

**Clinical trial results:**

**A phase I/II, partially blind, randomized, multicentre, age-stratified, dose-range study in healthy females aged 9 - 25 years to assess the safety and immunogenicity of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered intramuscularly according to a 2-dose schedule (0, 2-month or 0, 6-month) when compared to a standard 3-dose schedule of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine**

**Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2007-002777-32 |
| Trial protocol           | DE             |
| Global end of trial date | 18 March 2013  |

**Results information**

|                                |  |
|--------------------------------|--|
| Result version number          | v3 (current)   |
| This version publication date  | 09 May 2021  |
| First version publication date | 04 April 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Minor corrections in safety section.</li></ul> |

**Trial information****Trial identification**

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 110659 |
|-----------------------|--------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00541970 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium,   |
| Public contact               | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 08 January 2014 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 18 March 2013   |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 18 March 2013   |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of the HPV-16/18 L1 VLP AS04 vaccine one month after the last dose when administered at different dosages (20 or 40 µg of each HPV antigen) and on different schedules (0, 2- or 0, 6-months) compared with the standard HPV-16/18 L1 VLP AS04 vaccine administered on a 3-dose schedule (0, 1, 6-months).

To evaluate the reactogenicity of the HPV-16/18 L1 VLP AS04 vaccine when administered at different dosages (20 or 40 µg of each HPV type) and on different schedules (0, 2- or 0, 6-months) with respect to the occurrence, intensity and relationship to vaccination of solicited local and general symptoms reported within 7 days (Days 0 - 6) after each and any vaccination.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine.

For this reason, the vaccinee remained under medical supervision for 30 minutes after vaccination.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 17 October 2007 |
| Long term follow-up planned                               | Yes             |
| Long term follow-up rationale                             | Safety          |
| Long term follow-up duration                              | 60 Months       |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 479 |
| Country: Number of subjects enrolled | Canada: 482  |
| Worldwide total number of subjects   | 961          |
| EEA total number of subjects         | 479          |

Notes:

### Subjects enrolled per age group

|          |   |
|----------|---|
| In utero | 0 |
|----------|---|

|   |     |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 961 |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study included two phases, an active vaccination phase (Months 0-7) followed by a safety follow-up phase (up to the end of the study at Month 60).

### Pre-assignment

Screening details:

The study was run in an open manner for subjects in the groups receiving the Cervarix vaccine on a 3-dose vaccination schedule. For subjects in the group receiving the Cervarix vaccine on a 2-dose vaccination schedule, the study was run in an observer-blind manner until Month 24, and then in an open manner.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 961 |
| Number of subjects completed | 960 |

### Pre-assignment subject non-completion reasons

|                            |                       |
|----------------------------|-----------------------|
| Reason: Number of subjects | Protocol deviation: 1 |
|----------------------------|-----------------------|

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Single blind                   |
| Roles blinded                | Subject                        |

### Arms

|                              |                          |
|------------------------------|--------------------------|
| Are arms mutually exclusive? | Yes                      |
| <b>Arm title</b>             | Cervarix 1/Placebo Group |

Arm description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Cervarix   |
| Investigational medicinal product code |  |
| Other name                             | GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299 |
| Pharmaceutical forms                   | Injection  |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

Intramuscular injection, different dosing /schedule

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

Dosage and administration details:

Intramuscular injection, different dosing /schedule

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Cervarix 1/Placebo/Cervarix 1 Group |
|------------------|-------------------------------------|

**Arm description:**

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Cervarix   |
| Investigational medicinal product code |  |
| Other name                             | GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299 |
| Pharmaceutical forms                   | Injection  |
| Routes of administration               | Intramuscular use  |

**Dosage and administration details:**

Intramuscular injection, different dosing /schedule

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

**Dosage and administration details:**

Intramuscular injection, different dosing /schedule

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Cervarix 2/Placebo/Cervarix 2 Group |
|------------------|-------------------------------------|

**Arm description:**

Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Cervarix   |
| Investigational medicinal product code |  |
| Other name                             | GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299 |
| Pharmaceutical forms                   | Injection  |
| Routes of administration               | Intramuscular use  |

**Dosage and administration details:**

Intramuscular injection, different dosing /schedule

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

**Dosage and administration details:**

Intramuscular injection, different dosing /schedule

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Cervarix 2 Group |
|------------------|------------------|

**Arm description:**

Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

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

**Dosage and administration details:**

Intramuscular injection, different dosing /schedule

|  |  |
|--|--|
| Investigational medicinal product name | Cervarix   |
| Investigational medicinal product code |  |
| Other name                             | GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299 |
| Pharmaceutical forms                   | Injection  |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

Intramuscular injection, different dosing /schedule

| Number of subjects in period 1 <sup>[1]</sup> | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|
|   |                          |                                     |                                     |
| Started                                       | 240                      | 241                                 | 240                                 |
| Month 7                                       | 240                      | 241                                 | 240                                 |
| Month 12                                      | 240                      | 241                                 | 240                                 |
| Month 18                                      | 240                      | 241                                 | 240                                 |
| Month 24                                      | 240                      | 241                                 | 240                                 |
| Month 36                                      | 240                      | 241                                 | 240                                 |
| Month 48                                      | 240                      | 241                                 | 240                                 |
| Completed                                     | 162                      | 164                                 | 158                                 |
| Not completed                                 | 78                       | 77                                  | 82                                  |
| Protocol deviation                            | 78                       | 77                                  | 82                                  |

| Number of subjects in period 1 <sup>[1]</sup> | Cervarix 2 Group |
|---|------------------|
|   |                  |
| Started                                       | 239              |
| Month 7                                       | 239              |
| Month 12                                      | 239              |
| Month 18                                      | 239              |
| Month 24                                      | 239              |
| Month 36                                      | 239              |
| Month 48                                      | 239              |
| Completed                                     | 167              |
| Not completed                                 | 72               |
| Protocol deviation                            | 72               |

Notes:

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

Justification: Although 961 subjects were enrolled, only 960 subjects were vaccinated and started the study.

