br>to 69.95)                | 19.86 (13.83<br>to 28.52)            |  |  |
| Serotype 5 (n=47, 147)                      | 4.11 (2.86 to<br>5.9)                    | 2.7 (2.15 to<br>3.39)                |  |  |
| Serotype 6A (n=48, 147)                     | 7.49 (4.79 to<br>11.72)                  | 4.79 (3.57 to<br>6.44)               |  |  |
| Serotype 6B (n=47, 145)                     | 6.02 (3.79 to<br>9.55)                   | 4.94 (3.6 to<br>6.77)                |  |  |
| Serotype 7F (n=48, 147)                     | 14.65 (9.63 to<br>22.28)                 | 9.15 (6.95 to<br>12.05)              |  |  |
| Serotype 9V (n=48, 148)                     | 7.64 (5.4 to<br>10.82)                   | 5.26 (4.02 to<br>6.87)               |  |  |
| Serotype 14 (n=49, 148)                     | 5.01 (2.83 to<br>8.86)                   | 4.92 (3.53 to<br>6.87)               |  |  |
| Serotype 18C (n=49, 147)                    | 12.59 (7.84 to<br>20.21)                 | 7.13 (5.27 to<br>9.65)               |  |  |
| Serotype 19A (n=49, 147)                    | 5.04 (3.38 to<br>7.51)                   | 3.58 (2.72 to<br>4.7)                |  |  |
| Serotype 19F (n=49, 146)                    | 7.66 (4.67 to<br>12.57)                  | 6.44 (4.69 to<br>8.85)               |  |  |
| Serotype 23F (n=49, 148)                    | 9.73 (5.79 to<br>16.34)                  | 7.52 (5.46 to<br>10.35)              |  |  |

Notes:

[9] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[10] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 4 in Pediatric, Adult and All Subjects

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From Before 13vPnC Dose 1 to 1 Month After 13vPnC Dose 4 in Pediatric, Adult and All Subjects |
|-----------------|--|

End point description:

GMFR for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) from before 13vPnC Dose 1 to 1 month after 13vPnC Dose 4 were computed using the logarithmically transformed assay results. CI for GMFR were back transformations of a CI based on the Student t

distribution for the mean logarithm of the mean fold rise. GMFRs were calculated using all subjects with available data from both before 13vPnC Dose 1 and after 13vPnC Dose 4 blood draws. Evaluable immunogenicity population. Here, 'n' signifies all subjects who were evaluable for specified serotype for each treatment arm, respectively.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Before 13vPnC Dose 1 (pre-vaccination), 1 month after 13vPnC Dose 4 |           |

| End point values                         | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|--|--|--------------------------------------|---------------------------------|--|
| Subject group type                       | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed              | 38 <sup>[11]</sup>                       | 123 <sup>[12]</sup>                  | 161 <sup>[13]</sup>             |  |
| Units: Fold rise                         |  |                                      |                                 |  |
| geometric mean (confidence interval 95%) |  |                                      |                                 |  |
| Serotype 1 (n=37, 120, 157)              | 70.66 (39.2 to 127.36)                   | 35.81 (25.06 to 51.18)               | 42.03 (30.94 to 57.11)          |  |
| Serotype 3 (n=37, 120, 157)              | 5.88 (3.25 to 10.61)                     | 6.41 (4.74 to 8.66)                  | 6.28 (4.81 to 8.19)             |  |
| Serotype 4 (n=36, 121, 157)              | 90.31 (48.05 to 169.77)                  | 47.47 (32.09 to 70.22)               | 55.02 (39.39 to 76.85)          |  |
| Serotype 5 (n=37, 119, 156)              | 7.76 (4.81 to 12.51)                     | 7.29 (5.32 to 9.99)                  | 7.4 (5.69 to 9.63)              |  |
| Serotype 6A (n=36, 121, 157)             | 15.62 (9.63 to 25.34)                    | 17.02 (11.95 to 24.23)               | 16.7 (12.47 to 22.34)           |  |
| Serotype 6B (n=37, 122, 159)             | 16.9 (9.76 to 29.25)                     | 20.09 (13.94 to 28.94)               | 19.29 (14.22 to 26.18)          |  |
| Serotype 7F (n=38, 123, 161)             | 19.18 (11.75 to 31.33)                   | 18.69 (13.7 to 25.5)                 | 18.81 (14.48 to 24.43)          |  |
| Serotype 9V (n=36, 122, 158)             | 14.9 (9.55 to 23.25)                     | 11.13 (8.27 to 14.99)                | 11.9 (9.27 to 15.27)            |  |
| Serotype 14 (n=37, 123, 160)             | 12.61 (6.47 to 24.56)                    | 9.69 (6.8 to 13.8)                   | 10.3 (7.55 to 14.03)            |  |
| Serotype 18C (n=38, 121, 159)            | 21.22 (12.05 to 37.36)                   | 14.4 (10.17 to 20.41)                | 15.8 (11.76 to 21.24)           |  |
| Serotype 19A (n=37, 123, 160)            | 11.46 (7.22 to 18.2)                     | 9.52 (6.9 to 13.12)                  | 9.94 (7.61 to 12.98)            |  |
| Serotype 19F (n=38, 120, 158)            | 29.31 (16.63 to 51.64)                   | 25.63 (17.56 to 37.43)               | 26.47 (19.31 to 36.29)          |  |
| Serotype 23F (n=38, 122, 160)            | 25.37 (14.69 to 43.83)                   | 23.02 (15.63 to 33.92)               | 23.56 (17.11 to 32.45)          |  |

Notes:

[11] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[12] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[13] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From 1 Month After 13vPnC Dose 3 to 1 Month After 13vPnC Dose 4 in Pediatric, Adult and All Subjects

|                 |   |
|-----------------|---|
| End point title | Geometric Mean Fold Rise (GMFR) for Serotype-specific Pneumococcal Immunoglobulin G (IgG) Antibody From 1 Month |
|-----------------|---|

End point description:

GMFR for the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) from 1 month after 13vPnC Dose 3 to 1 month after 13vPnC Dose 4 were computed using the logarithmically transformed assay results. CI for GMFR were back transformations of a CI based on the Student t distribution for the mean logarithm of the mean fold rise. GMFRs were calculated using all subjects with available data from both after 13vPnC Dose 3 and after 13vPnC Dose 4 blood draws. Evaluable immunogenicity population. Here, 'n' signifies all subjects who were evaluable for specified serotype for each treatment arm, respectively.

End point type Secondary

End point timeframe:

1 month after 13vPnC Dose 3, 1 month after 13vPnC Dose 4

| End point values                            | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---|--|--------------------------------------|---------------------------------|--|
| Subject group type                          | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                 | 37 <sup>[14]</sup>                       | 121 <sup>[15]</sup>                  | 157 <sup>[16]</sup>             |  |
| Units: Fold rise                            |  |                                      |                                 |  |
| geometric mean (confidence interval<br>95%) |  |                                      |                                 |  |
| Serotype 1 (n=37, 119, 156)                 | 2.8 (1.99 to<br>3.95)                    | 2.16 (1.65 to<br>2.82)               | 2.3 (1.85 to<br>2.86)           |  |
| Serotype 3 (n=37, 119, 156)                 | 0.88 (0.64 to<br>1.22)                   | 1.32 (1.07 to<br>1.62)               | 1.2 (1.01 to<br>1.43)           |  |
| Serotype 4 (n=35, 121, 156)                 | 2.19 (1.51 to<br>3.19)                   | 2.32 (1.88 to<br>2.86)               | 2.29 (1.91 to<br>2.74)          |  |
| Serotype 5 (n=37, 119, 156)                 | 2.25 (1.74 to<br>2.93)                   | 2.43 (1.94 to<br>3.06)               | 2.39 (1.99 to<br>2.87)          |  |
| Serotype 6A (n=36, 119, 155)                | 2.36 (1.87 to<br>2.99)                   | 3.06 (2.35 to<br>3.98)               | 2.88 (2.34 to<br>3.55)          |  |
| Serotype 6B (n=37, 120, 157)                | 2.96 (2.09 to<br>4.19)                   | 3.1 (2.44 to<br>3.95)                | 3.07 (2.51 to<br>3.75)          |  |
| Serotype 7F (n=36, 121, 157)                | 1.51 (1.08 to<br>2.11)                   | 1.83 (1.47 to<br>2.29)               | 1.75 (1.46 to<br>2.11)          |  |
| Serotype 9V (n=36, 121, 157)                | 2.08 (1.43 to<br>3.03)                   | 1.82 (1.48 to<br>2.23)               | 1.88 (1.57 to<br>2.24)          |  |
| Serotype 14 (n=36, 121, 157)                | 2.5 (1.65 to<br>3.8)                     | 1.68 (1.32 to<br>2.13)               | 1.84 (1.5 to<br>2.26)           |  |
| Serotype 18C (n=37, 118, 155)               | 1.64 (1.24 to<br>2.16)                   | 1.87 (1.54 to<br>2.28)               | 1.81 (1.54 to<br>2.13)          |  |
| Serotype 19A (n=36, 121, 157)               | 2.25 (1.6 to<br>3.17)                    | 2.33 (1.91 to<br>2.85)               | 2.31 (1.95 to<br>2.74)          |  |
| Serotype 19F (n=37, 120, 157)               | 3.5 (2.15 to<br>5.68)                    | 3.65 (2.9 to<br>4.59)                | 3.61 (2.94 to<br>4.44)          |  |
| Serotype 23F (n=37, 120, 157)               | 2.49 (1.72 to<br>3.61)                   | 2.59 (2.04 to<br>3.3)                | 2.57 (2.1 to<br>3.14)           |  |

Notes:

[14] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[15] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

[16] - N (number of subjects analyzed) signifies all subjects who were evaluable for this measure.

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 1

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 1 |
|-----------------|--|

End point description:

Specific local reactions were prompted for each day, and reported using an electronic diary. Redness and Swelling were scaled as Any (redness present or swelling present); Mild (0.5 to 2.0 centimeters [cm] for subjects aged 2 to less than [ $<$ ]12 years and 2.5 to 5.0 cm for subjects aged greater than or equal to [ $\geq$ ] 12 years); Moderate (2.5 to 7.0 cm for subjects aged 2 to  $<$ 12 years and 5.5 to 10.0 cm for subjects aged  $\geq$ 12 years); Severe (greater than [ $>$ ] 7.0 cm for subjects aged 2 to  $<$ 12 years and  $>$ 10.0 cm for subjects aged  $\geq$ 12 years). Pain at injection site was scaled as Any (pain present); Mild (did not interfere with activity); Moderate (interfered with activity); Severe (prevented daily activity). Population analysed was the safety population. Here, 'n' signifies subjects with known values for specified local reaction. Subjects may be represented in more than 1 category.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Within 14 days after 13vPnC Dose 1

| End point values                      | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---------------------------------------|--|--------------------------------------|---------------------------------|--|
| Subject group type                    | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed           | 52 <sup>[17]</sup>                       | 171 <sup>[18]</sup>                  | 223 <sup>[19]</sup>             |  |
| Units: Percentage of subjects         |  |                                      |                                 |  |
| number (confidence interval 95%)      |  |                                      |                                 |  |
| Redness: any (n = 38, 130, 168)       | 21.1 (9.6 to 37.3)                       | 11.5 (6.6 to 18.3)                   | 13.7 (8.9 to 19.8)              |  |
| Redness: mild (n = 38, 130, 168)      | 15.8 (0 to 9.5)                          | 10.8 (6 to 17.4)                     | 11.9 (7.4 to 17.8)              |  |
| Redness: moderate (n = 37, 128, 165)  | 10.8 (12.7 to 41.2)                      | 1.6 (0.2 to 5.5)                     | 3.6 (1.3 to 7.7)                |  |
| Redness: severe (n = 37, 128, 165)    | 0 (2.9 to 24.2)                          | 0 (0 to 2.8)                         | 0 (0 to 2.2)                    |  |
| Swelling: any (n = 40, 130, 170)      | 25 (9.3 to 36.5)                         | 11.5 (6.6 to 18.3)                   | 14.7 (9.7 to 20.9)              |  |
| Swelling: mild (n = 39, 130, 169)     | 10.3 (0 to 9.5)                          | 10.8 (6 to 17.4)                     | 10.7 (6.4 to 16.3)              |  |
| Swelling: moderate (n = 39, 128, 167) | 20.5 (64.7 to 88.7)                      | 0.8 (0 to 4.3)                       | 5.4 (2.5 to 10)                 |  |
| Swelling: severe (n = 37, 128, 165)   | 0 (53.7 to 81.3)                         | 0.8 (0 to 4.3)                       | 0.6 (0 to 3.3)                  |  |
| Pain: any (n = 51, 171, 222)          | 78.4 (29.8 to 61.3)                      | 73.1 (65.8 to 79.6)                  | 74.3 (68.1 to 79.9)             |  |
| Pain: mild (n = 48, 169, 217)         | 68.8 (0.7 to 18.2)                       | 69.8 (62.3 to 76.6)                  | 69.6 (63 to 75.6)               |  |
| Pain: moderate (n = 42, 138, 180)     | 45.2 (9.6 to 37.3)                       | 22.5 (15.8 to 30.3)                  | 27.8 (21.4 to 34.9)             |  |
| Pain: severe (n = 37, 129, 166)       | 5.4 (0.7 to 18.2)                        | 2.3 (0.5 to 6.6)                     | 3 (1 to 6.9)                    |  |

Notes:

[17] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[18] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[19] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

## Statistical analyses

**Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 2**

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 2 |
|-----------------|--|

## End point description:

Specific local reactions were prompted for each day, and reported using an electronic diary. Redness and Swelling were scaled as Any (redness present or swelling present); Mild (0.5 to 2.0 cm for subjects aged 2 to <12 years and 2.5 to 5.0 cm for subjects aged ≥12 years); Moderate (2.5 to 7.0 cm for subjects aged 2 to <12 years and 5.5 to 10.0 cm for subjects aged ≥12 years); Severe >7.0 cm for subjects aged 2 to <12 years and >10.0 cm for subjects aged ≥12 years). Pain at injection site was scaled as Any (pain present); Mild (did not interfere with activity); Moderate (interfered with activity); Severe (prevented daily activity). Population analysed was the safety population. Here, 'n' signifies subjects with known values for specified local reaction. Subjects may be represented in more than 1 category.

|                                    |                     |
|------------------------------------|---------------------|
| End point type                     | Other pre-specified |
| End point timeframe:               |                     |
| Within 14 days after 13vPnC Dose 2 |                     |

| End point values                      | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---------------------------------------|--|--------------------------------------|---------------------------------|--|
| Subject group type                    | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed           | 41 <sup>[20]</sup>                       | 157 <sup>[21]</sup>                  | 198 <sup>[22]</sup>             |  |
| Units: Percentage of subjects         |  |                                      |                                 |  |
| number (confidence interval 95%)      |  |                                      |                                 |  |
| Redness: any (n = 28, 109, 137)       | 42.9 (24.5 to 62.8)                      | 16.5 (10.1 to 24.8)                  | 21.9 (15.3 to 29.8)             |  |
| Redness: mild (n = 26, 108, 134)      | 34.6 (17.2 to 55.7)                      | 15.7 (9.4 to 24)                     | 19.4 (13.1 to 27.1)             |  |
| Redness: moderate (n = 26, 103, 129)  | 26.9 (11.6 to 47.8)                      | 1.9 (0.2 to 6.8)                     | 7 (3.2 to 12.8)                 |  |
| Redness: severe (n = 24, 103, 127)    | 4.2 (0.1 to 21.1)                        | 1 (0 to 5.3)                         | 1.6 (0.2 to 5.6)                |  |
| Swelling: any (n = 28, 105, 133)      | 35.7 (18.6 to 55.9)                      | 14.3 (8.2 to 22.5)                   | 18.8 (12.5 to 26.5)             |  |
| Swelling: mild (n = 26, 105, 131)     | 15.4 (4.4 to 34.9)                       | 14.3 (8.2 to 22.5)                   | 14.5 (9 to 21.7)                |  |
| Swelling: moderate (n = 26, 102, 128) | 26.9 (11.6 to 47.8)                      | 0 (0 to 3.6)                         | 5.5 (2.2 to 10.9)               |  |
| Swelling: severe (n = 24, 102, 126)   | 0 (0 to 14.2)                            | 0 (0 to 3.6)                         | 0 (0 to 2.9)                    |  |
| Pain: any (n = 40, 154, 194)          | 77.5 (61.5 to 89.2)                      | 74.7 (67 to 81.3)                    | 75.3 (68.6 to 81.2)             |  |
| Pain: mild (n = 36, 148, 184)         | 66.7 (49 to 81.4)                        | 70.9 (62.9 to 78.1)                  | 70.1 (62.9 to 76.6)             |  |
| Pain: moderate (n = 32, 116, 148)     | 53.1 (34.7 to 70.9)                      | 27.6 (19.7 to 36.7)                  | 33.1 (25.6 to 41.3)             |  |
| Pain: severe (n = 27, 104, 131)       | 14.8 (4.2 to 33.7)                       | 1.9 (0.2 to 6.8)                     | 4.6 (1.7 to 9.7)                |  |

## Notes:

[20] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[21] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[22] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 3

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 3 |
|-----------------|--|

End point description:

Specific local reactions were prompted for each day, and reported using an electronic diary. Redness and Swelling were scaled as Any (redness present or swelling present); Mild (0.5 to 2.0 cm for subjects aged 2 to <12 years and 2.5 to 5.0 cm for subjects aged ≥12 years); Moderate (2.5 to 7.0 cm for subjects aged 2 to <12 years and 5.5 to 10.0 cm for subjects aged ≥12 years); Severe >7.0 cm for subjects aged 2 to <12 years and >10.0 cm for subjects aged ≥12 years). Pain at injection site was scaled as Any (pain present); Mild (did not interfere with activity); Moderate (interfered with activity); Severe (prevented daily activity). Population analysed was the safety population. Here, 'n' signifies subjects with known values for specified local reaction. Subjects may be represented in more than 1 category.

|                                    |                     |
|------------------------------------|---------------------|
| End point type                     | Other pre-specified |
| End point timeframe:               |                     |
| Within 14 days after 13vPnC Dose 3 |                     |

| End point values                     | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|--------------------------------------|--|--------------------------------------|---------------------------------|--|
| Subject group type                   | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed          | 37 <sup>[23]</sup>                       | 138 <sup>[24]</sup>                  | 175 <sup>[25]</sup>             |  |
| Units: Percentage of subjects        |  |                                      |                                 |  |
| number (confidence interval 95%)     |  |                                      |                                 |  |
| Redness: any (n = 25, 95, 120)       | 32 (45.25 to 80.8)                       | 9.5 (4.4 to 17.2)                    | 14.2 (8.5 to 21.7)              |  |
| Redness: mild (n = 24, 94, 118)      | 20.8 (22.2 to 56.4)                      | 8.5 (3.7 to 16.1)                    | 11 (6 to 18.1)                  |  |
| Redness: moderate (n = 24, 93, 117)  | 20.8 (14.9 to 53.5)                      | 1.1 (0 to 5.8)                       | 5.1 (1.9 to 10.8)               |  |
| Redness: severe (n = 23, 93, 116)    | 4.3 (7.1 to 42.2)                        | 1.1 (0 to 5.8)                       | 1.7 (0.2 to 6.1)                |  |
| Swelling: any (n = 28, 93, 121)      | 35.7 (7.1 to 42.2)                       | 8.6 (3.8 to 16.2)                    | 14.9 (9.1 to 22.5)              |  |
| Swelling: mild (n = 27, 93, 120)     | 25.9 (0.1 to 21.9)                       | 8.6 (3.8 to 16.2)                    | 12.5 (7.2 to 19.8)              |  |
| Swelling: moderate (n = 25, 92, 117) | 20 (18.6 to 55.9)                        | 0 (0 to 3.9)                         | 4.3 (1.4 to 9.7)                |  |
| Swelling: severe (n = 23, 92, 115)   | 4.3 (11.1 to 46.3)                       | 0 (0 to 3.9)                         | 0.9 (0 to 4.7)                  |  |
| Pain: any (n = 37, 138, 175)         | 70.3 (6.8 to 40.7)                       | 73.2 (65 to 80.4)                    | 72.6 (65.3 to 79)               |  |
| Pain: mild (n = 31, 132, 163)        | 64.5 (0.1 to 21.9)                       | 67.4 (58.7 to 75.3)                  | 66.9 (59.1 to 74)               |  |
| Pain: moderate (n = 34, 107, 141)    | 38.2 (53 to 84.1)                        | 27.1 (19 to 36.6)                    | 29.8 (22.4 to 38.1)             |  |
| Pain: severe (n = 24, 93, 117)       | 8.3 (1 to 27)                            | 3.2 (0.7 to 9.1)                     | 4.3 (1.4 to 9.7)                |  |

Notes:

[23] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[24] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.



## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 4

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Local Reactions: 13vPnC Dose 4 |
|-----------------|--|

End point description:

Specific local reactions were prompted for each day, and reported using an electronic diary. Redness and Swelling were scaled as Any (redness present or swelling present); Mild (0.5 to 2.0 cm for subjects aged 2 to <12 years and 2.5 to 5.0 cm for subjects aged ≥12 years); Moderate (2.5 to 7.0 cm for subjects aged 2 to <12 years and 5.5 to 10.0 cm for subjects aged ≥12 years); Severe >7.0 cm for subjects aged 2 to <12 years and >10.0 cm for subjects aged ≥12 years). Pain at injection site was scaled as Any (pain present); Mild (did not interfere with activity); Moderate (interfered with activity); Severe (prevented daily activity). Population analysed was the safety population. Here, 'n' signifies subjects with known values for specified local reaction. Subjects may be represented in more than 1 category.

|                                    |                     |
|------------------------------------|---------------------|
| End point type                     | Other pre-specified |
| End point timeframe:               |                     |
| Within 14 days after 13vPnC Dose 4 |                     |

| End point values                    | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|-------------------------------------|--|--------------------------------------|---------------------------------|--|
| Subject group type                  | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed         | 35 <sup>[26]</sup>                       | 116 <sup>[27]</sup>                  | 151 <sup>[28]</sup>             |  |
| Units: Percentage of subjects       |  |                                      |                                 |  |
| number (confidence interval 95%)    |  |                                      |                                 |  |
| Redness: any (n = 21, 79, 100)      | 71.4 (47.8 to 88.7)                      | 22.8 (14.1 to 33.6)                  | 33 (23.9 to 43.1)               |  |
| Redness: mild (n = 20, 77, 97)      | 50 (27.2 to 72.8)                        | 15.6 (8.3 to 25.6)                   | 22.7 (14.8 to 32.3)             |  |
| Redness: moderate (n = 18, 72, 90)  | 50 (26 to 74)                            | 9.7 (4 to 19)                        | 17.8 (10.5 to 27.3)             |  |
| Redness: severe (n = 16, 73, 89)    | 12.5 (1.6 to 38.3)                       | 4.1 (0.9 to 11.5)                    | 5.6 (1.8 to 12.6)               |  |
| Swelling: any (n = 27, 81, 108)     | 66.7 (46 to 83.5)                        | 28.4 (18.9 to 39.5)                  | 38 (28.8 to 47.8)               |  |
| Swelling: mild (n = 21, 79, 100)    | 38.1 (18.1 to 61.6)                      | 21.5 (13.1 to 32.2)                  | 25 (16.9 to 34.7)               |  |
| Swelling: moderate (n = 23, 72, 95) | 52.2 (30.6 to 73.2)                      | 6.9 (2.3 to 15.5)                    | 17.9 (10.8 to 27.1)             |  |
| Swelling: severe (n = 15, 73, 88)   | 6.7 (0.2 to 31.9)                        | 4.1 (0.9 to 11.5)                    | 4.5 (1.3 to 11.2)               |  |
| Pain: any (n = 30, 113, 143)        | 86.7 (69.3 to 96.2)                      | 77 (68.1 to 84.4)                    | 79 (71.4 to 85.4)               |  |
| Pain: mild (n = 25, 105, 130)       | 76 (54.9 to 90.6)                        | 71.4 (61.8 to 79.8)                  | 72.3 (63.8 to 79.8)             |  |

|                                  |                     |                     |                     |  |
|----------------------------------|---------------------|---------------------|---------------------|--|
| Pain: moderate (n = 24, 85, 109) | 62.5 (40.6 to 81.2) | 31.8 (22.1 to 42.8) | 38.5 (29.4 to 48.3) |  |
| Pain: severe (n = 16, 74, 90)    | 12.5 (1.6 to 38.3)  | 5.4 (1.5 to 13.3)   | 6.7 (2.5 to 13.9)   |  |

Notes:

[26] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[27] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

[28] - N (number of subjects analyzed) signifies subjects with known values for any local reaction.

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 1

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 1 |
|-----------------|--|

End point description:

Specific systemic events (fever  $\geq 38$  degrees Celsius [C], fatigue, headache, vomiting, diarrhea, muscle pain, joint pain and use of medication to treat pain/fever) were prompted for each day, and reported using an e-diary. Fatigue, headache, muscle pain and joint pain were scaled as: Any (symptom present); Mild (did not interfere with activity); Moderate (some interference with activity); Severe (prevented routine daily activity). Vomiting was scaled as: Any (vomiting present); Mild (1-2 times in 24 hours); Moderate ( $>2$  times in 24 hours); Severe (required intravenous hydration). Diarrhea was scaled as: Any (diarrhea present); Mild (2-3 loose stools in 24 hours); Moderate (4-5 loose stools 24 hours); Severe ( $\geq 6$  loose stools in 24 hours). Safety population. Here, 'n' signifies subjects with known values for specified systemic event. Subjects may be represented in more than 1 category.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Within 14 days after 13vPnC Dose 1

| End point values  | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---|--|--------------------------------------|---------------------------------|--|
| Subject group type  | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                               | 51 <sup>[29]</sup>                       | 172 <sup>[30]</sup>                  | 223 <sup>[31]</sup>             |  |
| Units: Percentage of subjects                             |  |                                      |                                 |  |
| number (confidence interval 95%)                          |  |                                      |                                 |  |
| Fever: $\geq 38$ degrees C (n = 39, 130, 169)             | 12.8 (4.3 to 27.4)                       | 6.2 (2.7 to 11.8)                    | 7.7 (4.2 to 12.8)               |  |
| Fever: $\geq 38$ , $<38.5$ degrees C (n = 37, 130, 167)   | 5.4 (0.7 to 18.2)                        | 6.2 (2.7 to 11.8)                    | 6 (2.9 to 10.7)                 |  |
| Fever: $\geq 38.5$ , $<39$ degrees C (n = 37, 128, 165)   | 5.4 (0.7 to 18.2)                        | 0 (0 to 2.8)                         | 1.2 (0.1 to 4.3)                |  |
| Fever: $\geq 39$ , $\leq 40$ degrees C (n = 39, 128, 167) | 7.7 (1.6 to 20.9)                        | 0 (0 to 2.8)                         | 1.8 (0.4 to 5.2)                |  |
| Fever: $>40$ degrees C (n = 37, 128, 165)                 | 0 (0 to 9.5)                             | 0 (0 to 2.8)                         | 0 (0 to 2.2)                    |  |
| Fatigue: Any (n = 45, 159, 204)                           | 53.3 (37.9 to 68.3)                      | 59.7 (51.7 to 67.4)                  | 58.3 (51.2 to 65.2)             |  |
| Fatigue: Mild (n = 41, 149, 190)                          | 36.6 (22.1 to 53.1)                      | 49 (40.7 to 57.3)                    | 46.3 (39.1 to 53.7)             |  |
| Fatigue: Moderate (n = 44, 148, 192)                      | 36.4 (22.4 to 52.2)                      | 35.8 (28.1 to 44.1)                  | 35.9 (29.2 to 43.2)             |  |
| Fatigue: Severe (n = 37, 136, 173)                        | 10.8 (3 to 25.4)                         | 11.8 (6.9 to 18.4)                   | 11.6 (7.2 to 17.3)              |  |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Headache: Any (n = 42, 147, 189)                   | 45.2 (29.8 to 61.3) | 44.2 (36 to 52.6)   | 44.4 (37.2 to 51.8) |
| Headache: Mild (n = 41, 145, 186)                  | 39 (24.2 to 55.5)   | 37.9 (30 to 46.4)   | 38.2 (31.2 to 45.6) |
| Headache: Moderate (n = 40, 134, 174)              | 20 (9.1 to 35.6)    | 17.2 (11.2 to 24.6) | 17.8 (12.4 to 24.3) |
| Headache: Severe (n = 37, 130, 167)                | 2.7 (0.1 to 14.2)   | 2.3 (0.5 to 6.6)    | 2.4 (0.7 to 6)      |
| Vomiting: Any (n = 39, 134, 173)                   | 20.5 (9.3 to 36.5)  | 20.9 (14.4 to 28.8) | 20.8 (15 to 27.6)   |
| Vomiting: Mild (n = 38, 134, 172)                  | 18.4 (7.7 to 34.3)  | 17.9 (11.8 to 25.5) | 18 (12.6 to 24.6)   |
| Vomiting: Moderate (n = 38, 128, 166)              | 2.6 (0.1 to 13.8)   | 3.9 (1.3 to 8.9)    | 3.6 (1.3 to 7.7)    |
| Vomiting: Severe (n = 37, 128, 165)                | 5.4 (0.7 to 18.2)   | 0 (0 to 2.8)        | 1.2 (0.1 to 4.3)    |
| Diarrhea: Any (n = 44, 145, 189)                   | 31.8 (18.6 to 47.6) | 35.9 (28.1 to 44.2) | 34.9 (28.1 to 42.2) |
| Diarrhea: Mild (n = 44, 142, 186)                  | 31.8 (18.6 to 47.6) | 33.8 (26.1 to 42.2) | 33.3 (26.6 to 40.6) |
| Diarrhea: Moderate (n = 38, 133, 171)              | 5.3 (0.6 to 17.7)   | 9 (4.7 to 15.2)     | 8.2 (4.5 to 13.4)   |
| Diarrhea: Severe (n = 37, 131, 168)                | 0 (0 to 9.5)        | 3.8 (1.3 to 8.7)    | 3 (1 to 6.8)        |
| Muscle Pain: Any (n = 47, 154, 201)                | 55.3 (40.1 to 69.8) | 50 (41.8 to 58.2)   | 51.2 (44.1 to 58.3) |
| Muscle Pain: Mild (n = 43, 148, 191)               | 46.5 (31.2 to 62.3) | 42.6 (34.5 to 51)   | 43.5 (36.3 to 50.8) |
| Muscle Pain: Moderate (n = 44, 139, 183)           | 36.4 (22.4 to 52.2) | 21.6 (15.1 to 29.4) | 25.1 (19 to 32.1)   |
| Muscle Pain: Severe (n = 37, 131, 168)             | 5.4 (0.7 to 18.2)   | 5.3 (2.2 to 10.7)   | 5.4 (2.5 to 9.9)    |
| Joint Pain: Any (n = 38, 143, 181)                 | 26.3 (13.4 to 43.1) | 26.6 (19.5 to 34.6) | 26.5 (20.2 to 33.6) |
| Joint Pain: Mild (n = 37, 139, 176)                | 18.9 (8 to 35.2)    | 19.4 (13.2 to 27)   | 19.3 (13.8 to 25.9) |
| Joint Pain: Moderate (n = 38, 137, 175)            | 15.8 (6 to 31.3)    | 14.6 (9.2 to 21.6)  | 14.9 (9.9 to 21)    |
| Joint Pain: Severe (n = 37, 130, 167)              | 2.7 (0.1 to 14.2)   | 3.1 (0.8 to 7.7)    | 3 (1 to 6.8)        |
| Use of Medication to Treat Pain (n= 40, 136, 176)  | 25 (12.7 to 41.2)   | 13.2 (8 to 20.1)    | 15.9 (10.8 to 22.2) |
| Use of Medication to Treat Fever (n= 41, 133, 174) | 24.4 (12.4 to 40.3) | 14.3 (8.8 to 21.4)  | 16.7 (11.5 to 23.1) |

Notes:

[29] - N signifies subjects with known values for any systemic event.

[30] - N signifies subjects with known values for any systemic event.

[31] - N signifies subjects with known values for any systemic event.

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 2

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 2 |
|-----------------|--|

End point description:

Specific systemic events (fever  $\geq 38$  degrees Celsius [C], fatigue, headache, vomiting, diarrhea, muscle pain, joint pain and use of medication to treat pain/fever) were prompted for each day, and reported using an e-diary. Fatigue, headache, muscle pain and joint pain were scaled as: Any (symptom

present); Mild (did not interfere with activity); Moderate (some interference with activity); Severe (prevented routine daily activity). Vomiting was scaled as: Any (vomiting present); Mild (1-2 times in 24 hours); Moderate (>2 times in 24 hours); Severe (required intravenous hydration). Diarrhea was scaled as: Any (diarrhea present); Mild (2-3 loose stools in 24 hours); Moderate (4-5 loose stools 24 hours); Severe (>=6 loose stools in 24 hours). Safety population. Here, 'n' signifies subjects with known values for specified systemic event. Subjects may be represented in more than 1 category.

|                                    |                     |
|------------------------------------|---------------------|
| End point type                     | Other pre-specified |
| End point timeframe:               |                     |
| Within 14 days after 13vPnC Dose 2 |                     |

| End point values                                | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---|--|--------------------------------------|---------------------------------|--|
| Subject group type                              | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                     | 45 <sup>[32]</sup>                       | 146 <sup>[33]</sup>                  | 191                             |  |
| Units: Percentage of subjects                   |  |                                      |                                 |  |
| number (confidence interval 95%)                |  |                                      |                                 |  |
| Fever: >=38 degrees C (n = 26, 105, 131)        | 23.1 (9 to 43.6)                         | 6.7 (2.7 to 13.3)                    | 27.5 (5.4 to 16.4)              |  |
| Fever: >=38, <38.5 degrees C (n = 26, 105, 131) | 19.2 (6.6 to 39.4)                       | 5.7 (2.1 to 12)                      | 9.7 (4.3 to 14.5)               |  |
| Fever: >=38.5, <39 degrees C (n = 24, 102, 126) | 8.3 (1 to 27)                            | 1 (0 to 5.3)                         | 1.6 (0.5 to 6.8)                |  |
| Fever: >=39, <=40 degrees C (n = 24, 102, 126)  | 8.3 (1 to 27)                            | 1 (0 to 5.3)                         | 45 (0.5 to 6.8)                 |  |
| Fever: >40 degrees C (n = 24, 102, 126)         | 0 (0 to 14.2)                            | 0 (0 to 3.6)                         | 36 (0 to 2.9)                   |  |
| Fatigue: Any (n = 38, 133, 171)                 | 60.5 (43.4 to 76)                        | 56.4 (47.5 to 65)                    | 28 (49.5 to 64.8)               |  |
| Fatigue: Mild (n = 31, 125, 156)                | 45.2 (27.3 to 64)                        | 39.2 (30.6 to 48.3)                  | 6.1 (32.6 to 48.5)              |  |
| Fatigue: Moderate (n = 33, 122, 155)            | 45.5 (28.1 to 63.6)                      | 37.7 (29.1 to 46.9)                  | 25.2 (31.6 to 47.5)             |  |
| Fatigue: Severe (n = 24, 107, 131)              | 12.5 (2.7 to 32.4)                       | 9.3 (4.6 to 16.5)                    | 21.1 (5.4 to 16.4)              |  |
| Headache: Any (n = 31, 121, 152)                | 32.3 (16.7 to 51.4)                      | 35.5 (27 to 44.8)                    | 14.7 (27.3 to 43)               |  |
| Headache: Mild (n = 30, 117, 147)               | 30 (14.7 to 49.4)                        | 29.9 (21.8 to 39.1)                  | 2.3 (22.7 to 38)                |  |
| Headache: Moderate (n = 26, 110, 136)           | 7.7 (0.9 to 25.1)                        | 16.4 (10 to 24.6)                    | 11.3 (9.2 to 21.8)              |  |
| Headache: Severe (n = 24, 104, 128)             | 0 (0 to 14.2)                            | 1.9 (0.2 to 6.8)                     | 14.9 (0.2 to 5.5)               |  |
| Vomiting: Any (n = 28, 107, 135)                | 21.4 (8.3 to 41)                         | 13.1 (7.3 to 21)                     | 9.9 (9.3 to 21.9)               |  |
| Vomiting: Mild (n = 27, 107, 134)               | 18.5 (6.3 to 38.1)                       | 10.3 (5.2 to 17.7)                   | 8.4 (7 to 18.7)                 |  |
| Vomiting: Moderate (n = 28, 103, 131)           | 14.3 (4 to 32.7)                         | 4.9 (1.6 to 11)                      | 2.4 (3.2 to 12.6)               |  |
| Vomiting: Severe (n = 24, 102, 126)             | 0 (0 to 14.2)                            | 1 (0 to 5.3)                         | 2.4 (0 to 4.3)                  |  |
| Diarrhea: Any (n = 29, 121, 150)                | 31 (15.3 to 50.8)                        | 28.9 (21 to 37.9)                    | 0 (22.2 to 37.3)                |  |
| Diarrhea: Mild (n = 29, 120, 149)               | 31 (15.3 to 50.8)                        | 26.7 (19 to 35.5)                    | 57.3 (20.5 to 35.4)             |  |
| Diarrhea: Moderate (n = 25, 109, 134)           | 8 (1 to 26)                              | 10.1 (5.1 to 17.3)                   | 40.4 (5.3 to 16)                |  |

|  |                     |                     |                     |  |
|--|---------------------|---------------------|---------------------|--|
| Diarrhea: Severe (n = 24, 103, 127)                | 0 (0 to 14.2)       | 1.9 (0.2 to 6.8)    | 39.4 (0.2 to 5.6)   |  |
| Muscle Pain: Any (n = 36, 124, 160)                | 44.4 (27.9 to 61.9) | 45.2 (36.2 to 54.3) | 9.9 (37.1 to 53.1)  |  |
| Muscle Pain: Mild (n = 32, 118, 150)               | 31.3 (16.1 to 50)   | 37.3 (28.6 to 46.7) | 34.9 (28.3 to 44.2) |  |
| Muscle Pain: Moderate (n = 32, 111, 143)           | 37.5 (21.1 to 56.3) | 25.2 (17.5 to 34.4) | 29.9 (20.8 to 36.1) |  |
| Muscle Pain: Severe (n = 25, 106, 131)             | 8 (1 to 26)         | 5.7 (2.1 to 11.9)   | 14.7 (2.7 to 11.7)  |  |
| Joint Pain: Any (n = 31, 116, 147)                 | 32.3 (16.7 to 51.4) | 23.3 (15.9 to 32)   | 1.6 (18.4 to 33)    |  |
| Joint Pain: Mild (n = 27, 115, 142)                | 18.5 (6.3 to 38.1)  | 21.7 (14.6 to 30.4) | 14.8 (14.7 to 28.8) |  |
| Joint Pain: Moderate (n = 30, 106, 136)            | 30 (14.7 to 49.4)   | 10.4 (5.3 to 17.8)  | 11.9 (9.2 to 21.8)  |  |
| Joint Pain: Severe (n = 25, 104, 129)              | 4 (0.1 to 20.4)     | 1.9 (0.2 to 6.8)    | 6.9 (0.5 to 6.6)    |  |
| Use of Medication to Treat Pain (n= 28, 105, 133)  | 25 (10.7 to 44.9)   | 7.6 (3.3 to 14.5)   | 0.8 (6.5 to 17.9)   |  |
| Use of Medication to Treat Fever (n= 27, 107, 134) | 33.3 (16.5 to 54)   | 10.3 (5.2 to 17.7)  | 29.3 (9.4 to 22.1)  |  |

Notes:

[32] - N signifies subjects with known values for any systemic event.

[33] - N signifies subjects with known values for any systemic event.