## Baseline characteristics

### Reporting groups

|  |                                     |
|--|-------------------------------------|
| Reporting group title  | Cervarix 1/Placebo Group            |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 1/Placebo/Cervarix 1 Group |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 2/Placebo/Cervarix 2 Group |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 2 Group                    |
| Reporting group description:<br>Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.                                       |                                     |

| Reporting group values                             | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|
| Number of subjects                                 | 240                      | 241                                 | 240                                 |
| Age categorical<br>Units: Subjects                 |                          |                                     |                                     |
| In utero   |                          |                                     |                                     |
| Preterm newborn infants (gestational age < 37 wks) |                          |                                     |                                     |
| Newborns (0-27 days)                               |                          |                                     |                                     |
| Infants and toddlers (28 days-23 months)           |                          |                                     |                                     |
| Children (2-11 years)                              |                          |                                     |                                     |
| Adolescents (12-17 years)                          |                          |                                     |                                     |
| Adults (18-64 years)                               |                          |                                     |                                     |
| From 65-84 years                                   |                          |                                     |                                     |
| 85 years and over                                  |                          |                                     |                                     |
| Age continuous<br>Units: years                     |                          |                                     |                                     |
| geometric mean                                     | 17.1                     | 17.2                                | 17.3                                |
| standard deviation                                 | ± 4.3                    | ± 4.3                               | ± 4.25                              |
| Gender categorical<br>Units: Subjects              |                          |                                     |                                     |
| Female   | 240                      | 241                                 | 240                                 |
| Male   | 0                        | 0                                   | 0                                   |

| Reporting group values | Cervarix 2 Group | Total |  |
|------------------------|------------------|-------|--|
| Number of subjects     | 239              | 960   |  |

|   |        |     |  |
|---|--------|-----|--|
| Age categorical<br>Units: Subjects                    |        |     |  |
| In utero  |        | 0   |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |        | 0   |  |
| Newborns (0-27 days)                                  |        | 0   |  |
| Infants and toddlers (28 days-23<br>months)           |        | 0   |  |
| Children (2-11 years)                                 |        | 0   |  |
| Adolescents (12-17 years)                             |        | 0   |  |
| Adults (18-64 years)                                  |        | 0   |  |
| From 65-84 years                                      |        | 0   |  |
| 85 years and over                                     |        | 0   |  |
| Age continuous<br>Units: years                        |        |     |  |
| geometric mean  | 17.2   |     |  |
| standard deviation                                    | ± 4.38 | -   |  |
| Gender categorical<br>Units: Subjects                 |        |     |  |
| Female  | 239    | 960 |  |
| Male  | 0      | 0   |  |



## End points

### End points reporting groups

|  |                                     |
|--|-------------------------------------|
| Reporting group title  | Cervarix 1/Placebo Group            |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 1/Placebo/Cervarix 1 Group |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 2/Placebo/Cervarix 2 Group |
| Reporting group description:<br>Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm. |                                     |
| Reporting group title  | Cervarix 2 Group                    |
| Reporting group description:<br>Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.                                       |                                     |

### Primary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

|   |   |
|---|---|
| End point title   | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies <sup>[1]</sup> |
| End point description:<br>Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).   |   |
| End point type  | Primary   |
| End point timeframe:<br>One month after vaccination with the last dose of the Cervarix vaccine (Cervarix 1/Placebo Group: Month 3; Other groups: Month 7).  |   |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed. |   |

| End point values                         | Cervarix 1/Placebo Group  | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group             |
|--|---------------------------|-------------------------------------|-------------------------------------|------------------------------|
| Subject group type                       | Reporting group           | Reporting group                     | Reporting group                     | Reporting group              |
| Number of subjects analysed              | 224                       | 206                                 | 204                                 | 208                          |
| Units: EL.U/mL                           |                           |                                     |                                     |                              |
| geometric mean (confidence interval 95%) |                           |                                     |                                     |                              |
| Anti-HPV-16 [N=224;204;204;208]          | 5844.6 (5259.6 to 6494.7) | 10500.9 (9356.9 to 11784.8)         | 7741.6 (6868.2 to 8726.1)           | 13045.3 (11211.4 to 15179.2) |
| Anti-HPV-18 [N=223;206;204;208]          | 3543.2 (3126.6 to 4015.3) | 5997.5 (5310.9 to 6772.8)           | 4811.4 (4282.7 to 5405.3)           | 5087.1 (4460.2 to 5802.1)    |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with report of any, and grade 3 solicited local symptoms

|                 |  |
|-----------------|--|
| End point title | Number of subjects with report of any, and grade 3 solicited local symptoms <sup>[2]</sup> |
|-----------------|--|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the solicited local symptom irrespective of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling larger than (>) 50 millimeters (mm).

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

End point timeframe:

Within 7 days (Day 0-6) after vaccination.

Notes:

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

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

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 238                      | 239                                 | 238                                 | 238              |
| Units: Subjects             |                          |                                     |                                     |                  |
| Any Pain                    | 222                      | 225                                 | 222                                 | 225              |
| Grade 3 Pain                | 18                       | 27                                  | 26                                  | 35               |
| Any Redness                 | 109                      | 112                                 | 123                                 | 145              |
| Redness > 50 mm             | 3                        | 4                                   | 1                                   | 3                |
| Any Swelling                | 92                       | 88                                  | 83                                  | 118              |
| Swelling > 50 mm            | 4                        | 3                                   | 1                                   | 5                |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with any, grade 3 and related solicited general symptoms

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related solicited general symptoms <sup>[3]</sup> |
|-----------------|--|

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, fever (defined as axillary temperature equal or above ( $\geq$ ) 37.5 degrees Celsius ( $^{\circ}$ C)), gastrointestinal symptoms, which included nausea, vomiting, diarrhoea and/or abdominal pain, headache, myalgia, rash and urticaria. Grade 3 symptoms =

symptoms that prevented normal activity. Grade 3 fever = axillary temperature  $\geq 39^{\circ}\text{C}$ . Grade 3 urticaria = urticaria distributed on at least 4 body areas. Related symptom = symptom assessed by the investigator to be causally related to vaccination.

|  |         |
|--|---------|
| End point type                             | Primary |
| End point timeframe:                       |         |
| Within 7 days (Day 0-6) after vaccination. |         |

Notes:

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

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

| End point values  | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type  | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                                       | 238                      | 239                                 | 238                                 | 238              |
| Units: Subjects   |                          |                                     |                                     |                  |
| Any Arthralgia  | 45                       | 57                                  | 39                                  | 43               |
| Related Arthralgia  | 39                       | 43                                  | 35                                  | 35               |
| Grade 3 Arthralgia  | 0                        | 3                                   | 4                                   | 3                |
| Any Fatigue   | 100                      | 109                                 | 104                                 | 107              |
| Related Fatigue   | 76                       | 82                                  | 87                                  | 83               |
| Grade 3 Fatigue   | 11                       | 4                                   | 5                                   | 8                |
| Any Fever (Axillary Temperature $\geq 37.5^{\circ}\text{C}$ )     | 23                       | 20                                  | 22                                  | 39               |
| Related Fever   | 18                       | 15                                  | 16                                  | 27               |
| Grade 3 Fever (Axillary Temperature $\geq 39.0^{\circ}\text{C}$ ) | 1                        | 0                                   | 1                                   | 0                |
| Any Gastrointestinal Symptoms                                     | 48                       | 48                                  | 36                                  | 68               |
| Related Gastrointestinal Symptoms                                 | 36                       | 43                                  | 27                                  | 50               |
| Grade 3 Gastrointestinal Symptoms                                 | 3                        | 7                                   | 2                                   | 7                |
| Any Headache  | 101                      | 116                                 | 112                                 | 125              |
| Related Headache  | 79                       | 81                                  | 91                                  | 95               |
| Grade 3 Headache  | 9                        | 9                                   | 7                                   | 12               |
| Any Myalgia   | 79                       | 109                                 | 98                                  | 99               |
| Related Myalgia   | 62                       | 87                                  | 75                                  | 77               |
| Grade 3 Myalgia   | 3                        | 9                                   | 6                                   | 7                |
| Any Rash  | 12                       | 12                                  | 10                                  | 15               |
| Related Rash  | 8                        | 9                                   | 8                                   | 9                |
| Grade 3 Rash  | 0                        | 0                                   | 1                                   | 1                |
| Any Urticaria   | 2                        | 4                                   | 4                                   | 5                |
| Related Urticaria   | 1                        | 3                                   | 4                                   | 3                |
| Grade 3 Urticaria   | 0                        | 0                                   | 1                                   | 0                |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies.

|                 |   |
|-----------------|---|
| End point title | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human |
|-----------------|---|

## End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The analysis was performed on the subjects who were administered a 2-dose vaccination schedule.

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

## End point timeframe:

At Month 3, 1 month after the second dose of vaccine or placebo

## Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                         | Cervarix 1/Placebo Group  | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group |  |
|--|---------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type                       | Reporting group           | Reporting group                     | Reporting group                     |  |
| Number of subjects analysed              | 224                       | 206                                 | 203                                 |  |
| Units: EL.U/mL                           |                           |                                     |                                     |  |
| geometric mean (confidence interval 95%) |                           |                                     |                                     |  |
| Anti-HPV-16 [N=224;204;203]              | 5844.6 (5259.6 to 6494.7) | 397.9 (337.4 to 469.2)              | 266.4 (227.2 to 312.4)              |  |
| Anti-HPV-18 [N=223;206;203]              | 3543.2 (3126.6 to 4015.3) | 228.3 (196.7 to 265)                | 181.9 (156.8 to 211.1)              |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

|                 |  |
|-----------------|--|
| End point title | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies |
|-----------------|--|

## End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). Groups were stratified into 3 age strata: 9-14, 15-19 and 20-25 years of age at the time of first vaccination. The 15-19 years age stratum in the group receiving the Cervarix vaccine on a 3-dose vaccination schedule was considered an active comparator.

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

## End point timeframe:

At Month 7, 1 month after the last dose of vaccine or placebo.

| End point values                         | Cervarix 1/Placebo Group  | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group             |
|--|---------------------------|-------------------------------------|-------------------------------------|------------------------------|
| Subject group type                       | Reporting group           | Reporting group                     | Reporting group                     | Reporting group              |
| Number of subjects analysed              | 221                       | 206                                 | 204                                 | 208                          |
| Units: EL.U/mL                           |                           |                                     |                                     |                              |
| geometric mean (confidence interval 95%) |                           |                                     |                                     |                              |
| 9-14 years, Anti-HPV-16 [N=76;62;69;75]  | 2003.9 (1635.7 to 2455)   | 15028.4 (12611.3 to 17908.6)        | 11058.6 (9273.8 to 13186.7)         | 22066.3 (18140.7 to 26841.2) |
| 15-19 years, Anti-HPV-16 [N=72;74;70;66] | 1168.5 (957.4 to 1426.2)  | 10818.7 (8979.8 to 13034.2)         | 7869.6 (6488.9 to 9543.9)           | 12817.4 (9723.2 to 16896.2)  |
| 20-25 years, Anti-HPV-16 [N=73;68;65;67] | 1371.2 (1092.2 to 1721.6) | 7331.4 (5965.2 to 9010.4)           | 5209.2 (4166.5 to 6512.7)           | 7370 (5673.6 to 9573.6)      |
| 9-14 years, Anti-HPV-18 [N=76;64;69;75]  | 1134.3 (922.8 to 1394.3)  | 8085.8 (6654.5 to 9825)             | 5630.7 (4772.1 to 6643.7)           | 7192.9 (5952.6 to 8691.6)    |
| 15-19 years, Anti-HPV-18 [N=72;74;69;66] | 719.8 (571.2 to 907)      | 6170.1 (5046.8 to 7543.5)           | 5039.3 (4283.4 to 5928.5)           | 4907 (3780.8 to 6368.7)      |
| 20-25 years, Anti-HPV-18 [N=72;68;66;67] | 656.5 (514.6 to 837.5)    | 4389.6 (3525.6 to 5465.4)           | 3889.2 (2980.9 to 5074.3)           | 3576.8 (2886.5 to 4432.2)    |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