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 3

|                 |  |
|-----------------|--|
| End point title | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 3 |
|-----------------|--|

End point description:

Specific systemic events (fever  $\geq 38$  degrees Celsius [C], fatigue, headache, vomiting, diarrhea, muscle pain, joint pain and use of medication to treat pain/fever) were prompted for each day, and reported using an e-diary. Fatigue, headache, muscle pain and joint pain were scaled as: Any (symptom present); Mild (did not interfere with activity); Moderate (some interference with activity); Severe (prevented routine daily activity). Vomiting was scaled as: Any (vomiting present); Mild (1-2 times in 24 hours); Moderate ( $>2$  times in 24 hours); Severe (required intravenous hydration). Diarrhea was scaled as: Any (diarrhea present); Mild (2-3 loose stools in 24 hours); Moderate (4-5 loose stools 24 hours); Severe ( $\geq 6$  loose stools in 24 hours). Safety population. Here, 'n' signifies subjects with known values for specified systemic event. Subjects may be represented in more than 1 category.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Within 14 days after 13vPnC Dose 3

| End point values                             | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|--|--|--------------------------------------|---------------------------------|--|
| Subject group type                           | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                  | 42 <sup>[34]</sup>                       | 136 <sup>[35]</sup>                  | 178 <sup>[36]</sup>             |  |
| Units: Percentage of subjects                |  |                                      |                                 |  |
| number (confidence interval 95%)             |  |                                      |                                 |  |
| Fever: $\geq 38$ degrees C (n = 27, 93, 120) | 14.8 (0.1 to 21.1)                       | 4.3 (1.2 to 10.6)                    | 6.7 (2.9 to 12.7)               |  |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Fever: $\geq 38$ , $< 38.5$ degrees C (n = 26, 93, 119)  | 11.5 (0.1 to 21.1)  | 3.2 (0.7 to 9.1)    | 5 (1.9 to 10.7)     |
| Fever: $\geq 38.5$ , $< 39$ degrees C (n = 24, 93, 117)  | 4.2 (0 to 14.8)     | 3.2 (0.7 to 9.1)    | 3.4 (0.9 to 8.5)    |
| Fever: $\geq 39$ , $\leq 40$ degrees C (n = 24, 92, 116) | 4.2 (31.4 to 66)    | 1.1 (0 to 5.9)      | 1.7 (0.2 to 6.1)    |
| Fever: $> 40$ degrees C (n = 23, 92, 115)                | 0 (23.7 to 59.4)    | 0 (0 to 3.9)        | 0 (0 to 3.2)        |
| Fatigue: Any (n = 35, 122, 157)                          | 48.6 (17.3 to 52.8) | 49.2 (40 to 58.4)   | 49 (41 to 57.1)     |
| Fatigue: Mild (n = 32, 116, 148)                         | 40.6 (0.1 to 21.1)  | 38.8 (29.9 to 48.3) | 39.2 (31.3 to 47.5) |
| Fatigue: Moderate (n = 30, 107, 137)                     | 33.3 (4.2 to 33.7)  | 29.9 (21.4 to 39.5) | 30.7 (23.1 to 39.1) |
| Fatigue: Severe (n = 24, 96, 120)                        | 4.2 (2.4 to 30.2)   | 7.3 (3 to 14.4)     | 6.7 (2.9 to 12.7)   |
| Headache: Any (n = 32, 110, 142)                         | 37.5 (21.1 to 56.3) | 37.3 (28.2 to 47)   | 37.3 (29.4 to 45.8) |
| Headache: Mild (n = 30, 108, 138)                        | 30 (14.7 to 49.4)   | 32.4 (23.7 to 42.1) | 31.9 (24.2 to 40.4) |
| Headache: Moderate (n = 27, 95, 122)                     | 22.2 (8.6 to 42.3)  | 15.8 (9.1 to 24.7)  | 17.2 (11 to 25.1)   |
| Headache: Severe (n = 25, 94, 119)                       | 8 (1 to 26)         | 2.1 (0.3 to 7.5)    | 3.4 (0.9 to 8.4)    |
| Vomiting: Any (n = 25, 95, 120)                          | 8 (1 to 26)         | 11.6 (5.9 to 19.8)  | 10.8 (5.9 to 17.8)  |
| Vomiting: Mild (n = 24, 95, 119)                         | 4.2 (0.1 to 21.1)   | 5.3 (1.7 to 11.9)   | 5 (1.9 to 10.7)     |
| Vomiting: Moderate (n = 24, 93, 117)                     | 4.2 (0.1 to 21.1)   | 7.5 (3.1 to 14.9)   | 6.8 (3 to 13)       |
| Vomiting: Severe (n = 23, 92, 115)                       | 0 (0 to 14.8)       | 0 (0 to 3.9)        | 0 (0 to 3.2)        |
| Diarrhea: Any (n = 26, 104, 130)                         | 15.4 (4.4 to 34.9)  | 25 (17 to 34.4)     | 23.1 (16.1 to 31.3) |
| Diarrhea: Mild (n = 26, 102, 128)                        | 15.4 (4.4 to 34.9)  | 21.6 (14 to 30.8)   | 20.3 (13.7 to 28.3) |
| Diarrhea: Moderate (n = 24, 95, 119)                     | 4.2 (0.1 to 21.1)   | 5.3 (1.7 to 11.9)   | 5 (1.9 to 10.7)     |
| Diarrhea: Severe (n = 23, 94, 117)                       | 0 (0 to 14.8)       | 2.1 (0.3 to 7.5)    | 1.7 (0.2 to 6)      |
| Muscle Pain: Any (n = 35, 117, 152)                      | 45.7 (28.8 to 63.4) | 38.5 (29.6 to 47.9) | 40.1 (32.3 to 48.4) |
| Muscle Pain: Mild (n = 30, 112, 142)                     | 33.3 (17.3 to 52.8) | 33 (24.4 to 42.6)   | 33.1 (25.4 to 41.5) |
| Muscle Pain: Moderate (n = 31, 101, 132)                 | 32.3 (16.7 to 51.4) | 16.8 (10.1 to 25.6) | 20.5 (13.9 to 28.3) |
| Muscle Pain: Severe (n = 24, 94, 118)                    | 4.2 (0.1 to 21.1)   | 3.2 (0.7 to 9)      | 3.4 (0.9 to 8.5)    |
| Joint Pain: Any (n = 28, 104, 132)                       | 25 (10.7 to 44.9)   | 20.2 (13 to 29.2)   | 21.2 (14.6 to 29.2) |
| Joint Pain: Mild (n = 26, 102, 128)                      | 19.2 (6.6 to 39.4)  | 17.6 (10.8 to 26.4) | 18 (11.7 to 25.7)   |
| Joint Pain: Moderate (n = 27, 95, 122)                   | 18.5 (6.3 to 38.1)  | 8.4 (3.7 to 15.9)   | 10.7 (5.8 to 17.5)  |
| Joint Pain: Severe (n = 25, 94, 119)                     | 8 (1 to 26)         | 2.1 (0.3 to 7.5)    | 3.4 (0.9 to 8.4)    |
| Use of Medication to Treat Pain (n = 28, 97, 125)        | 21.4 (8.3 to 41)    | 12.4 (6.6 to 20.6)  | 14.4 (8.8 to 21.8)  |
| Use of Medication to Treat Fever (n = 30, 101, 131)      | 26.7 (12.3 to 45.9) | 15.8 (9.3 to 24.4)  | 18.3 (12.1 to 26)   |

Notes:

[34] - N signifies subjects with known values for any systemic event.

[35] - N signifies subjects with known values for any systemic event.

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 4

|   |  |
|---|--|
| End point title   | Percentage of Pediatric, Adult and All Subjects Reporting Pre-specified Systemic Events: 13vPnC Dose 4 |
| End point description:  |  |
| Specific systemic events (fever $\geq 38$ degrees Celsius [C], fatigue, headache, vomiting, diarrhea, muscle pain, joint pain and use of medication to treat pain/fever) were prompted for each day, and reported using an e-diary. Fatigue, headache, muscle pain and joint pain were scaled as: Any (symptom present); Mild (did not interfere with activity); Moderate (some interference with activity); Severe (prevented routine daily activity). Vomiting was scaled as: Any (vomiting present); Mild (1-2 times in 24 hours); Moderate ( $>2$ times in 24 hours); Severe (required intravenous hydration). Diarrhea was scaled as: Any (diarrhea present); Mild (2-3 loose stools in 24 hours); Moderate (4-5 loose stools 24 hours); Severe ( $\geq 6$ loose stools in 24 hours). Safety population. Here, 'n' signifies subjects with known values for specified systemic event. Subjects may be represented in more than 1 category. |  |
| End point type  | Other pre-specified  |
| End point timeframe:  |  |
| Within 14 days after 13vPnC Dose 4  |  |

| End point values  | 13vPnC, 23vPS<br>(Pediatric<br>Subjects) | 13vPnC, 23vPS<br>(Adult<br>Subjects) | 13vPnC, 23vPS<br>(All Subjects) |  |
|---|--|--------------------------------------|---------------------------------|--|
| Subject group type                                      | Reporting group                          | Reporting group                      | Subject analysis set            |  |
| Number of subjects analysed                             | 32 <sup>[37]</sup>                       | 116 <sup>[38]</sup>                  | 148 <sup>[39]</sup>             |  |
| Units: Percentage of subjects                           |  |                                      |                                 |  |
| number (confidence interval 95%)                        |  |                                      |                                 |  |
| Fever: $\geq 38$ degrees C (n = 18, 78, 96)             | 27.8 (9.7 to 53.5)                       | 15.4 (8.2 to 25.3)                   | 17.7 (10.7 to 26.8)             |  |
| Fever: $\geq 38$ , $<38.5$ degrees C (n = 16, 76, 92)   | 12.5 (1.6 to 38.3)                       | 13.2 (6.5 to 22.9)                   | 13 (6.9 to 21.7)                |  |
| Fever: $\geq 38.5$ , $<39$ degrees C (n = 17, 73, 90)   | 17.6 (3.8 to 43.4)                       | 2.7 (0.3 to 9.5)                     | 5.6 (1.8 to 12.5)               |  |
| Fever: $\geq 39$ , $\leq 40$ degrees C (n = 15, 72, 87) | 0 (0 to 21.8)                            | 2.8 (0.3 to 9.7)                     | 2.3 (0.3 to 8.1)                |  |
| Fever: $>40$ degrees C (n = 15, 71, 86)                 | 0 (0 to 21.8)                            | 0 (0 to 5.1)                         | 0 (0 to 4.2)                    |  |
| Fatigue: Any (n = 28, 100, 128)                         | 67.9 (47.6 to 84.1)                      | 67 (56.9 to 76.1)                    | 67.2 (58.3 to 75.2)             |  |
| Fatigue: Mild (n = 26, 95, 121)                         | 61.5 (40.6 to 79.8)                      | 54.7 (44.2 to 65)                    | 56.2 (46.9 to 65.2)             |  |
| Fatigue: Moderate (n = 20, 86, 106)                     | 45 (23.1 to 68.5)                        | 45.3 (34.6 to 56.5)                  | 45.3 (35.6 to 55.2)             |  |
| Fatigue: Severe (n = 16, 77, 93)                        | 12.5 (1.6 to 38.3)                       | 13 (6.4 to 22.6)                     | 12.9 (6.8 to 21.5)              |  |
| Headache: Any (n = 21, 93, 114)                         | 52.4 (29.8 to 74.3)                      | 45.2 (34.8 to 55.8)                  | 46.5 (37.1 to 56.1)             |  |

|  |                     |                     |                     |  |
|--|---------------------|---------------------|---------------------|--|
| Headache: Mild (n = 21, 88, 109)                 | 47.6 (25.7 to 70.2) | 38.6 (28.4 to 49.6) | 40.4 (31.1 to 50.2) |  |
| Headache: Moderate (n = 16, 82, 98)              | 18.8 (4 to 45.6)    | 28 (18.7 to 39.1)   | 26.5 (18.1 to 36.4) |  |
| Headache: Severe (n = 16, 74, 90)                | 12.5 (1.6 to 38.3)  | 5.4 (1.5 to 13.3)   | 6.7 (2.5 to 13.9)   |  |
| Vomiting: Any (n = 16, 73, 89)                   | 6.3 (0.2 to 30.2)   | 5.5 (1.5 to 13.4)   | 5.6 (1.8 to 12.6)   |  |
| Vomiting: Mild (n = 16, 73, 89)                  | 6.3 (0.2 to 30.2)   | 5.5 (1.5 to 13.4)   | 5.6 (1.8 to 12.6)   |  |
| Vomiting: Moderate (n = 15, 71, 86)              | 0 (0 to 21.8)       | 0 (0 to 5.1)        | 0 (0 to 4.2)        |  |
| Vomiting: Severe (n = 15, 71, 86)                | 0 (0 to 21.8)       | 0 (0 to 5.1)        | 0 (0 to 4.2)        |  |
| Diarrhea: Any (n = 18, 83, 101)                  | 22.2 (6.4 to 47.6)  | 30.1 (20.5 to 41.2) | 28.7 (20.1 to 38.6) |  |
| Diarrhea: Mild (n = 18, 82, 100)                 | 22.2 (6.4 to 47.6)  | 29.3 (19.7 to 40.4) | 28 (19.5 to 37.9)   |  |
| Diarrhea: Moderate (n = 15, 72, 87)              | 0 (0 to 21.8)       | 4.2 (0.9 to 11.7)   | 3.4 (0.7 to 9.7)    |  |
| Diarrhea: Severe (n = 15, 72, 87)                | 0 (0 to 21.8)       | 1.4 (0 to 7.5)      | 1.1 (0 to 6.2)      |  |
| Muscle Pain: Any (n = 24, 99, 123)               | 58.3 (36.6 to 77.9) | 60.6 (50.3 to 70.3) | 60.2 (50.9 to 68.9) |  |
| Muscle Pain: Mild (n = 22, 92, 114)              | 50 (28.2 to 71.8)   | 50 (39.4 to 60.6)   | 50 (40.5 to 59.5)   |  |
| Muscle Pain: Moderate (n = 19, 80, 99)           | 36.8 (16.3 to 61.6) | 30 (20.3 to 41.3)   | 31.3 (22.4 to 41.4) |  |
| Muscle Pain: Severe (n = 16, 75, 91)             | 12.5 (1.6 to 38.3)  | 6.7 (2.2 to 14.9)   | 7.7 (3.1 to 15.2)   |  |
| Joint Pain: Any (n = 16, 83, 99)                 | 25 (7.3 to 52.4)    | 32.5 (22.6 to 43.7) | 31.3 (22.4 to 41.4) |  |
| Joint Pain: Mild (n = 15, 78, 93)                | 13.3 (1.7 to 40.5)  | 24.4 (15.3 to 35.4) | 22.6 (14.6 to 32.4) |  |
| Joint Pain: Moderate (n = 16, 75, 91)            | 12.5 (1.6 to 38.3)  | 17.3 (9.6 to 27.8)  | 16.5 (9.5 to 25.7)  |  |
| Joint Pain: Severe (n = 16, 74, 90)              | 6.3 (0.2 to 30.2)   | 4.1 (0.8 to 11.4)   | 4.4 (1.2 to 11)     |  |
| Use of Medication to Treat Pain (n= 16, 77, 93)  | 18.8 (4 to 45.6)    | 16.9 (9.3 to 27.1)  | 17.2 (10.2 to 26.4) |  |
| Use of Medication to Treat Fever (n= 17, 77, 94) | 23.5 (6.8 to 49.9)  | 15.6 (8.3 to 25.6)  | 17 (10.1 to 26.2)   |  |

Notes:

[37] - N signifies subjects with known values for any systemic event.

[38] - N signifies subjects with known values for any systemic event.

[39] - N signifies subjects with known values for any systemic event.

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs/SAEs: recorded from 13vPnC Dose 1 to completion of study. Subjects recorded pre-specified AEs in electronic diary: local reactions; systemic events (up to 14 days after 13vPnC vaccination)

Adverse event reporting additional description:

AEs/SAEs were grouped by system organ class and summarized. AEs included AEs collected in electronic diary (local, systemic reactions for dose 1, 2, 3, 4 of 13vPnC; systematic assessment), on case report form at each visit (non systematic assessment). Safety population was analysed. Version was not captured, 0.0 is mentioned for dictionary version.

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 0.0 |
|--------------------|-----|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | 13vPnC Dose 3 Blood Draw to 13vPnC Dose 4 |
|-----------------------|---|

Reporting group description:

All subjects aged 2 years and above who received 4 single 0.5 mL doses of 13vPnC intramuscular injections, 13vPnC Doses 1 to 3 at 1-month intervals and 13vPnC Dose 4 at 6 months after 13vPnC Dose 3, were assessed from blood draw 1 month after 13vPnC Dose 3 to prior to administration of 13vPnC Dose 4.

|                       |   |
|-----------------------|---|
| Reporting group title | 13vPnC Dose 1 to 13vPnC Dose 3 Blood Draw |
|-----------------------|---|

Reporting group description:

All subjects aged 2 years and above who received 3 single 0.5 mL doses of 13vPnC intramuscular injections at 1-month intervals, were assessed from 13vPnC Dose 1 to the blood draw 1 month after 13vPnC Dose 3.

|                       |               |
|-----------------------|---------------|
| Reporting group title | 13vPnC Dose 4 |
|-----------------------|---------------|

Reporting group description:

All subjects aged 2 years and above who received 4 single 0.5 mL doses of 13vPnC intramuscular injections, 13vPnC Doses 1 to 3 at 1-month intervals and 13vPnC Dose 4 at 6 months after 13vPnC Dose 3, were assessed from 13vPnC Dose 4 to the blood draw 1 month after 13vPnC Dose 4.

|                       |            |
|-----------------------|------------|
| Reporting group title | 23vPS Dose |
|-----------------------|------------|

Reporting group description:

All subjects aged 2 years and above who received 4 single 0.5 mL doses of 13vPnC intramuscular injections, 13vPnC Doses 1 to 3 at 1-month intervals and 13vPnC Dose 4 at 6 months after 13vPnC Dose 3, followed by single 0.5 mL dose of 23vPS intramuscular injection at 1 month after 13vPnC Dose 4, were assessed from 23vPS Dose to the blood draw 1 month after 23vPS Dose.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Follow-up |
|-----------------------|-----------|

Reporting group description:

All subjects aged 2 years and above who received 4 single 0.5 mL doses of 13vPnC intramuscular injections, 13vPnC Doses 1 to 3 at 1-month intervals and 13vPnC Dose 4 at 6 months after 13vPnC Dose 3, followed by single 0.5 mL dose of 23vPS intramuscular injection at 1 month after 13vPnC Dose 4, were assessed from blood draw 1 month after 23vPS Dose to 6-month follow-up.

| Serious adverse events                            | 13vPnC Dose 3<br>Blood Draw to<br>13vPnC Dose 4 | 13vPnC Dose 1 to<br>13vPnC Dose 3<br>Blood Draw | 13vPnC Dose 4    |
|---|---|---|------------------|
| Total subjects affected by serious adverse events |   |   |                  |
| subjects affected / exposed                       | 42 / 221 (19.00%)                               | 58 / 247 (23.48%)                               | 11 / 192 (5.73%) |
| number of deaths (all causes)                     | 1   | 11  | 2                |
| number of deaths resulting from adverse events    | 0   | 0   | 0                |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Acute myeloid leukaemia   |                 |                 |                 |
| subjects affected / exposed   | 2 / 221 (0.90%) | 6 / 247 (2.43%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 2           | 0 / 6           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Leukaemia recurrent   |                 |                 |                 |
| subjects affected / exposed   | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Non-Hodgkin's lymphoma  |                 |                 |                 |
| subjects affected / exposed   | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Plasma cell myeloma recurrent                                       |                 |                 |                 |
| subjects affected / exposed   | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Plasmacytoma  |                 |                 |                 |
| subjects affected / exposed   | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Post transplant lymphoproliferative disorder                        |                 |                 |                 |
| subjects affected / exposed   | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Acute lymphocytic leukaemia   |                 |                 |                 |
| subjects affected / exposed   | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 1           | 0 / 0           |
| Acute lymphocytic leukaemia recurrent                               |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Ependymoma                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Mantle cell lymphoma                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Myelodysplastic syndrome                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Refractory anaemia with an excess of blasts     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Chronic myeloid leukaemia                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Juvenile chronic myelomonocytic leukaemia       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Leukaemia                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Acute myeloid leukaemia recurrent               |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 4 / 221 (1.81%) | 6 / 247 (2.43%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all      | 0 / 4           | 0 / 6           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                                   |                 |                 |                 |
| Hypovolaemic shock                                   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           | 0 / 0           |
| Hypotension  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| General disorders and administration site conditions |                 |                 |                 |
| Pyrexia  |                 |                 |                 |
| subjects affected / exposed                          | 4 / 221 (1.81%) | 6 / 247 (2.43%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 4           | 1 / 8           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Injection site erythema                              |                 |                 |                 |
| subjects affected / exposed                          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Oedema peripheral                                    |                 |                 |                 |
| subjects affected / exposed                          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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 physical health deterioration                |                 |                 |                 |
| subjects affected / exposed                          | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Death  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 1           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Systemic inflammatory response syndrome         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Immune system disorders                         |                 |                 |                 |
| Graft versus host disease                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 5 / 247 (2.02%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 5           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 2           | 0 / 0           |
| Graft versus host disease in intestine          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (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           |
| Chronic graft versus host disease               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Graft versus host disease in liver              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Graft versus host disease in skin               |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders        |                 |                 |                 |
| Benign prostatic hyperplasia                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Epididymitis                                    |                 |                 |                 |