|   |  |
|---|--|
| End point title   | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies |
| End point description:  |  |
| Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| At Month 12, at Month 18, at Month 24, at Month 36, and at Month 48 during the safety follow-up phase.                                  |  |

| End point values                         | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                       | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed              | 216                      | 198                                 | 195                                 | 198              |
| Units: EL.U/mL                           |                          |                                     |                                     |                  |
| geometric mean (confidence interval 95%) |                          |                                     |                                     |                  |

|  |                             |                              |                              |                              |
|--|-----------------------------|------------------------------|------------------------------|------------------------------|
| Anti-HPV-16 at Month 12<br>[216;191;195;198] | 1064.7 (937.5<br>to 1209.1) | 3256 (2918.8<br>to 3632.1)   | 2438.7 (2167.2<br>to 2744.2) | 4726.7 (4036.8<br>to 5534.6) |
| Anti-HPV-16 at Month 18<br>[212;196;194;197] | 968.1 (845.2<br>to 1109)    | 2229.4 (1983.2<br>to 2506.2) | 1659.1 (1466.9<br>to 1876.4) | 3185.1 (2735.1<br>to 3709.2) |
| Anti-HPV-16 at Month 24<br>[199;184;186;190] | 821.2 (718.5<br>to 938.5)   | 1756.4 (1556.6<br>to 1981.9) | 1285.1 (1139.6<br>to 1449.2) | 2425.9 (2071.1<br>to 2841.5) |
| Anti-HPV-16 at Month 36<br>[166;158;162;153] | 688.3 (592.2<br>to 799.9)   | 1462.2 (1288.8<br>to 1658.8) | 1094 (961.1 to<br>1245.1)    | 2195.4 (1850.8<br>to 2604.1) |
| Anti-HPV-16 at Month 48<br>[160;151;157;148] | 649.5 (556 to<br>758.8)     | 1261.2 (1106.4<br>to 1437.7) | 953.5 (835.5<br>to 1088.2)   | 1892.3 (1594.2<br>to 2246)   |
| Anti-HPV-18 at Month 12<br>[215;193;194;198] | 472.9 (410.5<br>to 544.8)   | 1760.1 (1531.5<br>to 2022.8) | 1426.2 (1250.8<br>to 1626.1) | 1714.5 (1469.7<br>to 2000)   |
| Anti-HPV-18 at Month 18<br>[211;198;193;197] | 389.2 (338.7<br>to 447.2)   | 1025.2 (889 to<br>1182.2)    | 883.1 (774.7<br>to 1006.8)   | 1096.6 (939.4<br>to 1280.1)  |
| Anti-HPV-18 at Month 24<br>[198;186;185;190] | 345.9 (299.3<br>to 399.8)   | 818.2 (706.5<br>to 947.5)    | 674.6 (591.8<br>to 769)      | 866.8 (741.2<br>to 1013.6)   |
| Anti-HPV-18 at Month 36<br>[166;160;162;153] | 302.2 (254.9<br>to 358.2)   | 712.8 (605.4<br>to 839.3)    | 617.9 (532.3<br>to 717.2)    | 874.2 (734.9<br>to 1040)     |
| Anti-HPV-18 at Month 48<br>[160;153;157;148] | 260.4 (218.5<br>to 310.2)   | 626.3 (531 to<br>738.7)      | 517 (446.2 to<br>599.1)      | 723.2 (607.2<br>to 861.4)    |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

|                 |  |
|-----------------|--|
| End point title | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies |
|-----------------|--|

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).

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

End point timeframe:

At Month 7, 1 month after the last dose of vaccine or placebo.

| End point values                         | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group             |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------------------|
| Subject group type                       | Reporting group          | Reporting group                     | Reporting group                     | Reporting group              |
| Number of subjects analysed              | 221                      | 206                                 | 204                                 | 208                          |
| Units: EL.U/mL                           |                          |                                     |                                     |                              |
| geometric mean (confidence interval 95%) |                          |                                     |                                     |                              |
| Anti-HPV-16 [N=221;204;204;208]          | 1483 (1311 to 1677.5)    | 10500.9 (9356.9 to 11784.8)         | 7741.6 (6868.2 to 8726.1)           | 13045.3 (11211.4 to 15179.2) |

|                                 |                        |                           |                           |                           |
|---------------------------------|------------------------|---------------------------|---------------------------|---------------------------|
| Anti-HPV-18 [N=220;206;204;208] | 817.3 (715.6 to 933.4) | 5997.5 (5310.9 to 6772.8) | 4811.4 (4282.7 to 5405.3) | 5087.1 (4460.2 to 5802.1) |
|---------------------------------|------------------------|---------------------------|---------------------------|---------------------------|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents BAS results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 223                      | 221                                 | 221                                 | 225              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| BAS, PRE NORMAL [N=222;219;218;220], M7 NORMAL  | 219                      | 214                                 | 208                                 | 214              |
| BAS, PRE NORMAL [N=222;219;218;220], M7 BELOW   | 0                        | 0                                   | 0                                   | 0                |
| BAS, PRE NORMAL [N=222;219;218;220], M7 ABOVE   | 2                        | 3                                   | 6                                   | 3                |
| BAS, PRE NORMAL [N=222;219;218;220], M7 MISSING | 1                        | 2                                   | 4                                   | 3                |
| BAS, PRE BELOW [N=0;0;1;1], M7 NORMAL           | 0                        | 0                                   | 1                                   | 0                |
| BAS, PRE BELOW [N=0;0;1;1], M7 BELOW            | 0                        | 0                                   | 0                                   | 1                |
| BAS, PRE BELOW [N=0;0;1;1], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| BAS, PRE ABOVE [N=1;2;2;4], M7 NORMAL           | 1                        | 2                                   | 2                                   | 4                |
| BAS, PRE ABOVE [N=1;2;2;4], M7 BELOW            | 0                        | 0                                   | 0                                   | 0                |
| BAS, PRE ABOVE [N=1;2;2;4], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents EOS results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 226                      | 223                                 | 223                                 | 226              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| EOS, PRE NORMAL [N=209;214;212;214], M7 NORMAL  | 203                      | 207                                 | 200                                 | 205              |
| EOS, PRE NORMAL [N=209;214;212;214], M7 BELOW   | 0                        | 0                                   | 0                                   | 0                |
| EOS, PRE NORMAL [N=209;214;212;214], M7 ABOVE   | 5                        | 6                                   | 8                                   | 6                |
| EOS, PRE NORMAL [N=209;214;212;214], M7 MISSING | 1                        | 1                                   | 4                                   | 3                |
| EOS, PRE BELOW [N=1;2;1;0], M7 NORMAL           | 0                        | 1                                   | 0                                   | 0                |
| EOS, PRE BELOW [N=1;2;1;0], M7 BELOW            | 0                        | 1                                   | 1                                   | 0                |
| EOS, PRE BELOW [N=1;2;1;0], M7 ABOVE            | 1                        | 0                                   | 0                                   | 0                |
| EOS, PRE ABOVE [N=16;7;10;12], M7 NORMAL        | 8                        | 3                                   | 3                                   | 7                |
| EOS, PRE ABOVE [N=16;7;10;12], M7 BELOW         | 0                        | 0                                   | 0                                   | 0                |
| EOS, PRE ABOVE [N=16;7;10;12], M7 ABOVE         | 8                        | 3                                   | 7                                   | 5                |
| EOS, PRE ABOVE [N=16;7;10;12], M7 MISSING       | 0                        | 1                                   | 0                                   | 0                |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents CREA results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                 | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                               | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                      | 226                      | 225                                 | 228                                 | 229              |
| Units: Subjects                                  |                          |                                     |                                     |                  |
| CREA, PRE NORMAL [N=215;211;215;218], M7 NORMAL  | 202                      | 200                                 | 210                                 | 206              |
| CREA, PRE NORMAL [N=215;211;215;218], M7 BELOW   | 7                        | 4                                   | 3                                   | 6                |
| CREA, PRE NORMAL [N=215;211;215;218], M7 ABOVE   | 5                        | 7                                   | 1                                   | 4                |
| CREA, PRE NORMAL [N=215;211;215;218], M7 MISSING | 1                        | 0                                   | 1                                   | 2                |
| CREA, PRE BELOW [N=8;7;7;6], M7 NORMAL           | 6                        | 3                                   | 3                                   | 2                |
| CREA, PRE BELOW [N=8;7;7;6], M7 BELOW            | 2                        | 4                                   | 4                                   | 3                |
| CREA, PRE BELOW [N=8;7;7;6], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| CREA, PRE BELOW [N=8;7;7;6], M7 MISSING          | 0                        | 0                                   | 0                                   | 1                |
| CREA, PRE ABOVE [N=3;7;6;5], M7 NORMAL           | 2                        | 4                                   | 4                                   | 2                |
| CREA, PRE ABOVE [N=3;7;6;5], M7 BELOW            | 0                        | 0                                   | 0                                   | 0                |
| CREA, PRE ABOVE [N=3;7;6;5], M7 ABOVE            | 1                        | 3                                   | 2                                   | 3                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents ALT results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 229                      | 227                                 | 229                                 | 233              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| ALT, PRE NORMAL [N=215;219;225;218], M7 NORMAL  | 211                      | 211                                 | 213                                 | 209              |
| ALT, PRE NORMAL [N=215;219;225;218], M7 BELOW   | 3                        | 2                                   | 4                                   | 4                |
| ALT, PRE NORMAL [N=215;219;225;218], M7 ABOVE   | 1                        | 6                                   | 7                                   | 5                |
| ALT, PRE NORMAL [N=215;219;225;218], M7 MISSING | 0                        | 0                                   | 1                                   | 0                |
| ALT, PRE BELOW [N=1;3;1;4], M7 NORMAL           | 0                        | 2                                   | 0                                   | 2                |
| ALT, PRE BELOW [N=1;3;1;4], M7 BELOW            | 1                        | 1                                   | 1                                   | 2                |
| ALT, PRE BELOW [N=1;3;1;4], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| ALT, PRE ABOVE [N=13;5;3;11], M7 NORMAL         | 9                        | 4                                   | 1                                   | 7                |
| ALT, PRE ABOVE [N=13;5;3;11], M7 BELOW          | 0                        | 0                                   | 0                                   | 0                |
| ALT, PRE ABOVE [N=13;5;3;11], M7 ABOVE          | 4                        | 1                                   | 2                                   | 3                |
| ALT, PRE ABOVE [N=13;5;3;11], M7 MISSING        | 0                        | 0                                   | 0                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents Hct results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 229                      | 228                                 | 227                                 | 233              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| Hct, PRE NORMAL [N=215;208;208;217], M7 NORMAL  | 196                      | 193                                 | 189                                 | 208              |
| Hct, PRE NORMAL [N=215;208;208;217], M7 BELOW   | 6                        | 5                                   | 8                                   | 2                |
| Hct, PRE NORMAL [N=215;208;208;217], M7 ABOVE   | 11                       | 8                                   | 7                                   | 6                |
| Hct, PRE NORMAL [N=215;208;208;217], M7 MISSING | 2                        | 2                                   | 4                                   | 1                |
| Hct, PRE BELOW [N=6;7;7;3], M7 NORMAL           | 3                        | 5                                   | 4                                   | 2                |
| Hct, PRE BELOW [N=6;7;7;3], M7 BELOW            | 3                        | 2                                   | 3                                   | 1                |
| Hct, PRE BELOW [N=6;7;7;3], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| Hct, PRE ABOVE [N=8;13;12;13], M7 NORMAL        | 7                        | 8                                   | 10                                  | 7                |