|   |  |                 |                 |
|---|--|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 221 (0.00%)  | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |  |                 |                 |
| Uncoded   | Additional description: Term was not coded because it violated sponsor's coding conventions. |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%)  | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1  | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0           |
| Acute respiratory distress syndrome             |  |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%)  | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1           | 0 / 0           |
| Oropharyngeal pain                              |  |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%)  | 1 / 247 (0.40%) | 0 / 192 (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           |
| Organising pneumonia                            |  |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%)  | 0 / 247 (0.00%) | 0 / 192 (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           |
| Dyspnoea  |  |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%)  | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0           |
| Respiratory failure                             |  |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%)  | 0 / 247 (0.00%) | 0 / 192 (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           |
| Psychiatric disorders                           |  |                 |                 |
| Alcohol abuse                                   |  |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%)  | 0 / 247 (0.00%) | 0 / 192 (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           |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Completed suicide<br>subjects affected / exposed                   | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 1           | 0 / 0           | 0 / 0           |
| Investigations   |                 |                 |                 |
| Cytomegalovirus test positive<br>subjects affected / exposed       | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| False positive investigation result<br>subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural<br>complications                  |                 |                 |                 |
| Spinal fracture<br>subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tibia fracture<br>subjects affected / exposed                      | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sternal fracture<br>subjects affected / exposed                    | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders  |                 |                 |                 |
| Pericarditis<br>subjects affected / exposed                        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac failure acute  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| <b>Nervous system disorders</b>                 |                 |                 |                 |
| VIIth nerve paralysis                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Guillain-Barre syndrome                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Transient ischaemic attack                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Headache  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Blood and lymphatic system disorders</b>     |                 |                 |                 |
| Haemolytic anaemia                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Thrombocytopenia                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Anaemia haemolytic autoimmune                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pancytopenia                                    |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Febrile neutropenia                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Leukopenia                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Lymphadenitis                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Warm type haemolytic anaemia                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Pancreatitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Hernial eventration                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Pancreatitis acute                              |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Gastrointestinal haemorrhage                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Cholelithiasis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Hepatocellular injury                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Renal and urinary disorders                     |                 |                 |                 |
| Renal failure                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal failure acute                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Haematuria                                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Nephrotic syndrome                              |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Musculoskeletal and connective tissue           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| disorders                                       |                 |                 |                 |
| Musculoskeletal stiffness                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Osteonecrosis                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Escherichia sepsis                              |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 2 / 247 (0.81%) | 0 / 192 (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           |
| Herpes zoster                                   |                 |                 |                 |
| subjects affected / exposed                     | 4 / 221 (1.81%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory tract infection                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Septic shock                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Bacterial sepsis                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Bronchopulmonary aspergillosis                  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebral toxoplasmosis                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| Ear infection                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Enterocolitis viral                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Gingivitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Infection                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Influenza                                       |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Klebsiella sepsis                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Molluscum contagiosum                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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 haemophilus                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Post procedural infection                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory syncytial virus infection           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Sepsis  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Sinusitis                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Staphylococcal infection                        |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Cellulitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Cytomegalovirus infection                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Haemophilus sepsis                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Hepatic candidiasis                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Hepatitis B                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Herpes virus infection                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Herpes zoster disseminated                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Meningitis                                      |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Nasopharyngitis                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Oral herpes                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Pneumonia pneumococcal                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Pneumonia pseudomonas aeruginosa                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Urinary tract infection                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Viral upper respiratory tract infection         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| H1N1 influenza                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Staphylococcal sepsis                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Streptococcal sepsis                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Device related infection                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Thrombophlebitis septic                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Varicella                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Urinary tract infection bacterial               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Bacterial infection                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Bronchiolitis                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Oral candidiasis                                |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Pseudomonal sepsis                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Metabolism and nutrition disorders              |                 |                 |                 |
| Decreased appetite                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Diabetes mellitus                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (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           |
| Hypernatraemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (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           |
| Hyperglycaemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (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           |

| <b>Serious adverse events</b>                                       | 23vPS Dose       | Follow-up         |  |
|---|------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                  |                   |  |
| subjects affected / exposed   | 11 / 184 (5.98%) | 28 / 247 (11.34%) |  |
| number of deaths (all causes)                                       | 0                | 0                 |  |
| number of deaths resulting from adverse events                      | 0                | 0                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                   |  |
| Acute myeloid leukaemia   |                  |                   |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Leukaemia recurrent                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Non-Hodgkin's lymphoma                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Plasma cell myeloma recurrent                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Plasmacytoma                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Post transplant lymphoproliferative disorder    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute lymphocytic leukaemia                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute lymphocytic leukaemia recurrent           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ependymoma                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mantle cell lymphoma                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myelodysplastic syndrome                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Refractory anaemia with an excess of blasts     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Chronic myeloid leukaemia                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Juvenile chronic myelomonocytic leukaemia       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Leukaemia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute myeloid leukaemia recurrent               |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 3 / 247 (1.21%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vascular disorders                              |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| Hypovolaemic shock                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Hypotension  |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 4 / 247 (1.62%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 5           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Injection site erythema                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Oedema peripheral                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General physical health deterioration                |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Death  |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Systemic inflammatory response syndrome              |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|   |  |                 |  |
|---|--|-----------------|--|
| Immune system disorders                         |  |                 |  |
| Graft versus host disease                       |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 2 / 247 (0.81%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Graft versus host disease in intestine          |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Chronic graft versus host disease               |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Graft versus host disease in liver              |  |                 |  |
| subjects affected / exposed                     | 2 / 184 (1.09%)  | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Graft versus host disease in skin               |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Reproductive system and breast disorders        |  |                 |  |
| Benign prostatic hyperplasia                    |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Epididymitis                                    |  |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |  |                 |  |
| Uncoded   | Additional description: Term was not coded because it violated sponsor's coding conventions. |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute respiratory distress syndrome             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oropharyngeal pain                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Organising pneumonia                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory failure                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Alcohol abuse                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Completed suicide                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Investigations                                  |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| Cytomegalovirus test positive<br>subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| False positive investigation result<br>subjects affected / exposed | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural<br>complications                  |                 |                 |  |
| Spinal fracture  |                 |                 |  |
| subjects affected / exposed  | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Tibia fracture   |                 |                 |  |
| subjects affected / exposed  | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Sternal fracture   |                 |                 |  |
| subjects affected / exposed  | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders  |                 |                 |  |
| Pericarditis   |                 |                 |  |
| subjects affected / exposed  | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Cardiac failure acute  |                 |                 |  |
| subjects affected / exposed  | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders   |                 |                 |  |
| VIIth nerve paralysis  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Guillain-Barre syndrome                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Transient ischaemic attack                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Headache  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Haemolytic anaemia                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombocytopenia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Anaemia haemolytic autoimmune                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancytopenia                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Febrile neutropenia                             |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 2 / 247 (0.81%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Leukopenia                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphadenitis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Warm type haemolytic anaemia                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Diarrhoea                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hernial eventration                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis acute                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal haemorrhage                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Cholelithiasis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatocellular injury                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal failure                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal failure acute                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haematuria                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nephrotic syndrome                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Musculoskeletal stiffness                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Osteonecrosis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Escherichia sepsis                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Herpes zoster                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 2 / 247 (0.81%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 4 / 247 (1.62%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 5           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory tract infection                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Septic shock                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Appendicitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bacterial sepsis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchopulmonary aspergillosis                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cerebral toxoplasmosis                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ear infection                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Enterocolitis viral                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gingivitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infection                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Influenza                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Klebsiella sepsis                               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Molluscum contagiosum                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia haemophilus                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Post procedural infection                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus infection           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sinusitis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Staphylococcal infection                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cytomegalovirus infection                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haemophilus sepsis                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatic candidiasis                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatitis B                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Herpes virus infection                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Herpes zoster disseminated                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nasopharyngitis                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oral herpes                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia pneumococcal                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia pseudomonas aeruginosa                |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Viral upper respiratory tract infection         |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| H1N1 influenza                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Staphylococcal sepsis                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Streptococcal sepsis                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Device related infection                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombophlebitis septic                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Varicella                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection bacterial               |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bacterial infection                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oral candidiasis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pseudomonal sepsis                              |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Metabolism and nutrition disorders</b>       |                 |                 |  |
| Decreased appetite                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Diabetes mellitus</b>                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Hypernatraemia</b>                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Hyperglycaemia</b>                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>  | 13vPnC Dose 3<br>Blood Draw to<br>13vPnC Dose 4 | 13vPnC Dose 1 to<br>13vPnC Dose 3<br>Blood Draw | 13vPnC Dose 4      |
|--|---|---|--------------------|
| <b>Total subjects affected by non-serious adverse events</b>               |   |   |                    |
| subjects affected / exposed  | 89 / 221 (40.27%)                               | 203 / 247 (82.19%)                              | 127 / 192 (66.15%) |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |   |   |                    |
| Plasmacytoma   |   |   |                    |
| subjects affected / exposed  | 0 / 221 (0.00%)                                 | 1 / 247 (0.40%)                                 | 0 / 192 (0.00%)    |
| occurrences (all)  | 0   | 1   | 0                  |
| Precursor B-lymphoblastic lymphoma   |   |   |                    |
| subjects affected / exposed  | 0 / 221 (0.00%)                                 | 1 / 247 (0.40%)                                 | 0 / 192 (0.00%)    |
| occurrences (all)  | 0   | 1   | 0                  |
| Acute leukaemia  |   |   |                    |

|                                   |                 |                 |                 |
|-----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed       | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Acute myeloid leukaemia recurrent |                 |                 |                 |
| subjects affected / exposed       | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Kaposi's sarcoma                  |                 |                 |                 |
| subjects affected / exposed       | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Anogenital warts                  |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)                 | 0               | 0               | 1               |
| Vascular disorders                |                 |                 |                 |
| Hypertension                      |                 |                 |                 |
| subjects affected / exposed       | 1 / 221 (0.45%) | 7 / 247 (2.83%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 1               | 7               | 0               |
| Hypotension                       |                 |                 |                 |
| subjects affected / exposed       | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                 | 1               | 2               | 1               |
| Orthostatic hypotension           |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 2               | 0               |
| Thrombophlebitis                  |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 2               | 0               |
| Flushing                          |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Hypovolaemic shock                |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Vasodilatation                    |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Venous insufficiency              |                 |                 |                 |
| subjects affected / exposed       | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |

|   |                      |                        |                      |
|---|----------------------|------------------------|----------------------|
| Venous thrombosis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1   | 0 / 192 (0.00%)<br>0 |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)               | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| Vena cava thrombosis<br>subjects affected / exposed<br>occurrences (all)    | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| General disorders and administration<br>site conditions                     |                      |                        |                      |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 221 (1.36%)<br>4 | 15 / 247 (6.07%)<br>17 | 3 / 192 (1.56%)<br>3 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                 | 5 / 221 (2.26%)<br>5 | 16 / 247 (6.48%)<br>17 | 3 / 192 (1.56%)<br>3 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)       | 6 / 221 (2.71%)<br>6 | 12 / 247 (4.86%)<br>12 | 0 / 192 (0.00%)<br>0 |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 2 / 221 (0.90%)<br>2 | 10 / 247 (4.05%)<br>10 | 1 / 192 (0.52%)<br>1 |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 4 / 247 (1.62%)<br>4   | 3 / 192 (1.56%)<br>4 |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 3 / 247 (1.21%)<br>3   | 4 / 192 (2.08%)<br>5 |
| Oedema<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 221 (0.00%)<br>0 | 3 / 247 (1.21%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Chest pain  |                      |                        |                      |

|                                    |                 |                 |                 |
|------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed        | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                  | 0               | 2               | 1               |
| Catheter site rash                 |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Chest discomfort                   |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Complication of device removal     |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Feeling cold                       |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                  | 0               | 1               | 1               |
| Feeling hot                        |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Gait disturbance                   |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Influenza like illness             |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                  | 1               | 1               | 1               |
| Injection site movement impairment |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Injection site pain                |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 5 / 192 (2.60%) |
| occurrences (all)                  | 0               | 1               | 5               |
| Medical device complication        |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Pain                               |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 1               | 1               | 0               |
| Vaccination site haematoma         |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 1               | 1               |
| Vaccination site pain       |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Vaccination site reaction   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Inflammation                |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Spinal pain                 |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Chills                      |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Injection site pruritus     |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Injection site reaction     |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Mucosal inflammation        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Vaccination site erythema   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Vaccination site swelling   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Injection site induration   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Injection site inflammation |                 |                 |                 |

|   |  |                   |                  |
|---|--|-------------------|------------------|
| subjects affected / exposed                           | 0 / 221 (0.00%)  | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)                                     | 0  | 0                 | 0                |
| Vaccination site oedema                               |  |                   |                  |
| subjects affected / exposed                           | 0 / 221 (0.00%)  | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)                                     | 0  | 0                 | 0                |
| Vaccination site rash                                 |  |                   |                  |
| subjects affected / exposed                           | 0 / 221 (0.00%)  | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)                                     | 0  | 0                 | 0                |
| Hernia  |  |                   |                  |
| subjects affected / exposed                           | 0 / 221 (0.00%)  | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)                                     | 0  | 0                 | 0                |
| Fever >=38 degrees C: 13vPnC Dose 1 and Dose 4        | Additional description: Subjects affected and occurrences for LR and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic               |  |                   |                  |
| subjects affected / exposed <sup>[1]</sup>            | 0 / 221 (0.00%)  | 13 / 169 (7.69%)  | 17 / 96 (17.71%) |
| occurrences (all)                                     | 0  | 13                | 17               |
| Fever >=38, <38.5 degrees C: 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LR and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic               |  |                   |                  |
| subjects affected / exposed <sup>[2]</sup>            | 0 / 221 (0.00%)  | 10 / 167 (5.99%)  | 12 / 92 (13.04%) |
| occurrences (all)                                     | 0  | 10                | 12               |
| Fever >=38.5, <39 degrees C: 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LR and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic               |  |                   |                  |
| subjects affected / exposed <sup>[3]</sup>            | 0 / 221 (0.00%)  | 2 / 165 (1.21%)   | 5 / 90 (5.56%)   |
| occurrences (all)                                     | 0  | 2                 | 5                |
| Fever >=39, <=40 degrees C: 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LR and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic               |  |                   |                  |
| subjects affected / exposed <sup>[4]</sup>            | 0 / 221 (0.00%)  | 3 / 167 (1.80%)   | 2 / 87 (2.30%)   |
| occurrences (all)                                     | 0  | 3                 | 2                |
| Fatigue (Any): 13vPnC Dose 3                          | Additional description: Subjects affected and occurrences for LR and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic               |  |                   |                  |
| subjects affected / exposed <sup>[5]</sup>            | 0 / 221 (0.00%)  | 77 / 157 (49.04%) | 0 / 192 (0.00%)  |
| occurrences (all)                                     | 0  | 77                | 0                |
| Fatigue (Moderate): 13vPnC Dose 3                     | Additional description: Subjects affected and occurrences for LR and SEs is  |                   |                  |

|  |   |                   |                 |
|--|---|-------------------|-----------------|
| same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |   |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[6]</sup>   | 0 / 221 (0.00%)   | 42 / 137 (30.66%) | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 42                | 0               |
| Fatigue (Severe): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[7]</sup>   | 0 / 221 (0.00%)   | 8 / 120 (6.67%)   | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 8                 | 0               |
| Headache (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[8]</sup>   | 0 / 221 (0.00%)   | 53 / 142 (37.32%) | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 53                | 0               |
| Headache (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[9]</sup>   | 0 / 221 (0.00%)   | 44 / 138 (31.88%) | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 44                | 0               |
| Headache (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[10]</sup>  | 0 / 221 (0.00%)   | 21 / 122 (17.21%) | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 21                | 0               |
| Headache (Severe): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[11]</sup>  | 0 / 221 (0.00%)   | 4 / 119 (3.36%)   | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 4                 | 0               |
| Vomiting (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |
| subjects affected / exposed <sup>[12]</sup>  | 0 / 221 (0.00%)   | 13 / 120 (10.83%) | 0 / 192 (0.00%) |
| occurrences (all)  | 0   | 13                | 0               |
| Vomiting (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic   |   |                   |                 |

|  |   |                         |                      |
|--|---|-------------------------|----------------------|
| subjects affected / exposed <sup>[13]</sup><br>occurrences (all)   | 0 / 221 (0.00%)<br>0  | 6 / 119 (5.04%)<br>6    | 0 / 192 (0.00%)<br>0 |
| Vomiting (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[14]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 8 / 117 (6.84%)<br>8    | 0 / 192 (0.00%)<br>0 |
| Diarrhea (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[15]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 30 / 130 (23.08%)<br>30 | 0 / 192 (0.00%)<br>0 |
| Diarrhea (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[16]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 26 / 128 (20.31%)<br>26 | 0 / 192 (0.00%)<br>0 |
| Diarrhea (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[17]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 6 / 119 (5.04%)<br>6    | 0 / 192 (0.00%)<br>0 |
| Diarrhea (Severe): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[18]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 2 / 117 (1.71%)<br>2    | 0 / 192 (0.00%)<br>0 |
| Muscle pain (Any): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[19]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 61 / 152 (40.13%)<br>61 | 0 / 192 (0.00%)<br>0 |
| Muscle pain (Mild): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[20]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 47 / 142 (33.10%)<br>47 | 0 / 192 (0.00%)<br>0 |



|   |   |                         |                      |
|---|---|-------------------------|----------------------|
| Muscle pain (Moderate): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[21]</sup><br><br>occurrences (all) | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 27 / 132 (20.45%)<br>27 | 0 / 192 (0.00%)<br>0 |
| Muscle pain (Severe): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[22]</sup><br><br>occurrences (all)   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 4 / 118 (3.39%)<br>4    | 0 / 192 (0.00%)<br>0 |
| Joint pain (Any): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[23]</sup><br><br>occurrences (all)       | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 28 / 132 (21.21%)<br>28 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Mild): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[24]</sup><br><br>occurrences (all)      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 23 / 128 (17.97%)<br>23 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Moderate): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[25]</sup><br><br>occurrences (all)  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 13 / 122 (10.66%)<br>13 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Severe): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[26]</sup><br><br>occurrences (all)    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 4 / 119 (3.36%)<br>4    | 0 / 192 (0.00%)<br>0 |
| Fever >=38 degrees C: 13vPnC Dose 2<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[27]</sup><br><br>occurrences (all)   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 13 / 131 (9.92%)<br>13  | 0 / 192 (0.00%)<br>0 |
| Fever >=38, <38.5 degrees C: 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |

|  |   |                        |                      |
|--|---|------------------------|----------------------|
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[28]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 11 / 131 (8.40%)<br>11 | 0 / 192 (0.00%)<br>0 |
| Fever >=38.5, <39 degrees C:<br>13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[29]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 3 / 126 (2.38%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Fever >=39, <=40 degrees C:<br>13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[30]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 3 / 126 (2.38%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Fever >=38 degrees C: 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[31]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 8 / 120 (6.67%)<br>8   | 0 / 192 (0.00%)<br>0 |
| Fever >=38, <38.5 degrees C:<br>13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[32]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 6 / 119 (5.04%)<br>6   | 0 / 192 (0.00%)<br>0 |
| Fever >=38.5, <39 degrees C:<br>13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[33]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 4 / 117 (3.42%)<br>4   | 0 / 192 (0.00%)<br>0 |
| Fever >=39, <=40 degrees C:<br>13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[34]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0  | 2 / 116 (1.72%)<br>2   | 0 / 192 (0.00%)<br>0 |
| Fatigue (Any): 13vPnC Dose 1 and<br>Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                        |                      |
| alternative assessment type:<br>Systematic   |   |                        |                      |

|  |   |                    |                   |
|--|---|--------------------|-------------------|
| subjects affected / exposed <sup>[35]</sup>  | 0 / 221 (0.00%)   | 119 / 204 (58.33%) | 86 / 128 (67.19%) |
| occurrences (all)                            | 0   | 119                | 86                |
| Fatigue (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[36]</sup>  | 0 / 221 (0.00%)   | 88 / 190 (46.32%)  | 68 / 121 (56.20%) |
| occurrences (all)                            | 0   | 88                 | 68                |
| Fatigue (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[37]</sup>  | 0 / 221 (0.00%)   | 69 / 192 (35.94%)  | 48 / 106 (45.28%) |
| occurrences (all)                            | 0   | 69                 | 48                |
| Fatigue (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[38]</sup>  | 0 / 221 (0.00%)   | 20 / 173 (11.56%)  | 12 / 93 (12.90%)  |
| occurrences (all)                            | 0   | 20                 | 12                |
| Fatigue (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[39]</sup>  | 0 / 221 (0.00%)   | 91 / 171 (53.22%)  | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 91                 | 0                 |
| Fatigue (Mild): 13vPnC Dose 2                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[40]</sup>  | 0 / 221 (0.00%)   | 63 / 156 (40.38%)  | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 63                 | 0                 |
| Fatigue (Moderate): 13vPnC Dose 2            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[41]</sup>  | 0 / 221 (0.00%)   | 61 / 155 (39.35%)  | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 61                 | 0                 |
| Fatigue (Severe): 13vPnC Dose 2              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
| alternative assessment type:<br>Systematic   |   |                    |                   |
| subjects affected / exposed <sup>[42]</sup>  | 0 / 221 (0.00%)   | 13 / 131 (9.92%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 13                 | 0                 |