| Hct, PRE ABOVE [N=8;13;12;13], M7 BELOW         | 0                        | 0                                   | 0                                   | 0                |
| Hct, PRE ABOVE [N=8;13;12;13], M7 ABOVE         | 1                        | 5                                   | 2                                   | 6                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents LYM results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 226                      | 223                                 | 223                                 | 227              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| LYM, PRE NORMAL [N=211;211;204;213], M7 NORMAL  | 201                      | 202                                 | 192                                 | 202              |
| LYM, PRE NORMAL [N=211;211;204;213], M7 BELOW   | 3                        | 0                                   | 3                                   | 1                |
| LYM, PRE NORMAL [N=211;211;204;213], M7 ABOVE   | 6                        | 7                                   | 5                                   | 7                |
| LYM, PRE NORMAL [N=211;211;204;213], M7 MISSING | 1                        | 2                                   | 4                                   | 3                |
| LYM, PRE BELOW [N=6;3;5;5], M7 NORMAL           | 4                        | 3                                   | 3                                   | 1                |
| LYM, PRE BELOW [N=6;3;5;5], M7 BELOW            | 2                        | 0                                   | 2                                   | 2                |
| LYM, PRE BELOW [N=6;3;5;5], M7 ABOVE            | 0                        | 0                                   | 0                                   | 2                |
| LYM, PRE ABOVE [N=9;9;14;9], M7 NORMAL          | 5                        | 7                                   | 8                                   | 5                |
| LYM, PRE ABOVE [N=9;9;14;9], M7 BELOW           | 0                        | 0                                   | 1                                   | 0                |
| LYM, PRE ABOVE [N=9;9;14;9], M7 ABOVE           | 4                        | 2                                   | 5                                   | 4                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents MON results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 226                      | 223                                 | 223                                 | 227              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| MON, PRE NORMAL [N=217;211;211;219], M7 NORMAL  | 212                      | 202                                 | 197                                 | 208              |
| MON, PRE NORMAL [N=217;211;211;219], M7 BELOW   | 0                        | 1                                   | 2                                   | 2                |
| MON, PRE NORMAL [N=217;211;211;219], M7 ABOVE   | 4                        | 6                                   | 9                                   | 6                |
| MON, PRE NORMAL [N=217;211;211;219], M7 MISSING | 1                        | 2                                   | 3                                   | 3                |
| MON, PRE BELOW [N=3;2;0;2], M7 NORMAL           | 1                        | 1                                   | 0                                   | 2                |
| MON, PRE BELOW [N=3;2;0;2], M7 BELOW            | 2                        | 1                                   | 0                                   | 0                |
| MON, PRE BELOW [N=3;2;0;2], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| MON, PRE ABOVE [N=6;10;12;6], M7 NORMAL         | 5                        | 6                                   | 6                                   | 4                |
| MON, PRE ABOVE [N=6;10;12;6], M7 BELOW          | 0                        | 0                                   | 0                                   | 0                |
| MON, PRE ABOVE [N=6;10;12;6], M7 ABOVE          | 1                        | 4                                   | 5                                   | 2                |
| MON, PRE ABOVE [N=6;10;12;6], M7 MISSING        | 0                        | 0                                   | 1                                   | 0                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents NEU results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 224                      | 223                                 | 223                                 | 226              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| NEU, PRE NORMAL [N=206;207;202;204], M7 NORMAL  | 184                      | 188                                 | 185                                 | 186              |
| NEU, PRE NORMAL [N=206;207;202;204], M7 BELOW   | 16                       | 16                                  | 9                                   | 9                |
| NEU, PRE NORMAL [N=206;207;202;204], M7 ABOVE   | 5                        | 1                                   | 1                                   | 3                |
| NEU, PRE NORMAL [N=206;207;202;204], M7 MISSING | 1                        | 2                                   | 7                                   | 6                |
| NEU, PRE BELOW [N=11;11;16;19], M7 NORMAL       | 8                        | 6                                   | 9                                   | 15               |
| NEU, PRE BELOW [N=11;11;16;19], M7 BELOW        | 2                        | 4                                   | 7                                   | 3                |
| NEU, PRE BELOW [N=11;11;16;19], M7 ABOVE        | 0                        | 0                                   | 0                                   | 0                |
| NEU, PRE ABOVE [N=7;5;5;3], M7 NORMAL           | 6                        | 5                                   | 5                                   | 1                |
| NEU, PRE ABOVE [N=7;5;5;3], M7 BELOW            | 0                        | 0                                   | 0                                   | 2                |
| NEU, PRE ABOVE [N=7;5;5;3], M7 ABOVE            | 1                        | 0                                   | 0                                   | 0                |
| NEU, PRE BELOW [N=11;11;16;19], M7 MISSING      | 1                        | 1                                   | 0                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents RBC results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 229                      | 228                                 | 228                                 | 233              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| RBC, PRE NORMAL [N=214;215;204;225], M7 NORMAL  | 204                      | 204                                 | 196                                 | 213              |
| RBC, PRE NORMAL [N=214;215;204;225], M7 BELOW   | 7                        | 7                                   | 2                                   | 7                |
| RBC, PRE NORMAL [N=214;215;204;225], M7 ABOVE   | 2                        | 3                                   | 2                                   | 3                |
| RBC, PRE NORMAL [N=214;215;204;225], M7 MISSING | 1                        | 1                                   | 4                                   | 2                |
| RBC, PRE BELOW [N=6;6;12;4], M7 NORMAL          | 4                        | 3                                   | 2                                   | 1                |
| RBC, PRE BELOW [N=6;6;12;4], M7 BELOW           | 2                        | 3                                   | 10                                  | 3                |
| RBC, PRE BELOW [N=6;6;12;4], M7 ABOVE           | 0                        | 0                                   | 0                                   | 0                |
| RBC, PRE ABOVE [N=9;7;12;4], M7 NORMAL          | 5                        | 4                                   | 6                                   | 3                |
| RBC, PRE ABOVE [N=9;7;12;4], M7 BELOW           | 0                        | 0                                   | 0                                   | 0                |
| RBC, PRE ABOVE [N=9;7;12;4], M7 ABOVE           | 4                        | 3                                   | 6                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents WBC results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 229                      | 228                                 | 229                                 | 233              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| WBC, PRE NORMAL [N=207;213;211;225], M7 NORMAL  | 197                      | 199                                 | 194                                 | 212              |
| WBC, PRE NORMAL [N=207;213;211;225], M7 BELOW   | 4                        | 9                                   | 5                                   | 9                |
| WBC, PRE NORMAL [N=207;213;211;225], M7 ABOVE   | 5                        | 4                                   | 8                                   | 3                |
| WBC, PRE NORMAL [N=207;213;211;225], M7 MISSING | 1                        | 1                                   | 4                                   | 1                |
| WBC, PRE BELOW [N=8;9;6;4], M7 NORMAL           | 4                        | 5                                   | 3                                   | 3                |
| WBC, PRE BELOW [N=8;9;6;4], M7 BELOW            | 4                        | 4                                   | 3                                   | 1                |
| WBC, PRE BELOW [N=8;9;6;4], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| WBC, PRE ABOVE [N=14;6;12;4], M7 NORMAL         | 10                       | 4                                   | 9                                   | 4                |
| WBC, PRE ABOVE [N=14;6;12;4], M7 BELOW          | 0                        | 0                                   | 0                                   | 0                |
| WBC, PRE ABOVE [N=14;6;12;4], M7 ABOVE          | 4                        | 2                                   | 3                                   | 0                |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed. |
|-----------------|--|

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocrits (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents PLA results.

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

End point timeframe:

At Month 7 (M7)

| End point values                                | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                              | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                     | 226                      | 227                                 | 228                                 | 232              |
| Units: Subjects                                 |                          |                                     |                                     |                  |
| PLA, PRE NORMAL [N=211;210;215;221], M7 NORMAL  | 204                      | 204                                 | 206                                 | 218              |
| PLA, PRE NORMAL [N=211;210;215;221], M7 BELOW   | 1                        | 2                                   | 3                                   | 0                |
| PLA, PRE NORMAL [N=211;210;215;221], M7 ABOVE   | 5                        | 2                                   | 2                                   | 1                |
| PLA, PRE NORMAL [N=211;210;215;221], M7 MISSING | 1                        | 2                                   | 4                                   | 2                |
| PLA, PRE BELOW [N=0;3;0;3], M7 NORMAL           | 0                        | 0                                   | 0                                   | 1                |
| PLA, PRE BELOW [N=0;3;0;3], M7 BELOW            | 0                        | 3                                   | 0                                   | 2                |
| PLA, PRE BELOW [N=0;3;0;3], M7 ABOVE            | 0                        | 0                                   | 0                                   | 0                |
| PLA, PRE ABOVE [N=15;14;13;8], M7 NORMAL        | 9                        | 11                                  | 8                                   | 4                |
| PLA, PRE ABOVE [N=15;14;13;8], M7 BELOW         | 0                        | 0                                   | 0                                   | 0                |
| PLA, PRE ABOVE [N=15;14;13;8], M7 ABOVE         | 6                        | 3                                   | 5                                   | 4                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

|                 |  |
|-----------------|--|
| End point title | Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18) |
|-----------------|--|

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titers greater than or equal to ( $\geq$ ) cut-off value) in the serum of subjects seronegative before vaccination. Assay cut-off was defined as  $\geq 8$  ELISA units per milliliter (EL.U/mL) for HPV-16, and 7 EL.U/mL for HPV-18. Seronegative subjects are subjects who had an antibody concentration below cut-off value. Cut-off values were 8 EL.U/mL for antibody concentrations against HPV-16, and 7 EL.U/mL for antibody concentrations against HPV-18.

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

End point timeframe:

At Month 12, at Month 18, at Month 24, at Month 36, and at Month 48 during the safety follow-up phase.

| End point values                               | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                             | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                    | 216                      | 198                                 | 195                                 | 198              |
| Units: Subjects                                |                          |                                     |                                     |                  |
| Anti-HPV-16 at Month 12<br>[N=216;191;195;198] | 194                      | 162                                 | 172                                 | 169              |
| Anti-HPV-16 at Month 18<br>[N=212;196;194;197] | 192                      | 166                                 | 172                                 | 168              |
| Anti-HPV-16 at Month 24<br>[N=199;184;186;190] | 185                      | 155                                 | 165                                 | 162              |
| Anti-HPV-16 at Month 36<br>[N=166;158;162;153] | 156                      | 135                                 | 146                                 | 135              |
| Anti-HPV-16 at Month 48<br>[N=160;151;157;148] | 149                      | 130                                 | 139                                 | 129              |
| Anti-HPV-18 at Month 12<br>[N=215;193;194;198] | 187                      | 173                                 | 166                                 | 173              |
| Anti-HPV-18 at Month 18<br>[N=211;198;193;197] | 184                      | 177                                 | 166                                 | 173              |
| Anti-HPV-18 at Month 24<br>[N=198;186;185;190] | 173                      | 165                                 | 159                                 | 166              |
| Anti-HPV-18 at Month 36<br>[N=166;160;162;153] | 144                      | 145                                 | 139                                 | 132              |
| Anti-HPV-18 at Month 48<br>[N=160;153;157;148] | 138                      | 139                                 | 135                                 | 129              |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

|                 |  |
|-----------------|--|
| End point title | Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies |
|-----------------|--|

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The assay cut-off for Month 60 was defined as  $\geq 19$  ELISA units per milliliter (EL.U/mL).

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

End point timeframe:

At Month 60 of the safety follow-up phase

| End point values                               | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group          |
|--|--------------------------|-------------------------------------|-------------------------------------|---------------------------|
| Subject group type                             | Reporting group          | Reporting group                     | Reporting group                     | Reporting group           |
| Number of subjects analysed                    | 137                      | 134                                 | 131                                 | 146                       |
| Units: EL.U/mL                                 |                          |                                     |                                     |                           |
| geometric mean (confidence interval 95%)       |                          |                                     |                                     |                           |
| Anti-HPV-16 at Month 60<br>[N=137;132;131;146] | 658 (560.4 to 772.5)     | 1254 (1088.5 to 1444.8)             | 976.1 (846.1 to 1126.1)             | 1858.5 (1586.2 to 2177.6) |
| Anti-HPV-18 at Month 60<br>[N=137;134;131;146] | 269.4 (223 to 325.5)     | 622.2 (519 to 745.9)                | 557.9 (473.7 to 657)                | 745.3 (629.3 to 882.7)    |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

|                 |  |
|-----------------|--|
| End point title | Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18) |
|-----------------|--|