|   |   |                             |                             |
|---|---|-----------------------------|-----------------------------|
| Headache (Any): 13vPnC Dose 1 and Dose 4<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[43]</sup><br><br>occurrences (all)      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 84 / 189 (44.44%)<br><br>84 | 53 / 114 (46.49%)<br><br>53 |
| Headache (Mild): 13vPnC Dose 1 and Dose 4<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[44]</sup><br><br>occurrences (all)     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 71 / 186 (38.17%)<br><br>71 | 44 / 109 (40.37%)<br><br>44 |
| Headache (Moderate): 13vPnC Dose 1 and Dose 4<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[45]</sup><br><br>occurrences (all) | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 31 / 174 (17.82%)<br><br>31 | 26 / 98 (26.53%)<br><br>26  |
| Headache (Severe): 13vPnC Dose 1 and Dose 4<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[46]</sup><br><br>occurrences (all)   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 6 / 167 (3.59%)<br><br>4    | 6 / 90 (6.67%)<br><br>6     |
| Headache (Any): 13vPnC Dose 2<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[47]</sup><br><br>occurrences (all)                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 53 / 152 (34.87%)<br><br>53 | 0 / 192 (0.00%)<br><br>0    |
| Headache (Mild): 13vPnC Dose 2<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[48]</sup><br><br>occurrences (all)                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 44 / 147 (29.93%)<br><br>44 | 0 / 192 (0.00%)<br><br>0    |
| Headache (Moderate): 13vPnC Dose 2<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[49]</sup><br><br>occurrences (all)            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |
|   | 0 / 221 (0.00%)<br><br>0  | 20 / 136 (14.71%)<br><br>0  | 0 / 192 (0.00%)<br><br>0    |
| Headache (Severe): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                             |                             |

|   |  |                   |                 |
|---|--|-------------------|-----------------|
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[50]</sup>   | 0 / 221 (0.00%)  | 2 / 128 (1.56%)   | 0 / 192 (0.00%) |
| occurrences (all)                             | 0  | 2                 | 0               |
| Vomiting (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[51]</sup>   | 0 / 221 (0.00%)  | 36 / 173 (20.81%) | 5 / 89 (5.62%)  |
| occurrences (all)                             | 0  | 36                | 5               |
| Vomiting (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[52]</sup>   | 0 / 221 (0.00%)  | 31 / 172 (18.02%) | 5 / 89 (5.62%)  |
| occurrences (all)                             | 0  | 31                | 5               |
| Vomiting (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[53]</sup>   | 0 / 221 (0.00%)  | 6 / 166 (3.61%)   | 0 / 86 (0.00%)  |
| occurrences (all)                             | 0  | 6                 | 0               |
| Vomiting (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[54]</sup>   | 0 / 221 (0.00%)  | 2 / 165 (1.21%)   | 0 / 86 (0.00%)  |
| occurrences (all)                             | 0  | 2                 | 0               |
| Vomiting (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[55]</sup>   | 0 / 221 (0.00%)  | 20 / 135 (14.81%) | 0 / 192 (0.00%) |
| occurrences (all)                             | 0  | 20                | 0               |
| Vomiting (Mild): 13vPnC Dose 2                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |
| subjects affected / exposed <sup>[56]</sup>   | 0 / 221 (0.00%)  | 16 / 134 (11.94%) | 0 / 192 (0.00%) |
| occurrences (all)                             | 0  | 16                | 0               |
| Vomiting (Moderate): 13vPnC Dose 2            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                 |
| alternative assessment type:<br>Systematic    |  |                   |                 |

|  |  |                         |                         |
|--|--|-------------------------|-------------------------|
| subjects affected / exposed <sup>[57]</sup><br>occurrences (all)   | 0 / 221 (0.00%)<br>0   | 9 / 131 (6.87%)<br>9    | 0 / 192 (0.00%)<br>0    |
| Vomiting (Severe): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[58]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 1 / 126 (0.79%)<br>1    | 0 / 192 (0.00%)<br>0    |
| Diarrhea (Any): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[59]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 66 / 189 (34.92%)<br>66 | 29 / 101 (28.71%)<br>29 |
| Diarrhea (Mild): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[60]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 62 / 186 (33.33%)<br>62 | 28 / 100 (28.00%)<br>28 |
| Diarrhea (Moderate): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[61]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 14 / 171 (8.19%)<br>14  | 3 / 87 (3.45%)<br>3     |
| Diarrhea (Severe): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[62]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 5 / 168 (2.98%)<br>5    | 1 / 87 (1.15%)<br>1     |
| Diarrhea (Any): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[63]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 44 / 150 (29.33%)<br>44 | 0 / 192 (0.00%)<br>0    |
| Diarrhea (Mild): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                         |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[64]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 41 / 149 (27.52%)<br>41 | 0 / 192 (0.00%)<br>0    |

|  |  |                    |                   |
|--|--|--------------------|-------------------|
| Diarrhea (Moderate): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[65]</sup>      | 0 / 221 (0.00%)  | 13 / 134 (9.70%)   | 0 / 192 (0.00%)   |
| occurrences (all)                                | 0  | 13                 | 0                 |
| Diarrhea (Severe): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[66]</sup>      | 0 / 221 (0.00%)  | 2 / 127 (1.57%)    | 0 / 192 (0.00%)   |
| occurrences (all)                                | 0  | 2                  | 0                 |
| Muscle pain (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[67]</sup>      | 0 / 221 (0.00%)  | 103 / 201 (51.24%) | 74 / 123 (60.16%) |
| occurrences (all)                                | 0  | 103                | 74                |
| Muscle pain (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[68]</sup>      | 0 / 221 (0.00%)  | 83 / 191 (43.46%)  | 57 / 114 (50.00%) |
| occurrences (all)                                | 0  | 83                 | 57                |
| Muscle pain (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[69]</sup>      | 0 / 221 (0.00%)  | 46 / 183 (25.14%)  | 31 / 99 (31.31%)  |
| occurrences (all)                                | 0  | 46                 | 31                |
| Muscle pain (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[70]</sup>      | 0 / 221 (0.00%)  | 9 / 168 (5.36%)    | 7 / 91 (7.69%)    |
| occurrences (all)                                | 0  | 9                  | 7                 |
| Muscle pain (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:<br>Systematic   |                    |                   |
| subjects affected / exposed <sup>[71]</sup>      | 0 / 221 (0.00%)  | 72 / 160 (45.00%)  | 0 / 192 (0.00%)   |
| occurrences (all)                                | 0  | 72                 | 0                 |
| Muscle pain (Mild): 13vPnC Dose 2                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                   |
|  | alternative assessment type:   |                    |                   |

|   |  |                   |                  |
|---|--|-------------------|------------------|
| Systematic                                      |  |                   |                  |
| subjects affected / exposed <sup>[72]</sup>     | 0 / 221 (0.00%)  | 54 / 150 (36.00%) | 0 / 192 (0.00%)  |
| occurrences (all)                               | 0  | 54                | 0                |
| Muscle pain (Moderate): 13vPnC Dose 2           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[73]</sup>     | 0 / 221 (0.00%)  | 40 / 143 (27.97%) | 0 / 192 (0.00%)  |
| occurrences (all)                               | 0  | 40                | 0                |
| Muscle pain (Severe): 13vPnC Dose 2             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[74]</sup>     | 0 / 221 (0.00%)  | 8 / 131 (6.11%)   | 0 / 192 (0.00%)  |
| occurrences (all)                               | 0  | 8                 | 0                |
| Joint pain (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[75]</sup>     | 0 / 221 (0.00%)  | 34 / 176 (19.32%) | 21 / 93 (22.58%) |
| occurrences (all)                               | 0  | 34                | 21               |
| Joint pain (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[76]</sup>     | 0 / 221 (0.00%)  | 34 / 176 (19.32%) | 21 / 93 (22.58%) |
| occurrences (all)                               | 0  | 34                | 21               |
| Joint pain (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[77]</sup>     | 0 / 221 (0.00%)  | 24 / 175 (13.71%) | 15 / 91 (16.48%) |
| occurrences (all)                               | 0  | 24                | 15               |
| Joint pain (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |
| subjects affected / exposed <sup>[78]</sup>     | 0 / 221 (0.00%)  | 5 / 167 (2.99%)   | 4 / 90 (4.44%)   |
| occurrences (all)                               | 0  | 5                 | 4                |
| Joint pain (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                  |
| alternative assessment type: Systematic         |  |                   |                  |



|  |  |                         |                      |
|--|--|-------------------------|----------------------|
| subjects affected / exposed <sup>[79]</sup><br>occurrences (all)   | 0 / 221 (0.00%)<br>0   | 37 / 147 (25.17%)<br>37 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Mild): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[80]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 30 / 142 (21.13%)<br>30 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Moderate): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[81]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 20 / 136 (14.71%)<br>20 | 0 / 192 (0.00%)<br>0 |
| Joint pain (Severe): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[82]</sup><br>occurrences (all) | 0 / 221 (0.00%)<br>0   | 3 / 129 (2.33%)<br>3    | 0 / 192 (0.00%)<br>0 |
| Immune system disorders  |  |                         |                      |
| Graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                                  | 8 / 221 (3.62%)<br>9   | 21 / 247 (8.50%)<br>24  | 2 / 192 (1.04%)<br>2 |
| Chronic graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 221 (1.36%)<br>3   | 12 / 247 (4.86%)<br>14  | 0 / 192 (0.00%)<br>0 |
| Graft versus host disease in liver<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 221 (0.45%)<br>1   | 5 / 247 (2.02%)<br>7    | 0 / 192 (0.00%)<br>0 |
| Graft versus host disease in skin<br>subjects affected / exposed<br>occurrences (all)                          | 6 / 221 (2.71%)<br>7   | 4 / 247 (1.62%)<br>4    | 0 / 192 (0.00%)<br>0 |
| Food allergy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0   | 2 / 247 (0.81%)<br>3    | 1 / 192 (0.52%)<br>1 |
| Hypogammaglobulinaemia<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 221 (0.00%)<br>0   | 2 / 247 (0.81%)<br>2    | 0 / 192 (0.00%)<br>0 |
| Acute graft versus host disease  |  |                         |                      |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 1               | 1               | 0               |
| Chronic graft versus host disease in liver      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Graft versus host disease in intestine          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Hypersensitivity                                |                 |                 |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 2               | 0               | 0               |
| Reproductive system and breast disorders        |                 |                 |                 |
| Erectile dysfunction                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Gynaecomastia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Vulvovaginal discomfort                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Vulvovaginal dryness                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Prostatitis                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 2               | 0               | 0               |
| Genital discharge                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Amenorrhoea                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |

|                             |                 |                  |                 |
|-----------------------------|-----------------|------------------|-----------------|
| Cough                       |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 24 / 247 (9.72%) | 4 / 192 (2.08%) |
| occurrences (all)           | 2               | 24               | 4               |
| Dyspnoea exertional         |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 4 / 247 (1.62%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 1               | 4                | 1               |
| Rhinorrhoea                 |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 4 / 247 (1.62%)  | 2 / 192 (1.04%) |
| occurrences (all)           | 1               | 4                | 2               |
| Lung disorder               |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 1                | 0               |
| Lung infiltration           |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Oropharyngeal plaque        |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Productive cough            |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Pulmonary mass              |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 1                | 0               |
| Dyspnoea                    |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 2               | 0                | 0               |
| Hyperventilation            |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0                | 0               |
| Nasal congestion            |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0                | 0               |
| Organising pneumonia        |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0                | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Oropharyngeal pain          |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 8 / 247 (3.24%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 8               | 0               |
| Pneumonitis                 |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Rhonchi                     |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Sputum discoloured          |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Epistaxis                   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Pleural effusion            |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Laryngeal oedema            |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Psychiatric disorders       |                 |                 |                 |
| Anxiety                     |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 5 / 247 (2.02%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 6               | 0               |
| Insomnia                    |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 4 / 247 (1.62%) | 1 / 192 (0.52%) |
| occurrences (all)           | 1               | 5               | 1               |
| Sleep disorder              |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 2               | 1               |
| Confusional state           |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Nervousness                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Stress                                      |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Depression                                  |                 |                 |                 |
| subjects affected / exposed                 | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Investigations                              |                 |                 |                 |
| Blood testosterone decreased                |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 2               | 0               |
| Liver function test abnormal                |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                           | 0               | 2               | 1               |
| Neutrophil count decreased                  |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 2               | 0               |
| Weight decreased                            |                 |                 |                 |
| subjects affected / exposed                 | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                           | 1               | 2               | 1               |
| Alanine aminotransferase increased          |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Blood potassium decreased                   |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Blood thyroid stimulating hormone increased |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| C-reactive protein increased                |                 |                 |                 |
| subjects affected / exposed                 | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Gamma-glutamyltransferase increased         |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Human herpes virus 6 serology positive |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Intraocular pressure increased         |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Thyroxine decreased                    |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Serum ferritin increased               |                 |                 |                 |
| subjects affected / exposed            | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)                      | 2               | 0               | 1               |
| Cystogram                              |                 |                 |                 |
| subjects affected / exposed            | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Ejection fraction abnormal             |                 |                 |                 |
| subjects affected / exposed            | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Hepatic enzyme increased               |                 |                 |                 |
| subjects affected / exposed            | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Blood creatine phosphokinase increased |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 0               | 0               |
| Blood creatinine increased             |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 0               | 0               |
| Body temperature increased             |                 |                 |                 |
| subjects affected / exposed            | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                      | 0               | 0               | 0               |
| Transaminases increased                |                 |                 |                 |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Injury, poisoning and procedural complications   |                      |                      |                      |
| Transfusion reaction                             |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 2 / 247 (0.81%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 3                    | 0                    |
| Laceration                                       |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 2 / 247 (0.81%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 2                    | 0                    |
| Ligament sprain                                  |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 2 / 247 (0.81%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 2                    | 0                    |
| Eye injury                                       |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 1 / 247 (0.40%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Fall   |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 1 / 247 (0.40%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Febrile nonhaemolytic transfusion reaction       |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 1 / 247 (0.40%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Infusion related reaction                        |                      |                      |                      |
| subjects affected / exposed                      | 0 / 221 (0.00%)      | 1 / 247 (0.40%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Conjunctival scar                                |                      |                      |                      |
| subjects affected / exposed                      | 1 / 221 (0.45%)      | 0 / 247 (0.00%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Drug administration error                        |                      |                      |                      |
| subjects affected / exposed                      | 1 / 221 (0.45%)      | 0 / 247 (0.00%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Post-traumatic pain                              |                      |                      |                      |
| subjects affected / exposed                      | 1 / 221 (0.45%)      | 0 / 247 (0.00%)      | 0 / 192 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Procedural pain                                  |                      |                      |                      |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 1 / 192 (0.52%)<br>1 |
| Arthropod bite<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Anaemia postoperative<br>subjects affected / exposed<br>occurrences (all)  | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Congenital, familial and genetic disorders<br>Myotonic dystrophy<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Ichthyosis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Cardiac disorders<br>Palpitations<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 221 (0.45%)<br>1 | 2 / 247 (0.81%)<br>2 | 0 / 192 (0.00%)<br>0 |
| Arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Atrial thrombosis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Dilatation ventricular<br>subjects affected / exposed<br>occurrences (all)   | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Myocardial infarction<br>subjects affected / exposed<br>occurrences (all)  | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Cardiomyopathy   |                      |                      |                      |



|                                |                 |                 |                 |
|--------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Tachycardia                    |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Nervous system disorders       |                 |                 |                 |
| Neuropathy peripheral          |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 1               | 0               |
| Polyneuropathy                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)              | 0               | 1               | 1               |
| Post herpetic neuralgia        |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Sciatica                       |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 1               | 0               |
| Sinus headache                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Amnesia                        |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Migraine with aura             |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Syncope                        |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Disturbance in attention       |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)              | 0               | 0               | 1               |
| Cranial nerve palsies multiple |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 0               | 0               |

|                             |                 |                  |                 |
|-----------------------------|-----------------|------------------|-----------------|
| Epilepsy                    |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0                | 0               |
| Hypoaesthesia               |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0                | 0               |
| Restless legs syndrome      |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0                | 0               |
| Dysgeusia                   |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 3 / 247 (1.21%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 3                | 0               |
| Headache                    |                 |                  |                 |
| subjects affected / exposed | 3 / 221 (1.36%) | 13 / 247 (5.26%) | 4 / 192 (2.08%) |
| occurrences (all)           | 3               | 13               | 5               |
| Balance disorder            |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 247 (0.81%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 2                | 0               |
| Dizziness                   |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 2 / 247 (0.81%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 2                | 0               |
| Paraesthesia                |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 2 / 247 (0.81%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 2               | 2                | 0               |
| Coordination abnormal       |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Hyperaesthesia              |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Myoclonus                   |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |
| Nervous system disorder     |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1                | 0               |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| Blood and lymphatic system disorders |                 |                 |                 |
| Thrombocytopenia                     |                 |                 |                 |
| subjects affected / exposed          | 2 / 221 (0.90%) | 5 / 247 (2.02%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 2               | 6               | 0               |
| Eosinophilia                         |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 3               | 0               |
| Anaemia                              |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 2               | 0               |
| Aplasia pure red cell                |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 2               | 0               |
| Anaemia macrocytic                   |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Aplastic anaemia                     |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Febrile neutropenia                  |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Histiocytosis haematophagic          |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Iron deficiency anaemia              |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Leukopenia                           |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Lymphadenopathy                      |                 |                 |                 |
| subjects affected / exposed          | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                    | 0               | 1               | 1               |
| Normochromic normocytic anaemia      |                 |                 |                 |

|                                     |                 |                 |                 |
|-------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Pancytopenia                        |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Splenomegaly                        |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Haemolytic uraemic syndrome         |                 |                 |                 |
| subjects affected / exposed         | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 1               | 0               | 0               |
| Idiopathic thrombocytopenic purpura |                 |                 |                 |
| subjects affected / exposed         | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 1               | 0               | 0               |
| Hypergammaglobulinaemia             |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)                   | 0               | 0               | 1               |
| Ear and labyrinth disorders         |                 |                 |                 |
| Ear pain                            |                 |                 |                 |
| subjects affected / exposed         | 2 / 221 (0.90%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 2               | 3               | 0               |
| Vertigo                             |                 |                 |                 |
| subjects affected / exposed         | 1 / 221 (0.45%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 1               | 3               | 0               |
| Tinnitus                            |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 2               | 0               |
| Ear discomfort                      |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Hearing impaired                    |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Hypoacusis                          |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| Middle ear effusion<br>subjects affected / exposed<br>occurrences (all)        | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Tympanic membrane disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Deafness neurosensory<br>subjects affected / exposed<br>occurrences (all)      | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Deafness unilateral<br>subjects affected / exposed<br>occurrences (all)        | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)          | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Ear pruritus<br>subjects affected / exposed<br>occurrences (all)               | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Eye disorders  |                      |                      |                      |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 221 (0.00%)<br>0 | 6 / 247 (2.43%)<br>7 | 0 / 192 (0.00%)<br>0 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 221 (1.36%)<br>3 | 5 / 247 (2.02%)<br>5 | 1 / 192 (0.52%)<br>1 |
| Allergic keratitis<br>subjects affected / exposed<br>occurrences (all)         | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Conjunctival hyperaemia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Diabetic retinopathy<br>subjects affected / exposed<br>occurrences (all)       | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Eye haemorrhage  |                      |                      |                      |

|                                |                 |                 |                 |
|--------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Eye irritation                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Foreign body sensation in eyes |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Keratitis                      |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Orbital oedema                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Vision blurred                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Visual acuity reduced          |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Visual impairment              |                 |                 |                 |
| subjects affected / exposed    | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Vitreous detachment            |                 |                 |                 |
| subjects affected / exposed    | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 2               | 0               | 0               |
| Blindness                      |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Cataract                       |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Periorbital oedema             |                 |                 |                 |
| subjects affected / exposed    | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Eye inflammation               |                 |                 |                 |

|                             |                 |                  |                 |
|-----------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0                | 1               |
| Retinal detachment          |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0                | 1               |
| Xerophthalmia               |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0                | 1               |
| Lacrimation increased       |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0                | 0               |
| Gastrointestinal disorders  |                 |                  |                 |
| Diarrhoea                   |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 24 / 247 (9.72%) | 3 / 192 (1.56%) |
| occurrences (all)           | 2               | 27               | 3               |
| Vomiting                    |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 15 / 247 (6.07%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 21               | 0               |
| Nausea                      |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 8 / 247 (3.24%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 10               | 0               |
| Abdominal pain              |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 8 / 247 (3.24%)  | 2 / 192 (1.04%) |
| occurrences (all)           | 1               | 9                | 2               |
| Abdominal pain upper        |                 |                  |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 5 / 247 (2.02%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 5                | 0               |
| Stomatitis                  |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 5 / 247 (2.02%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 2               | 5                | 1               |
| Constipation                |                 |                  |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 4 / 247 (1.62%)  | 1 / 192 (0.52%) |
| occurrences (all)           | 2               | 4                | 1               |
| Dry mouth                   |                 |                  |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 3 / 247 (1.21%)  | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 3                | 0               |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Dysphagia                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 3               | 0               |
| Gastrooesophageal reflux disease |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 3               | 0               |
| Aphthous stomatitis              |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 2               | 0               |
| Dyspepsia                        |                 |                 |                 |
| subjects affected / exposed      | 3 / 221 (1.36%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                | 3               | 2               | 1               |
| Gastrointestinal pain            |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 2               | 0               |
| Haemorrhoids                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                | 0               | 2               | 1               |
| Oesophagitis                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 2               | 0               |
| Abdominal pain lower             |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Aptyalism                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Ascites                          |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Eructation                       |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Faecaloma                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |



|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Glossodynia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hyperchlorhydria            |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Lip swelling                |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Mouth ulceration            |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral disorder               |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral mucosal discolouration |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Tongue coated               |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Tongue discolouration       |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Abdominal distension        |                 |                 |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Oral lichen planus          |                 |                 |                 |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Odynophagia                 |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |

|  |                      |                        |                      |
|--|----------------------|------------------------|----------------------|
| Sensitivity of teeth<br>subjects affected / exposed<br>occurrences (all)         | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| Gastrointestinal haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0   | 1 / 192 (0.52%)<br>1 |
| Gastrointestinal disorder<br>subjects affected / exposed<br>occurrences (all)    | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| Inguinal hernia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0   | 0 / 192 (0.00%)<br>0 |
| Hepatobiliary disorders  |                      |                        |                      |
| Hepatic function abnormal<br>subjects affected / exposed<br>occurrences (all)    | 1 / 221 (0.45%)<br>1 | 3 / 247 (1.21%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Hepatocellular injury<br>subjects affected / exposed<br>occurrences (all)        | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1   | 0 / 192 (0.00%)<br>0 |
| Hepatomegaly<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1   | 0 / 192 (0.00%)<br>0 |
| Cholestasis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 221 (0.00%)<br>0 | 5 / 247 (2.02%)<br>6   | 0 / 192 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders   |                      |                        |                      |
| Rash<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 221 (0.00%)<br>0 | 14 / 247 (5.67%)<br>14 | 2 / 192 (1.04%)<br>2 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 221 (0.90%)<br>2 | 11 / 247 (4.45%)<br>13 | 1 / 192 (0.52%)<br>1 |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 221 (0.00%)<br>0 | 5 / 247 (2.02%)<br>5   | 0 / 192 (0.00%)<br>0 |
| Eczema   |                      |                        |                      |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 221 (0.00%) | 4 / 247 (1.62%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 4               | 0               |
| Erythema                    |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 3               | 0               |
| Skin lesion                 |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 3               | 0               |
| Acne                        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Rash macular                |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Rash papular                |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Blister                     |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Dermatitis acneiform        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Dermatosis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Generalised erythema        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Lichenification             |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Night sweats                |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)           | 1               | 1               | 1               |
| Perivascular dermatitis     |                 |                 |                 |

|                                       |                 |                 |                 |
|---------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Rash generalised                      |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Rash maculo-papular                   |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Seborrhoeic dermatitis                |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Skin discolouration                   |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Skin hyperpigmentation                |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Skin mass                             |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Acute febrile neutrophilic dermatosis |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Hyperhidrosis                         |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Pityriasis rubra pilaris              |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Rash pruritic                         |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Dermatitis                            |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)                     | 0               | 0               | 1               |
| Dermatitis atopic                     |                 |                 |                 |

|  |   |                   |                   |
|--|---|-------------------|-------------------|
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 1 / 192 (0.52%)   |
| occurrences (all)                            | 0   | 0                 | 1                 |
| Angioedema                                   |   |                   |                   |
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 0                 | 0                 |
| Intertrigo                                   |   |                   |                   |
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 0                 | 0                 |
| Pruritus generalised                         |   |                   |                   |
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 0                 | 0                 |
| Urticaria                                    |   |                   |                   |
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 0                 | 0                 |
| Alopecia                                     |   |                   |                   |
| subjects affected / exposed                  | 0 / 221 (0.00%)   | 0 / 247 (0.00%)   | 0 / 192 (0.00%)   |
| occurrences (all)                            | 0   | 0                 | 0                 |
| Redness (Any) : 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                   |
| alternative assessment type: Systematic      |   |                   |                   |
| subjects affected / exposed <sup>[83]</sup>  | 0 / 221 (0.00%)   | 23 / 168 (13.69%) | 33 / 100 (33.00%) |
| occurrences (all)                            | 0   | 23                | 33                |
| Redness (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                   |
| alternative assessment type: Systematic      |   |                   |                   |
| subjects affected / exposed <sup>[84]</sup>  | 0 / 221 (0.00%)   | 20 / 168 (11.90%) | 22 / 97 (22.68%)  |
| occurrences (all)                            | 0   | 20                | 22                |
| Redness (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                   |
| alternative assessment type: Systematic      |   |                   |                   |
| subjects affected / exposed <sup>[85]</sup>  | 0 / 221 (0.00%)   | 6 / 165 (3.64%)   | 16 / 90 (17.78%)  |
| occurrences (all)                            | 0   | 6                 | 16                |
| Redness (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                   |                   |
| alternative assessment type: Systematic      |   |                   |                   |

|   |   |                    |                    |
|---|---|--------------------|--------------------|
| subjects affected / exposed <sup>[86]</sup>   | 0 / 221 (0.00%)   | 0 / 247 (0.00%)    | 5 / 89 (5.62%)     |
| occurrences (all)                             | 0   | 0                  | 5                  |
| Swelling (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[87]</sup>   | 0 / 221 (0.00%)   | 25 / 170 (14.71%)  | 41 / 108 (37.96%)  |
| occurrences (all)                             | 0   | 25                 | 41                 |
| Swelling (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[88]</sup>   | 0 / 221 (0.00%)   | 18 / 169 (10.65%)  | 25 / 100 (25.00%)  |
| occurrences (all)                             | 0   | 18                 | 25                 |
| Swelling (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[89]</sup>   | 0 / 221 (0.00%)   | 9 / 167 (5.39%)    | 17 / 95 (17.89%)   |
| occurrences (all)                             | 0   | 9                  | 17                 |
| Swelling (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[90]</sup>   | 0 / 221 (0.00%)   | 1 / 165 (0.61%)    | 4 / 88 (4.55%)     |
| occurrences (all)                             | 0   | 1                  | 4                  |
| Pain (Any): 13vPnC Dose 1 and Dose 4          | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[91]</sup>   | 0 / 221 (0.00%)   | 165 / 222 (74.32%) | 113 / 143 (79.02%) |
| occurrences (all)                             | 0   | 165                | 113                |
| Pain (Mild): 13vPnC Dose 1 and Dose 4         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[92]</sup>   | 0 / 221 (0.00%)   | 151 / 217 (69.59%) | 94 / 130 (72.31%)  |
| occurrences (all)                             | 0   | 151                | 94                 |
| Pain (Moderate): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                    |
| alternative assessment type:<br>Systematic    |   |                    |                    |
| subjects affected / exposed <sup>[93]</sup>   | 0 / 221 (0.00%)   | 50 / 180 (27.78%)  | 42 / 109 (38.53%)  |
| occurrences (all)                             | 0   | 50                 | 42                 |

|  |   |                         |                      |
|--|---|-------------------------|----------------------|
| Pain (Severe): 13vPnC Dose 1 and Dose 4<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[94]</sup><br><br>occurrences (all) | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 5 / 166 (3.01%)<br>5    | 6 / 90 (6.67%)<br>6  |
| Redness (Any): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[95]</sup><br><br>occurrences (all)            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 30 / 137 (21.90%)<br>30 | 0 / 192 (0.00%)<br>0 |
| Redness (Mild): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[96]</sup><br><br>occurrences (all)           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 26 / 134 (19.40%)<br>26 | 0 / 192 (0.00%)<br>0 |
| Redness (Moderate): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[97]</sup><br><br>occurrences (all)       | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 9 / 129 (6.98%)<br>9    | 0 / 192 (0.00%)<br>0 |
| Redness (Severe): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[98]</sup><br><br>occurrences (all)         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 2 / 127 (1.57%)<br>2    | 0 / 192 (0.00%)<br>0 |
| Swelling (Any): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[99]</sup><br><br>occurrences (all)           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 25 / 133 (18.80%)<br>25 | 0 / 192 (0.00%)<br>0 |
| Swelling (Mild): 13vPnC Dose 2<br><br>alternative assessment type: Systematic<br>subjects affected / exposed <sup>[100]</sup><br><br>occurrences (all)         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  | 0 / 221 (0.00%)<br>0  | 19 / 131 (14.50%)<br>19 | 0 / 192 (0.00%)<br>0 |
| Swelling (Moderate): 13vPnC Dose 2<br><br>alternative assessment type:   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|  |   |                         |                      |

|  |   |                    |                 |
|--|---|--------------------|-----------------|
| Systematic                                   |   |                    |                 |
| subjects affected / exposed <sup>[101]</sup> | 0 / 221 (0.00%)   | 7 / 128 (5.47%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 7                  | 0               |
| Pain (Any): 13vPnC Dose 2                    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[102]</sup> | 0 / 221 (0.00%)   | 146 / 194 (75.26%) | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 146                | 0               |
| Pain (Mild): 13vPnC Dose 2                   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[103]</sup> | 0 / 221 (0.00%)   | 129 / 184 (70.11%) | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 129                | 0               |
| Pain (Moderate): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[104]</sup> | 0 / 221 (0.00%)   | 49 / 148 (33.11%)  | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 49                 | 0               |
| Pain (Severe): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[105]</sup> | 0 / 221 (0.00%)   | 6 / 131 (4.58%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 6                  | 0               |
| Redness (Any): 13vPnC Dose 3                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[106]</sup> | 0 / 221 (0.00%)   | 17 / 120 (14.17%)  | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 17                 | 0               |
| Redness (Mild): 13vPnC Dose 3                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[107]</sup> | 0 / 221 (0.00%)   | 13 / 118 (11.02%)  | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 13                 | 0               |
| Redness (Moderate): 13vPnC Dose 3            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |



|  |   |                    |                 |
|--|---|--------------------|-----------------|
| subjects affected / exposed <sup>[108]</sup> | 0 / 221 (0.00%)   | 6 / 117 (5.13%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 6                  | 0               |
| Redness (Severe): 13vPnC Dose 3              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[109]</sup> | 0 / 221 (0.00%)   | 2 / 116 (1.72%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 2                  | 0               |
| Swelling (Any): 13vPnC Dose 3                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[110]</sup> | 0 / 221 (0.00%)   | 18 / 121 (14.88%)  | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 18                 | 0               |
| Swelling (Mild): 13vPnC Dose 3               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[111]</sup> | 0 / 221 (0.00%)   | 15 / 120 (12.50%)  | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 15                 | 0               |
| Swelling (Moderate): 13vPnC Dose 3           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[112]</sup> | 0 / 221 (0.00%)   | 5 / 117 (4.27%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 5                  | 0               |
| Swelling (Severe): 13vPnC Dose 3             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[113]</sup> | 0 / 221 (0.00%)   | 1 / 115 (0.87%)    | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 1                  | 0               |
| Pain (Any): 13vPnC Dose 3                    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[114]</sup> | 0 / 221 (0.00%)   | 127 / 175 (72.57%) | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 127                | 0               |
| Pain (Mild): 13vPnC Dose 3                   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                    |                 |
| alternative assessment type:<br>Systematic   |   |                    |                 |
| subjects affected / exposed <sup>[115]</sup> | 0 / 221 (0.00%)   | 109 / 163 (66.87%) | 0 / 192 (0.00%) |
| occurrences (all)                            | 0   | 109                | 0               |

|   |   |                         |                      |
|---|---|-------------------------|----------------------|
| Pain (Moderate): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[116]</sup><br>occurrences (all) | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 42 / 141 (29.79%)<br>42 | 0 / 192 (0.00%)<br>0 |
| Pain (Severe): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[117]</sup><br>occurrences (all)   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 5 / 117 (4.27%)<br>5    | 0 / 192 (0.00%)<br>0 |
| Fatigue (Mild): 13vPnC Dose 3<br><br>alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[118]</sup><br>occurrences (all)  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                         |                      |
|   | 0 / 221 (0.00%)<br>0  | 58 / 148 (39.19%)<br>58 | 0 / 192 (0.00%)<br>0 |
| Renal and urinary disorders   |   |                         |                      |
| Polyuria  |   |                         |                      |
| subjects affected / exposed   | 0 / 221 (0.00%)   | 2 / 247 (0.81%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 0   | 4                       | 0                    |
| Renal failure   |   |                         |                      |
| subjects affected / exposed   | 0 / 221 (0.00%)   | 3 / 247 (1.21%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 0   | 3                       | 0                    |
| Dysuria   |   |                         |                      |
| subjects affected / exposed   | 1 / 221 (0.45%)   | 2 / 247 (0.81%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 1   | 2                       | 0                    |
| Nocturia  |   |                         |                      |
| subjects affected / exposed   | 0 / 221 (0.00%)   | 2 / 247 (0.81%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 0   | 2                       | 0                    |
| Pollakiuria   |   |                         |                      |
| subjects affected / exposed   | 1 / 221 (0.45%)   | 2 / 247 (0.81%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 1   | 2                       | 0                    |
| Haematuria  |   |                         |                      |
| subjects affected / exposed   | 0 / 221 (0.00%)   | 1 / 247 (0.40%)         | 1 / 192 (0.52%)      |
| occurrences (all)   | 0   | 1                       | 1                    |
| Incontinence  |   |                         |                      |
| subjects affected / exposed   | 0 / 221 (0.00%)   | 1 / 247 (0.40%)         | 0 / 192 (0.00%)      |
| occurrences (all)   | 0   | 1                       | 0                    |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| Renal impairment<br>subjects affected / exposed<br>occurrences (all)       | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Urethral pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)      | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Cystitis haemorrhagic<br>subjects affected / exposed<br>occurrences (all)  | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)            | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Urinary tract disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Urine abnormality<br>subjects affected / exposed<br>occurrences (all)      | 0 / 221 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Endocrine disorders  |                      |                      |                      |
| Cushingoid<br>subjects affected / exposed<br>occurrences (all)             | 0 / 221 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)        | 1 / 221 (0.45%)<br>1 | 1 / 247 (0.40%)<br>1 | 0 / 192 (0.00%)<br>0 |
| Cushing's syndrome<br>subjects affected / exposed<br>occurrences (all)     | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 0 / 192 (0.00%)<br>0 |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)         | 1 / 221 (0.45%)<br>1 | 0 / 247 (0.00%)<br>0 | 1 / 192 (0.52%)<br>1 |
| Oestrogen deficiency   |                      |                      |                      |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 221 (0.00%) | 0 / 247 (0.00%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 0                | 0               |
| Musculoskeletal and connective tissue disorders |                 |                  |                 |
| Arthralgia                                      |                 |                  |                 |
| subjects affected / exposed                     | 6 / 221 (2.71%) | 11 / 247 (4.45%) | 4 / 192 (2.08%) |
| occurrences (all)                               | 7               | 11               | 6               |
| Muscle spasms                                   |                 |                  |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 7 / 247 (2.83%)  | 2 / 192 (1.04%) |
| occurrences (all)                               | 2               | 9                | 2               |
| Back pain                                       |                 |                  |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 7 / 247 (2.83%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 1               | 8                | 0               |
| Myalgia   |                 |                  |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 5 / 247 (2.02%)  | 1 / 192 (0.52%) |
| occurrences (all)                               | 1               | 5                | 1               |
| Musculoskeletal pain                            |                 |                  |                 |
| subjects affected / exposed                     | 2 / 221 (0.90%) | 4 / 247 (1.62%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 2               | 4                | 0               |
| Pain in extremity                               |                 |                  |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 3 / 247 (1.21%)  | 1 / 192 (0.52%) |
| occurrences (all)                               | 0               | 3                | 1               |
| Musculoskeletal stiffness                       |                 |                  |                 |
| subjects affected / exposed                     | 1 / 221 (0.45%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 1               | 2                | 0               |
| Bone pain                                       |                 |                  |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1                | 0               |
| Flank pain                                      |                 |                  |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1                | 0               |
| Joint stiffness                                 |                 |                  |                 |
| subjects affected / exposed                     | 0 / 221 (0.00%) | 1 / 247 (0.40%)  | 0 / 192 (0.00%) |
| occurrences (all)                               | 0               | 1                | 0               |
| Muscular weakness                               |                 |                  |                 |

|                             |                 |                   |                  |
|-----------------------------|-----------------|-------------------|------------------|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 0               | 1                 | 0                |
| Myopathy                    |                 |                   |                  |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)   | 1 / 192 (0.52%)  |
| occurrences (all)           | 0               | 1                 | 1                |
| Osteonecrosis               |                 |                   |                  |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 0               | 1                 | 0                |
| Osteoporosis                |                 |                   |                  |
| subjects affected / exposed | 3 / 221 (1.36%) | 1 / 247 (0.40%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 3               | 1                 | 0                |
| Synovial cyst               |                 |                   |                  |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 0               | 1                 | 0                |
| Groin pain                  |                 |                   |                  |
| subjects affected / exposed | 2 / 221 (0.90%) | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 2               | 0                 | 0                |
| Osteopenia                  |                 |                   |                  |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 1               | 0                 | 0                |
| Spinal osteoarthritis       |                 |                   |                  |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 1               | 0                 | 0                |
| Tendonitis                  |                 |                   |                  |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 1               | 0                 | 0                |
| Sjogren's syndrome          |                 |                   |                  |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%)   | 1 / 192 (0.52%)  |
| occurrences (all)           | 0               | 0                 | 1                |
| Osteoarthritis              |                 |                   |                  |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%)   | 0 / 192 (0.00%)  |
| occurrences (all)           | 0               | 1                 | 0                |
| Infections and infestations |                 |                   |                  |
| Nasopharyngitis             |                 |                   |                  |
| subjects affected / exposed | 6 / 221 (2.71%) | 28 / 247 (11.34%) | 11 / 192 (5.73%) |
| occurrences (all)           | 6               | 32                | 11               |

|   |                      |                        |                      |
|---|----------------------|------------------------|----------------------|
| Cytomegalovirus infection<br>subjects affected / exposed<br>occurrences (all)         | 3 / 221 (1.36%)<br>4 | 10 / 247 (4.05%)<br>12 | 1 / 192 (0.52%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 6 / 221 (2.71%)<br>8 | 10 / 247 (4.05%)<br>12 | 3 / 192 (1.56%)<br>3 |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 5 / 221 (2.26%)<br>5 | 8 / 247 (3.24%)<br>11  | 0 / 192 (0.00%)<br>0 |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 221 (1.36%)<br>3 | 6 / 247 (2.43%)<br>6   | 1 / 192 (0.52%)<br>1 |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 221 (0.45%)<br>1 | 5 / 247 (2.02%)<br>6   | 0 / 192 (0.00%)<br>0 |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 221 (0.00%)<br>0 | 5 / 247 (2.02%)<br>5   | 1 / 192 (0.52%)<br>1 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 2 / 221 (0.90%)<br>2 | 4 / 247 (1.62%)<br>5   | 0 / 192 (0.00%)<br>0 |
| Oral fungal infection<br>subjects affected / exposed<br>occurrences (all)             | 1 / 221 (0.45%)<br>1 | 4 / 247 (1.62%)<br>4   | 0 / 192 (0.00%)<br>0 |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 221 (1.36%)<br>3 | 4 / 247 (1.62%)<br>4   | 0 / 192 (0.00%)<br>0 |
| Escherichia infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 221 (0.00%)<br>0 | 2 / 247 (0.81%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 221 (0.00%)<br>0 | 2 / 247 (0.81%)<br>3   | 0 / 192 (0.00%)<br>0 |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 221 (0.45%)<br>1 | 2 / 247 (0.81%)<br>3   | 0 / 192 (0.00%)<br>0 |

|                                       |                 |                 |                 |
|---------------------------------------|-----------------|-----------------|-----------------|
| Oral herpes                           |                 |                 |                 |
| subjects affected / exposed           | 4 / 221 (1.81%) | 3 / 247 (1.21%) | 1 / 192 (0.52%) |
| occurrences (all)                     | 4               | 3               | 1               |
| Candidiasis                           |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Enterobacter sepsis                   |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Escherichia sepsis                    |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Eye infection                         |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Otitis media                          |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 2               | 0               |
| Pharyngitis                           |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 1 / 192 (0.52%) |
| occurrences (all)                     | 0               | 2               | 1               |
| Respiratory syncytial virus infection |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Respiratory tract infection           |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Viral infection                       |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 2               | 0               |
| Adenovirus infection                  |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Aspergillosis                         |                 |                 |                 |
| subjects affected / exposed           | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |

|                                     |                 |                 |                 |
|-------------------------------------|-----------------|-----------------|-----------------|
| Bacterial infection                 |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Catheter site infection             |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Conjunctivitis viral                |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                   | 0               | 1               | 1               |
| Enterobacter infection              |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Enterococcal sepsis                 |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Epstein-Barr virus infection        |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Escherichia urinary tract infection |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                   | 0               | 1               | 1               |
| Febrile infection                   |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Folliculitis                        |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Fungal infection                    |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                   | 0               | 1               | 1               |
| Gastroenteritis viral               |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |
| Genital infection fungal            |                 |                 |                 |
| subjects affected / exposed         | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                   | 0               | 1               | 0               |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Herpes simplex                          |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                       | 0               | 1               | 1               |
| Infection                               |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)                       | 0               | 1               | 1               |
| Influenza                               |                 |                 |                 |
| subjects affected / exposed             | 3 / 221 (1.36%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 3               | 1               | 0               |
| Laryngitis                              |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Mycoplasma infection                    |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Pseudomonas infection                   |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Respiratory moniliasis                  |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Staphylococcal sepsis                   |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Systemic candida                        |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Viral upper respiratory tract infection |                 |                 |                 |
| subjects affected / exposed             | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 0               | 1               | 0               |
| Pneumonia                               |                 |                 |                 |
| subjects affected / exposed             | 2 / 221 (0.90%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 2               | 0               | 0               |
| Acute sinusitis                         |                 |                 |                 |
| subjects affected / exposed             | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                       | 1               | 0               | 0               |

|                                       |                 |                 |                 |
|---------------------------------------|-----------------|-----------------|-----------------|
| Bronchitis viral                      |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Fungal skin infection                 |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Hepatitis B                           |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Herpes zoster oticus                  |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Hordeolum                             |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Oesophageal candidiasis               |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Parainfluenzae virus infection        |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Periorbital cellulitis                |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Sepsis                                |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Staphylococcal infection              |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Streptococcal urinary tract infection |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Viral pharyngitis                     |                 |                 |                 |
| subjects affected / exposed           | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Chronic sinusitis           |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 2 / 192 (1.04%) |
| occurrences (all)           | 0               | 0               | 2               |
| Herpes virus infection      |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Infected dermal cyst        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Lung infection              |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Pharyngotonsillitis         |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Toxoplasmosis               |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Viral rhinitis              |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Ear infection               |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Gastrointestinal infection  |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Injection site cellulitis   |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Trichosporon infection      |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Rash pustular               |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                                    |                 |                 |                 |
|------------------------------------|-----------------|-----------------|-----------------|
| Metabolism and nutrition disorders |                 |                 |                 |
| Decreased appetite                 |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 7 / 247 (2.83%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 1               | 8               | 0               |
| Fluid retention                    |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 3               | 0               |
| Hypercholesterolaemia              |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 3 / 247 (1.21%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 1               | 3               | 0               |
| Diabetes mellitus                  |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 1               | 2               | 0               |
| Hyperglycaemia                     |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 2               | 0               |
| Hypocalcaemia                      |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 2 / 247 (0.81%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 2               | 0               |
| Cachexia                           |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Dehydration                        |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Folate deficiency                  |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Hypercreatininaemia                |                 |                 |                 |
| subjects affected / exposed        | 1 / 221 (0.45%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 1               | 1               | 0               |
| Hyperphosphataemia                 |                 |                 |                 |
| subjects affected / exposed        | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0               |
| Hyperuricaemia                     |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 1               | 1               |
| Hypophosphataemia           |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Metabolic acidosis          |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Vitamin D deficiency        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Vitamin K deficiency        |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 1 / 247 (0.40%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hyperkalaemia               |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Glucose tolerance impaired  |                 |                 |                 |
| subjects affected / exposed | 1 / 221 (0.45%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Haemochromatosis            |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hypomagnesaemia             |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 1 / 192 (0.52%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hyperlipidaemia             |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Hypertriglyceridaemia       |                 |                 |                 |
| subjects affected / exposed | 0 / 221 (0.00%) | 0 / 247 (0.00%) | 0 / 192 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |

| <b>Non-serious adverse events</b>                     | 23vPS Dose        | Follow-up        |  |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                   |                  |  |
| subjects affected / exposed                           | 93 / 184 (50.54%) | 19 / 247 (7.69%) |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |  |
| Plasmacytoma  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Precursor B-lymphoblastic lymphoma                                  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Acute leukaemia   |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Acute myeloid leukaemia recurrent                                   |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Kaposi's sarcoma  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Anogenital warts  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Vascular disorders  |                 |                 |  |
| Hypertension  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Hypotension   |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Orthostatic hypotension   |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Thrombophlebitis  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Flushing  |                 |                 |  |
| subjects affected / exposed   | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)   | 0               | 0               |  |
| Hypovolaemic shock  |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Vasodilatation                                       |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Venous insufficiency                                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Venous thrombosis                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Hot flush  |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 0               | 0               |  |
| Haematoma  |                 |                 |  |
| subjects affected / exposed                          | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 1               | 0               |  |
| Vena cava thrombosis                                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)                                    | 0               | 1               |  |
| General disorders and administration site conditions |                 |                 |  |
| Fatigue  |                 |                 |  |
| subjects affected / exposed                          | 5 / 184 (2.72%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 6               | 0               |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 8 / 184 (4.35%) | 1 / 247 (0.40%) |  |
| occurrences (all)                                    | 8               | 2               |  |
| Oedema peripheral                                    |                 |                 |  |
| subjects affected / exposed                          | 2 / 184 (1.09%) | 0 / 247 (0.00%) |  |
| occurrences (all)                                    | 2               | 0               |  |
| Asthenia   |                 |                 |  |
| subjects affected / exposed                          | 3 / 184 (1.63%) | 1 / 247 (0.40%) |  |
| occurrences (all)                                    | 3               | 1               |  |
| Injection site swelling                              |                 |                 |  |

|                                    |                 |                 |
|------------------------------------|-----------------|-----------------|
| subjects affected / exposed        | 8 / 184 (4.35%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 9               | 0               |
| Injection site erythema            |                 |                 |
| subjects affected / exposed        | 5 / 184 (2.72%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 5               | 0               |
| Oedema                             |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Chest pain                         |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                  | 0               | 1               |
| Catheter site rash                 |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Chest discomfort                   |                 |                 |
| subjects affected / exposed        | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 1               | 0               |
| Complication of device removal     |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Feeling cold                       |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Feeling hot                        |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Gait disturbance                   |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Influenza like illness             |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Injection site movement impairment |                 |                 |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                  | 0               | 0               |
| Injection site pain                |                 |                 |



|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 8 / 184 (4.35%) | 0 / 247 (0.00%) |
| occurrences (all)           | 8               | 0               |
| Medical device complication |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Pain                        |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Vaccination site haematoma  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Vaccination site pain       |                 |                 |
| subjects affected / exposed | 6 / 184 (3.26%) | 0 / 247 (0.00%) |
| occurrences (all)           | 6               | 0               |
| Vaccination site reaction   |                 |                 |
| subjects affected / exposed | 4 / 184 (2.17%) | 0 / 247 (0.00%) |
| occurrences (all)           | 4               | 0               |
| Inflammation                |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Spinal pain                 |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Chills                      |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Injection site pruritus     |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Injection site reaction     |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Mucosal inflammation        |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Vaccination site erythema   |                 |                 |

|   |   |                 |  |
|---|---|-----------------|--|
| subjects affected / exposed                           | 5 / 184 (2.72%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 5   | 0               |  |
| Vaccination site swelling                             |   |                 |  |
| subjects affected / exposed                           | 4 / 184 (2.17%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 4   | 0               |  |
| Injection site induration                             |   |                 |  |
| subjects affected / exposed                           | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 1   | 0               |  |
| Injection site inflammation                           |   |                 |  |
| subjects affected / exposed                           | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 1   | 0               |  |
| Vaccination site oedema                               |   |                 |  |
| subjects affected / exposed                           | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 1   | 0               |  |
| Vaccination site rash                                 |   |                 |  |
| subjects affected / exposed                           | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 1   | 0               |  |
| Hernia  |   |                 |  |
| subjects affected / exposed                           | 0 / 184 (0.00%)   | 1 / 247 (0.40%) |  |
| occurrences (all)                                     | 0   | 1               |  |
| Fever >=38 degrees C: 13vPnC Dose 1 and Dose 4        | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic               |   |                 |  |
| subjects affected / exposed <sup>[1]</sup>            | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 0   | 0               |  |
| Fever >=38, <38.5 degrees C: 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic               |   |                 |  |
| subjects affected / exposed <sup>[2]</sup>            | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 0   | 0               |  |
| Fever >=38.5, <39 degrees C: 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic               |   |                 |  |
| subjects affected / exposed <sup>[3]</sup>            | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                                     | 0   | 0               |  |
| Fever >=39, <=40 degrees C: 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |

|   |   |                 |  |
|---|---|-----------------|--|
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[4]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fatigue (Any): 13vPnC Dose 3                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[5]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fatigue (Moderate): 13vPnC Dose 3           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[6]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fatigue (Severe): 13vPnC Dose 3             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[7]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Headache (Any): 13vPnC Dose 3               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[8]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Headache (Mild): 13vPnC Dose 3              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[9]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Headache (Moderate): 13vPnC Dose 3          | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |
| subjects affected / exposed <sup>[10]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Headache (Severe): 13vPnC Dose 3            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic  |   |                 |  |

|  |   |                      |  |
|--|---|----------------------|--|
| subjects affected / exposed <sup>[11]</sup><br>occurrences (all)   | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[12]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[13]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[14]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Diarrhea (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[15]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Diarrhea (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[16]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Diarrhea (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[17]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Diarrhea (Severe): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[18]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |

|  |   |                      |  |
|--|---|----------------------|--|
| Muscle pain (Any): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[19]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Mild): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[20]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Moderate): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[21]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Severe): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[22]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Any): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[23]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[24]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Moderate): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[25]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Severe): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:   |   |                      |  |

|   |   |                 |  |
|---|---|-----------------|--|
| Systematic                                  |   |                 |  |
| subjects affected / exposed <sup>[26]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38 degrees C: 13vPnC Dose 2         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[27]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38, <38.5 degrees C: 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[28]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38.5, <39 degrees C: 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[29]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=39, <=40 degrees C: 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[30]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38 degrees C: 13vPnC Dose 3         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[31]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38, <38.5 degrees C: 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[32]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Fever >=38.5, <39 degrees C: 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |

|   |   |                 |  |
|---|---|-----------------|--|
| subjects affected / exposed <sup>[33]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fever >=39, =<40 degrees C:<br>13vPnC Dose 3    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[34]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Any): 13vPnC Dose 1 and<br>Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[35]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Mild): 13vPnC Dose 1 and<br>Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[36]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Moderate): 13vPnC Dose 1<br>and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[37]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Severe): 13vPnC Dose 1<br>and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[38]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Any): 13vPnC Dose 2                    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |
| subjects affected / exposed <sup>[39]</sup>     | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0   | 0               |  |
| Fatigue (Mild): 13vPnC Dose 2                   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic      |   |                 |  |

|   |   |                 |  |
|---|---|-----------------|--|
| subjects affected / exposed <sup>[40]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Fatigue (Moderate): 13vPnC Dose 2             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[41]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Fatigue (Severe): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[42]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Headache (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[43]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Headache (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[44]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Headache (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[45]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Headache (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |
| subjects affected / exposed <sup>[46]</sup>   | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0   | 0               |  |
| Headache (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |   |                 |  |



|  |  |                      |  |
|--|--|----------------------|--|
| subjects affected / exposed <sup>[47]</sup><br>occurrences (all)   | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Headache (Mild): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[48]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Headache (Moderate): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[49]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Headache (Severe): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[50]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Any): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[51]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Mild): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[52]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Moderate): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[53]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Vomiting (Severe): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[54]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |

|   |  |                 |  |
|---|--|-----------------|--|
| Vomiting (Any): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[55]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Vomiting (Mild): 13vPnC Dose 2                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[56]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Vomiting (Moderate): 13vPnC Dose 2            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[57]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Vomiting (Severe): 13vPnC Dose 2              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[58]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Diarrhea (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[59]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Diarrhea (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[60]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Diarrhea (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic    |  |                 |  |
| subjects affected / exposed <sup>[61]</sup>   | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                             | 0  | 0               |  |
| Diarrhea (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:                  |  |                 |  |

|  |  |                 |  |
|--|--|-----------------|--|
| Systematic                                       |  |                 |  |
| subjects affected / exposed <sup>[62]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Diarrhea (Any): 13vPnC Dose 2                    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[63]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Diarrhea (Mild): 13vPnC Dose 2                   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[64]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Diarrhea (Moderate): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[65]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Diarrhea (Severe): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[66]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Muscle pain (Any): 13vPnC Dose 1 and Dose 4      | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[67]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Muscle pain (Mild): 13vPnC Dose 1 and Dose 4     | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |
| subjects affected / exposed <sup>[68]</sup>      | 0 / 184 (0.00%)  | 0 / 247 (0.00%) |  |
| occurrences (all)                                | 0  | 0               |  |
| Muscle pain (Moderate): 13vPnC Dose 1 and Dose 4 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic       |  |                 |  |

|  |  |                      |  |
|--|--|----------------------|--|
| subjects affected / exposed <sup>[69]</sup><br>occurrences (all)   | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Severe): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[70]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Any): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[71]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Mild): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[72]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Moderate): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[73]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Muscle pain (Severe): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[74]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Any): 13vPnC Dose 1 and Dose 4   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[75]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |
| Joint pain (Mild): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[76]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0   | 0 / 247 (0.00%)<br>0 |  |

|  |   |                 |                 |   |   |                 |                 |   |   |
|--|---|-----------------|-----------------|---|---|-----------------|-----------------|---|---|
| <p>Joint pain (Moderate): 13vPnC Dose 1 and Dose 4</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[77]</sup></p> <p>occurrences (all)</p>   | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Joint pain (Severe): 13vPnC Dose 1 and Dose 4</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[78]</sup></p> <p>occurrences (all)</p>   | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Joint pain (Any): 13vPnC Dose 2</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[79]</sup></p> <p>occurrences (all)</p>   | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Joint pain (Mild): 13vPnC Dose 2</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[80]</sup></p> <p>occurrences (all)</p>  | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Joint pain (Moderate): 13vPnC Dose 2</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[81]</sup></p> <p>occurrences (all)</p>  | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Joint pain (Severe): 13vPnC Dose 2</p> <p>alternative assessment type:<br/>Systematic</p> <p>subjects affected / exposed<sup>[82]</sup></p> <p>occurrences (all)</p>  | <p>Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.</p> <table border="1"> <tr> <td>0 / 184 (0.00%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>0</td><td>0</td></tr> </table> | 0 / 184 (0.00%) | 0 / 247 (0.00%) | 0 | 0 |                 |                 |   |   |
| 0 / 184 (0.00%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 0  | 0   |                 |                 |   |   |                 |                 |   |   |
| <p>Immune system disorders</p> <p>Graft versus host disease</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Chronic graft versus host disease</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <table border="1"> <tr> <td>4 / 184 (2.17%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>4</td><td>0</td></tr> <tr> <td>3 / 184 (1.63%)</td><td>0 / 247 (0.00%)</td></tr> <tr> <td>3</td><td>0</td></tr> </table>   | 4 / 184 (2.17%) | 0 / 247 (0.00%) | 4 | 0 | 3 / 184 (1.63%) | 0 / 247 (0.00%) | 3 | 0 |
| 4 / 184 (2.17%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 4  | 0   |                 |                 |   |   |                 |                 |   |   |
| 3 / 184 (1.63%)  | 0 / 247 (0.00%)   |                 |                 |   |   |                 |                 |   |   |
| 3  | 0   |                 |                 |   |   |                 |                 |   |   |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Graft versus host disease in liver<br>subjects affected / exposed<br>occurrences (all)         | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Graft versus host disease in skin<br>subjects affected / exposed<br>occurrences (all)          | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Food allergy<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hypogammaglobulinaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Acute graft versus host disease<br>subjects affected / exposed<br>occurrences (all)            | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Chronic graft versus host disease in liver<br>subjects affected / exposed<br>occurrences (all) | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Graft versus host disease in intestine<br>subjects affected / exposed<br>occurrences (all)     | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Reproductive system and breast disorders   |                      |                      |  |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Gynaecomastia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Vulvovaginal discomfort<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Vulvovaginal dryness   |                      |                      |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 1               | 0               |  |
| Prostatitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Genital discharge                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Amenorrhoea                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Cough   |                 |                 |  |
| subjects affected / exposed                     | 7 / 184 (3.80%) | 2 / 247 (0.81%) |  |
| occurrences (all)                               | 7               | 2               |  |
| Dyspnoea exertional                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Rhinorrhoea                                     |                 |                 |  |
| subjects affected / exposed                     | 3 / 184 (1.63%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 3               | 0               |  |
| Lung disorder                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Lung infiltration                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Oropharyngeal plaque                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Productive cough                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Pulmonary mass                                  |                 |                 |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Dyspnoea                    |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Hyperventilation            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Nasal congestion            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Organising pneumonia        |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Oropharyngeal pain          |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Pneumonitis                 |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Rhonchi                     |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Sputum discoloured          |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Epistaxis                   |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)           | 0               | 2               |  |
| Pleural effusion            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 2 / 247 (0.81%) |  |
| occurrences (all)           | 0               | 2               |  |
| Laryngeal oedema            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Psychiatric disorders       |                 |                 |  |



|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| Anxiety                            |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Insomnia                           |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Sleep disorder                     |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Confusional state                  |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Nervousness                        |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Stress                             |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Depression                         |                 |                 |  |
| subjects affected / exposed        | 2 / 184 (1.09%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 2               | 0               |  |
| Investigations                     |                 |                 |  |
| Blood testosterone decreased       |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Liver function test abnormal       |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Neutrophil count decreased         |                 |                 |  |
| subjects affected / exposed        | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 0               | 0               |  |
| Weight decreased                   |                 |                 |  |
| subjects affected / exposed        | 3 / 184 (1.63%) | 0 / 247 (0.00%) |  |
| occurrences (all)                  | 3               | 0               |  |
| Alanine aminotransferase increased |                 |                 |  |

|   |                 |                 |
|---|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Blood potassium decreased                   |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Blood thyroid stimulating hormone increased |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| C-reactive protein increased                |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Gamma-glutamyltransferase increased         |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Human herpes virus 6 serology positive      |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Intraocular pressure increased              |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Thyroxine decreased                         |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                           | 0               | 1               |
| Serum ferritin increased                    |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Cystogram                                   |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Ejection fraction abnormal                  |                 |                 |
| subjects affected / exposed                 | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                           | 0               | 0               |
| Hepatic enzyme increased                    |                 |                 |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Blood creatine phosphokinase increased         |                 |                 |  |
| subjects affected / exposed                    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 1               | 0               |  |
| Blood creatinine increased                     |                 |                 |  |
| subjects affected / exposed                    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 1               | 0               |  |
| Body temperature increased                     |                 |                 |  |
| subjects affected / exposed                    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 1               | 0               |  |
| Transaminases increased                        |                 |                 |  |
| subjects affected / exposed                    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 1               | 0               |  |
| Injury, poisoning and procedural complications |                 |                 |  |
| Transfusion reaction                           |                 |                 |  |
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Laceration                                     |                 |                 |  |
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Ligament sprain                                |                 |                 |  |
| subjects affected / exposed                    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 1               | 0               |  |
| Eye injury                                     |                 |                 |  |
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Fall   |                 |                 |  |
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Febrile nonhaemolytic transfusion reaction     |                 |                 |  |
| subjects affected / exposed                    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                              | 0               | 0               |  |
| Infusion related reaction                      |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Conjunctival scar                          |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Drug administration error                  |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Post-traumatic pain                        |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Procedural pain                            |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Rib fracture                               |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Arthropod bite                             |                 |                 |  |
| subjects affected / exposed                | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Anaemia postoperative                      |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)                          | 0               | 1               |  |
| Congenital, familial and genetic disorders |                 |                 |  |
| Myotonic dystrophy                         |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Ichthyosis                                 |                 |                 |  |
| subjects affected / exposed                | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 1               | 0               |  |
| Cardiac disorders                          |                 |                 |  |
| Palpitations                               |                 |                 |  |
| subjects affected / exposed                | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                          | 0               | 0               |  |
| Arrhythmia                                 |                 |                 |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Atrial thrombosis           |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Dilatation ventricular      |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Myocardial infarction       |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Cardiomyopathy              |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Tachycardia                 |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Nervous system disorders    |                 |                 |  |
| Neuropathy peripheral       |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Polyneuropathy              |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Post herpetic neuralgia     |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Sciatica                    |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Sinus headache              |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Amnesia                     |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |