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titers greater than or equal to ( $\geq$ ) cut-off value) in the serum of subjects seronegative before vaccination. Assay cut-off was defined as  $\geq 19$  ELISA units per milliliter (EL.U/mL). Seronegative subjects are subjects who had an antibody concentration below cut-off value.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| At Month 60 of the safety follow-up phase |           |

| End point values                               | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                             | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                    | 130                      | 122                                 | 119                                 | 127              |
| Units: Subjects                                |                          |                                     |                                     |                  |
| Anti-HPV-16 at Month 60<br>[N=130;114;119;127] | 130                      | 114                                 | 119                                 | 127              |
| Anti-HPV-18 at Month 60<br>[N=117;122;116;125] | 116                      | 122                                 | 116                                 | 125              |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with pregnancy outcomes.

|   |   |
|---|---|
| End point title   | Number of subjects with pregnancy outcomes. |
| End point description:  |   |
| Pregnancy outcomes were ectopic pregnancy, elective termination with no apparent congenital anomaly (ACA), elective termination with congenital anomaly (CA), lost to follow up, pregnancy ongoing, spontaneous abortion with no ACA and live infant with no ACA. |   |
| End point type  | Secondary                                   |
| End point timeframe:  |   |
| From Month 0 to Month 48.   |   |

| End point values                 | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|----------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type               | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed      | 23                       | 16                                  | 24                                  | 20               |
| Units: Subjects                  |                          |                                     |                                     |                  |
| Ectopic pregnancy                | 1                        | 0                                   | 0                                   | 0                |
| Elective termination with NO ACA | 5                        | 3                                   | 3                                   | 5                |
| Elective termination with CA     | 0                        | 0                                   | 1                                   | 0                |
| Live infant with NO ACA          | 15                       | 12                                  | 15                                  | 12               |
| Lost to follow up                | 1                        | 0                                   | 0                                   | 0                |
| Pregnancy ongoing                | 0                        | 1                                   | 2                                   | 2                |
| Spontaneous abortion with NO ACA | 1                        | 0                                   | 3                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with pregnancy outcomes.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with pregnancy outcomes. |
|-----------------|---|

End point description:

Pregnancy outcomes were ectopic pregnancy, elective termination with no apparent congenital anomaly (ACA), elective termination with congenital anomaly (CA), lost to follow up, pregnancy ongoing, spontaneous abortion with no ACA and live infant with no ACA.

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

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

| End point values                                  | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                                | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                       | 32                       | 23                                  | 30                                  | 26               |
| Units: Subjects                                   |                          |                                     |                                     |                  |
| Ectopic pregnancy                                 | 1                        | 0                                   | 0                                   | 1                |
| Elective termination NO apparent congenital anom. | 5                        | 6                                   | 4                                   | 6                |
| Elective termination congenital anomaly           | 0                        | 0                                   | 1                                   | 0                |
| Live infant NO apparent congenital anomaly        | 22                       | 16                                  | 22                                  | 18               |
| Lost to follow up                                 | 1                        | 0                                   | 0                                   | 0                |
| Molar pregnancy                                   | 1                        | 0                                   | 0                                   | 0                |
| Spontaneous abortion NO apparent congenital anom. | 2                        | 1                                   | 3                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related unsolicited adverse events (AEs). |
|-----------------|--|

End point description:

An unsolicited adverse event (AE) is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Grade 3 = an event that prevented normal activity. Related = an event assessed by the investigator as causally related to the study vaccination.

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

End point timeframe:

Within 30 days (Day 0-29) after vaccination.

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| Any unsolicited AE(s)       | 83                       | 85                                  | 76                                  | 107              |
| Grade 3 unsolicited AE(s)   | 11                       | 8                                   | 6                                   | 14               |
| Related unsolicited AE(s)   | 26                       | 20                                  | 16                                  | 27               |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with Medically Significant Conditions (MSCs).

|                 |  |
|-----------------|--|
| End point title | Number of subjects with Medically Significant Conditions (MSCs). |
|-----------------|--|

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

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

End point timeframe:

From Month 0 to Month 7.

| End point values                             | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|--|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type                           | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed                  | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects                              |                          |                                     |                                     |                  |
| MSCs reported up to Month 7 [Units:subjects] | 40                       | 48                                  | 45                                  | 42               |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with Medically Significant Conditions (MSCs).

|                 |  |
|-----------------|--|
| End point title | Number of subjects with Medically Significant Conditions |
|-----------------|--|

(MSCs).

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

End point type Secondary

End point timeframe:

From Month 0 to Month 48.

| End point values             | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type           | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed  | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects              |                          |                                     |                                     |                  |
| MSCs reported up to Month 48 | 79                       | 94                                  | 88                                  | 82               |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Medically Significant Conditions (MSCs).

End point title Number of subjects with Medically Significant Conditions (MSCs).

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

End point type Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| MSCs                        | 85                       | 97                                  | 92                                  | 89               |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with New Onset of Autoimmune Diseases (NOADs) |
|-----------------|--|

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

From Month 0 to Month 7.

| End point values             | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type           | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed  | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects              |                          |                                     |                                     |                  |
| NOADs reported up to Month 7 | 1                        | 1                                   | 2                                   | 1                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with New Onset of Autoimmune Diseases (NOADs) |
|-----------------|--|

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

From Month 0 to Month 48.



| End point values              | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type            | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed   | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects               |                          |                                     |                                     |                  |
| NOADs reported up to Month 48 | 3                        | 4                                   | 5                                   | 4                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with New Onset of Autoimmune Diseases (NOADs) |
|-----------------|--|

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| (NOADs)                     | 4                        | 4                                   | 5                                   | 6                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with New Onset of Chronic Diseases (NOCDs) |
|-----------------|---|

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

From Month 0 to Month 7.

| End point values             | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type           | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed  | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects              |                          |                                     |                                     |                  |
| NOCDs reported up to Month 7 | 4                        | 2                                   | 6                                   | 3                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with New Onset of Chronic Diseases (NOCDs) |
|-----------------|---|

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

From Month 0 to Month 48.

| End point values              | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-------------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type            | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed   | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects               |                          |                                     |                