|                                |                 |                 |
|--------------------------------|-----------------|-----------------|
| Migraine with aura             |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Syncope                        |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Disturbance in attention       |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Cranial nerve palsies multiple |                 |                 |
| subjects affected / exposed    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)              | 1               | 0               |
| Epilepsy                       |                 |                 |
| subjects affected / exposed    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)              | 1               | 0               |
| Hypoaesthesia                  |                 |                 |
| subjects affected / exposed    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)              | 1               | 0               |
| Restless legs syndrome         |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Dysgeusia                      |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Headache                       |                 |                 |
| subjects affected / exposed    | 3 / 184 (1.63%) | 0 / 247 (0.00%) |
| occurrences (all)              | 3               | 0               |
| Balance disorder               |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Dizziness                      |                 |                 |
| subjects affected / exposed    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)              | 1               | 0               |
| Paraesthesia                   |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| Coordination abnormal<br>subjects affected / exposed<br>occurrences (all)   | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hyperaesthesia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Myoclonus<br>subjects affected / exposed<br>occurrences (all)               | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Nervous system disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Blood and lymphatic system disorders  |                      |                      |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)        | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Eosinophilia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 184 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Aplasia pure red cell<br>subjects affected / exposed<br>occurrences (all)   | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Anaemia macrocytic<br>subjects affected / exposed<br>occurrences (all)      | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Aplastic anaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Histiocytosis haematophagic   |                      |                      |  |

|                                     |                 |                 |  |
|-------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Iron deficiency anaemia             |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Leukopenia                          |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Lymphadenopathy                     |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Normochromic normocytic anaemia     |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Pancytopenia                        |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Splenomegaly                        |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Haemolytic uraemic syndrome         |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Idiopathic thrombocytopenic purpura |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Hypergammaglobulinaemia             |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |
| Ear and labyrinth disorders         |                 |                 |  |
| Ear pain                            |                 |                 |  |
| subjects affected / exposed         | 2 / 184 (1.09%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 2               | 0               |  |
| Vertigo                             |                 |                 |  |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                   | 0               | 0               |  |



|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Tinnitus                    |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Ear discomfort              |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Hearing impaired            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Hypoacusis                  |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Middle ear effusion         |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Tympanic membrane disorder  |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Deafness neurosensory       |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Deafness unilateral         |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Cerumen impaction           |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Ear pruritus                |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Eye disorders               |                 |                 |  |
| Conjunctivitis              |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Dry eye                     |                 |                 |  |

|                                |                 |                 |
|--------------------------------|-----------------|-----------------|
| subjects affected / exposed    | 2 / 184 (1.09%) | 0 / 247 (0.00%) |
| occurrences (all)              | 2               | 0               |
| Allergic keratitis             |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Conjunctival hyperaemia        |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Diabetic retinopathy           |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Eye haemorrhage                |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Eye irritation                 |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Foreign body sensation in eyes |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Keratitis                      |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)              | 0               | 1               |
| Orbital oedema                 |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)              | 0               | 1               |
| Vision blurred                 |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Visual acuity reduced          |                 |                 |
| subjects affected / exposed    | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)              | 0               | 0               |
| Visual impairment              |                 |                 |
| subjects affected / exposed    | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)              | 1               | 0               |
| Vitreous detachment            |                 |                 |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Blindness                   |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Cataract                    |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Periorbital oedema          |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Eye inflammation            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Retinal detachment          |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Xerophthalmia               |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Lacrimation increased       |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Gastrointestinal disorders  |                 |                 |  |
| Diarrhoea                   |                 |                 |  |
| subjects affected / exposed | 3 / 184 (1.63%) | 1 / 247 (0.40%) |  |
| occurrences (all)           | 3               | 1               |  |
| Vomiting                    |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Nausea                      |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 2 / 247 (0.81%) |  |
| occurrences (all)           | 1               | 2               |  |
| Abdominal pain              |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |

|                                  |                 |                 |
|----------------------------------|-----------------|-----------------|
| Abdominal pain upper             |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Stomatitis                       |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Constipation                     |                 |                 |
| subjects affected / exposed      | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Dry mouth                        |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Dysphagia                        |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                | 0               | 1               |
| Gastrooesophageal reflux disease |                 |                 |
| subjects affected / exposed      | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                | 1               | 0               |
| Aphthous stomatitis              |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Dyspepsia                        |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Gastrointestinal pain            |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Haemorrhoids                     |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Oesophagitis                     |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |
| Abdominal pain lower             |                 |                 |
| subjects affected / exposed      | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                | 0               | 0               |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Aptyalism                   |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Ascites                     |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Eructation                  |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Faecaloma                   |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Glossodynia                 |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hyperchlorhydria            |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Lip swelling                |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Mouth ulceration            |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Oral disorder               |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Oral mucosal discolouration |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Oral pain                   |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Tongue coated               |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Tongue discolouration<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Oral lichen planus<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Odynophagia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Sensitivity of teeth<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Gastrointestinal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Gastrointestinal disorder<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Inguinal hernia<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Hepatobiliary disorders<br>Hepatic function abnormal<br>subjects affected / exposed<br>occurrences (all) | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hepatocellular injury<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Hepatomegaly<br>subjects affected / exposed<br>occurrences (all)   | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Cholestasis  |                      |                      |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Skin and subcutaneous tissue disorders           |                      |                      |  |
| Rash   |                      |                      |  |
| subjects affected / exposed                      | 2 / 184 (1.09%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 2                    | 0                    |  |
| Pruritus   |                      |                      |  |
| subjects affected / exposed                      | 1 / 184 (0.54%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                    |  |
| Dry skin   |                      |                      |  |
| subjects affected / exposed                      | 1 / 184 (0.54%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                    |  |
| Eczema   |                      |                      |  |
| subjects affected / exposed                      | 1 / 184 (0.54%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                    |  |
| Erythema   |                      |                      |  |
| subjects affected / exposed                      | 1 / 184 (0.54%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 1                    | 0                    |  |
| Skin lesion                                      |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |
| Acne   |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |
| Rash macular                                     |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |
| Rash papular                                     |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |
| Blister  |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |
| Dermatitis acneiform                             |                      |                      |  |
| subjects affected / exposed                      | 0 / 184 (0.00%)      | 0 / 247 (0.00%)      |  |
| occurrences (all)                                | 0                    | 0                    |  |

|                                       |                 |                 |
|---------------------------------------|-----------------|-----------------|
| Dermatosis                            |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Generalised erythema                  |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Lichenification                       |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Night sweats                          |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Perivascular dermatitis               |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Rash generalised                      |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Rash maculo-papular                   |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Seborrhoeic dermatitis                |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Skin discolouration                   |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Skin hyperpigmentation                |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Skin mass                             |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Acute febrile neutrophilic dermatosis |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |



|   |   |                 |  |
|---|---|-----------------|--|
| Hyperhidrosis                               |   |                 |  |
| subjects affected / exposed                 | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 1   | 0               |  |
| Pityriasis rubra pilaris                    |   |                 |  |
| subjects affected / exposed                 | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Rash pruritic                               |   |                 |  |
| subjects affected / exposed                 | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Dermatitis                                  |   |                 |  |
| subjects affected / exposed                 | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Dermatitis atopic                           |   |                 |  |
| subjects affected / exposed                 | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Angioedema                                  |   |                 |  |
| subjects affected / exposed                 | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 1   | 0               |  |
| Intertrigo                                  |   |                 |  |
| subjects affected / exposed                 | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 1   | 0               |  |
| Pruritus generalised                        |   |                 |  |
| subjects affected / exposed                 | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 1   | 0               |  |
| Urticaria                                   |   |                 |  |
| subjects affected / exposed                 | 1 / 184 (0.54%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 1   | 0               |  |
| Alopecia                                    |   |                 |  |
| subjects affected / exposed                 | 0 / 184 (0.00%)   | 1 / 247 (0.40%) |  |
| occurrences (all)                           | 0   | 1               |  |
| Redness (Any) : 13vPnC Dose 1 and Dose 4    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type: Systematic     |   |                 |  |
| subjects affected / exposed <sup>[83]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                           | 0   | 0               |  |
| Redness (Mild): 13vPnC Dose 1 and Dose 4    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one   |                 |  |

|   |   |                 |
|---|---|-----------------|
| occurrence from another within a subject/vaccination. |   |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[84]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Redness (Moderate): 13vPnC Dose 1 and Dose 4          | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[85]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Redness (Severe): 13vPnC Dose 1 and Dose 4            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[86]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Swelling (Any): 13vPnC Dose 1 and Dose 4              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[87]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Swelling (Mild): 13vPnC Dose 1 and Dose 4             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[88]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Swelling (Moderate): 13vPnC Dose 1 and Dose 4         | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[89]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Swelling (Severe): 13vPnC Dose 1 and Dose 4           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |
| subjects affected / exposed <sup>[90]</sup>           | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                                     | 0   | 0               |
| Pain (Any): 13vPnC Dose 1 and Dose 4                  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic            |   |                 |

|  |   |                      |  |
|--|---|----------------------|--|
| subjects affected / exposed <sup>[91]</sup><br>occurrences (all)   | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Mild): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[92]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Moderate): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[93]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Severe): 13vPnC Dose 1 and Dose 4  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[94]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Redness (Any): 13vPnC Dose 2   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[95]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Redness (Mild): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[96]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Redness (Moderate): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[97]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Redness (Severe): 13vPnC Dose 2  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[98]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |

|  |   |                 |
|--|---|-----------------|
| Swelling (Any): 13vPnC Dose 2                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[99]</sup>  | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Swelling (Mild): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[100]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Swelling (Moderate): 13vPnC Dose 2           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[101]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Pain (Any): 13vPnC Dose 2                    | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[102]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Pain (Mild): 13vPnC Dose 2                   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[103]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Pain (Moderate): 13vPnC Dose 2               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[104]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Pain (Severe): 13vPnC Dose 2                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:<br>Systematic   |   |                 |
| subjects affected / exposed <sup>[105]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |
| occurrences (all)                            | 0   | 0               |
| Redness (Any): 13vPnC Dose 3                 | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |
| alternative assessment type:                 |   |                 |

|  |   |                 |  |
|--|---|-----------------|--|
| Systematic                                   |   |                 |  |
| subjects affected / exposed <sup>[106]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Redness (Mild): 13vPnC Dose 3                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[107]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Redness (Moderate): 13vPnC Dose 3            | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[108]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Redness (Severe): 13vPnC Dose 3              | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[109]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Swelling (Any): 13vPnC Dose 3                | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[110]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Swelling (Mild): 13vPnC Dose 3               | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[111]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Swelling (Moderate): 13vPnC Dose 3           | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |
| subjects affected / exposed <sup>[112]</sup> | 0 / 184 (0.00%)   | 0 / 247 (0.00%) |  |
| occurrences (all)                            | 0   | 0               |  |
| Swelling (Severe): 13vPnC Dose 3             | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                 |  |
| alternative assessment type:<br>Systematic   |   |                 |  |

|   |   |                      |  |
|---|---|----------------------|--|
| subjects affected / exposed <sup>[113]</sup><br>occurrences (all)   | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Any): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[114]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Mild): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[115]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Moderate): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[116]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Pain (Severe): 13vPnC Dose 3  | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[117]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Fatigue (Mild): 13vPnC Dose 3   | Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination. |                      |  |
| alternative assessment type:<br>Systematic<br>subjects affected / exposed <sup>[118]</sup><br>occurrences (all) | 0 / 184 (0.00%)<br>0  | 0 / 247 (0.00%)<br>0 |  |
| Renal and urinary disorders   |   |                      |  |
| Polyuria  |   |                      |  |
| subjects affected / exposed   | 0 / 184 (0.00%)   | 0 / 247 (0.00%)      |  |
| occurrences (all)   | 0   | 0                    |  |
| Renal failure   |   |                      |  |
| subjects affected / exposed   | 0 / 184 (0.00%)   | 0 / 247 (0.00%)      |  |
| occurrences (all)   | 0   | 0                    |  |
| Dysuria   |   |                      |  |
| subjects affected / exposed   | 0 / 184 (0.00%)   | 0 / 247 (0.00%)      |  |
| occurrences (all)   | 0   | 0                    |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Nocturia                    |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Pollakiuria                 |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Haematuria                  |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Incontinence                |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Renal impairment            |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Urethral pain               |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Urinary retention           |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Cystitis haemorrhagic       |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Proteinuria                 |                 |                 |  |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Urinary tract disorder      |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Urine abnormality           |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Endocrine disorders         |                 |                 |  |
| Cushingoid                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Hyperthyroidism                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Cushing's syndrome                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Hypothyroidism                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Oestrogen deficiency                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 1               | 0               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Arthralgia                                      |                 |                 |  |
| subjects affected / exposed                     | 3 / 184 (1.63%) | 2 / 247 (0.81%) |  |
| occurrences (all)                               | 3               | 2               |  |
| Muscle spasms                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 184 (0.54%) | 1 / 247 (0.40%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 2 / 184 (1.09%) | 1 / 247 (0.40%) |  |
| occurrences (all)                               | 2               | 1               |  |
| Myalgia   |                 |                 |  |
| subjects affected / exposed                     | 3 / 184 (1.63%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 3               | 0               |  |
| Musculoskeletal pain                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 0               | 0               |  |
| Pain in extremity                               |                 |                 |  |
| subjects affected / exposed                     | 2 / 184 (1.09%) | 0 / 247 (0.00%) |  |
| occurrences (all)                               | 2               | 0               |  |
| Musculoskeletal stiffness                       |                 |                 |  |



|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Bone pain                   |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Flank pain                  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Joint stiffness             |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Muscular weakness           |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Myopathy                    |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Osteonecrosis               |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Osteoporosis                |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Synovial cyst               |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Groin pain                  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Osteopenia                  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Spinal osteoarthritis       |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Tendonitis                  |                 |                 |

|                                   |                 |                 |  |
|-----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |
| Sjogren's syndrome                |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |
| Osteoarthritis                    |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |
| Infections and infestations       |                 |                 |  |
| Nasopharyngitis                   |                 |                 |  |
| subjects affected / exposed       | 9 / 184 (4.89%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 9               | 0               |  |
| Cytomegalovirus infection         |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |
| Upper respiratory tract infection |                 |                 |  |
| subjects affected / exposed       | 3 / 184 (1.63%) | 1 / 247 (0.40%) |  |
| occurrences (all)                 | 3               | 1               |  |
| Herpes zoster                     |                 |                 |  |
| subjects affected / exposed       | 1 / 184 (0.54%) | 2 / 247 (0.81%) |  |
| occurrences (all)                 | 1               | 2               |  |
| Bronchitis                        |                 |                 |  |
| subjects affected / exposed       | 2 / 184 (1.09%) | 1 / 247 (0.40%) |  |
| occurrences (all)                 | 2               | 1               |  |
| Sinusitis                         |                 |                 |  |
| subjects affected / exposed       | 2 / 184 (1.09%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 2               | 0               |  |
| Tonsillitis                       |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |
| Urinary tract infection           |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 1 / 247 (0.40%) |  |
| occurrences (all)                 | 0               | 1               |  |
| Oral fungal infection             |                 |                 |  |
| subjects affected / exposed       | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)                 | 0               | 0               |  |

|                                       |                 |                 |
|---------------------------------------|-----------------|-----------------|
| Rhinitis                              |                 |                 |
| subjects affected / exposed           | 2 / 184 (1.09%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 2               | 0               |
| Escherichia infection                 |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Gastroenteritis                       |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Oral candidiasis                      |                 |                 |
| subjects affected / exposed           | 3 / 184 (1.63%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 3               | 0               |
| Oral herpes                           |                 |                 |
| subjects affected / exposed           | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 1               | 0               |
| Candidiasis                           |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Enterobacter sepsis                   |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Escherichia sepsis                    |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Eye infection                         |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Otitis media                          |                 |                 |
| subjects affected / exposed           | 2 / 184 (1.09%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 2               | 0               |
| Pharyngitis                           |                 |                 |
| subjects affected / exposed           | 2 / 184 (1.09%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 2               | 0               |
| Respiratory syncytial virus infection |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |

|                                     |                 |                 |
|-------------------------------------|-----------------|-----------------|
| Respiratory tract infection         |                 |                 |
| subjects affected / exposed         | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 1               | 0               |
| Viral infection                     |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Adenovirus infection                |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Aspergillosis                       |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Bacterial infection                 |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Catheter site infection             |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Conjunctivitis viral                |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Enterobacter infection              |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Enterococcal sepsis                 |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Epstein-Barr virus infection        |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Escherichia urinary tract infection |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |
| Febrile infection                   |                 |                 |
| subjects affected / exposed         | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                   | 0               | 0               |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Folliculitis                |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Fungal infection            |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Gastroenteritis viral       |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 10              | 0               |
| Genital infection fungal    |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Herpes simplex              |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Infection                   |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Influenza                   |                 |                 |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Laryngitis                  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Mycoplasma infection        |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Pseudomonas infection       |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Respiratory moniliasis      |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Staphylococcal sepsis       |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |

|   |                 |                 |
|---|-----------------|-----------------|
| Systemic candida                        |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Viral upper respiratory tract infection |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Pneumonia                               |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                       | 0               | 1               |
| Acute sinusitis                         |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Bronchitis viral                        |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Fungal skin infection                   |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Hepatitis B                             |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Herpes zoster oticus                    |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Hordeolum                               |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Oesophageal candidiasis                 |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Parainfluenzae virus infection          |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |
| Periorbital cellulitis                  |                 |                 |
| subjects affected / exposed             | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                       | 0               | 0               |

|                                       |                 |                 |
|---------------------------------------|-----------------|-----------------|
| Sepsis                                |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Staphylococcal infection              |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 1 / 247 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Streptococcal urinary tract infection |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Viral pharyngitis                     |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Chronic sinusitis                     |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Herpes virus infection                |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Infected dermal cyst                  |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Lung infection                        |                 |                 |
| subjects affected / exposed           | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 1               | 0               |
| Pharyngotonsillitis                   |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Toxoplasmosis                         |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Viral rhinitis                        |                 |                 |
| subjects affected / exposed           | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 0               | 0               |
| Ear infection                         |                 |                 |
| subjects affected / exposed           | 1 / 184 (0.54%) | 0 / 247 (0.00%) |
| occurrences (all)                     | 1               | 0               |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Gastrointestinal infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Injection site cellulitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 184 (0.54%)<br>1 | 0 / 247 (0.00%)<br>0 |  |
| Trichosporon infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 184 (0.00%)<br>0 | 1 / 247 (0.40%)<br>1 |  |
| Rash pustular<br>subjects affected / exposed<br>occurrences (all)              | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Metabolism and nutrition disorders   |                      |                      |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)         | 1 / 184 (0.54%)<br>1 | 1 / 247 (0.40%)<br>1 |  |
| Fluid retention<br>subjects affected / exposed<br>occurrences (all)            | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)      | 3 / 184 (1.63%)<br>3 | 0 / 247 (0.00%)<br>0 |  |
| Diabetes mellitus<br>subjects affected / exposed<br>occurrences (all)          | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Cachexia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 184 (0.00%)<br>0 | 0 / 247 (0.00%)<br>0 |  |
| Dehydration  |                      |                      |  |



|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Folate deficiency           |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hypercreatininaemia         |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hyperphosphataemia          |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hyperuricaemia              |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hypophosphataemia           |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Metabolic acidosis          |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Vitamin D deficiency        |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Vitamin K deficiency        |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hyperkalaemia               |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Glucose tolerance impaired  |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Haemochromatosis            |                 |                 |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |
| occurrences (all)           | 0               | 0               |
| Hypomagnesaemia             |                 |                 |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 0               | 0               |  |
| Hyperlipidaemia             |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Hypertriglyceridaemia       |                 |                 |  |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 247 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.





Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.



Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.



[113] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[114] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[115] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[116] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[117] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[118] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 20 November 2009 | An exclusion criteria of receipt of advanced therapy medicinal products (ATMP) including gene therapy products, somatic cell therapy products and tissue engineered products at any time before enrollment was added. Clarification regarding administration of unassigned investigational product, relapse of underlying disease and receipt of chemotherapy were added.  |
| 14 February 2012 | An SAE was to be reported to Pfizer within 24 hours of investigator awareness and SAEs occurring to a subject after the study was over were to be reported to the sponsor if the investigator becomes aware of them were added. Addition of the definition of an AE (requiring documentation on CRF) was extended to include medication error and uses outside what was foreseen in the protocol, including overdose, misuse and dependency of the product, it also included drug withdrawal, extravasation, drug interactions, exposure during pregnancy, and exposure via breastfeeding. Addition of pregnancy of subject or partner required completion of the exposure in utero form (EIU) (and EIU Pregnant Partner Release of Information Form as appropriate) and additionally, if the outcome was not a live healthy birth, an SAE form was completed. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported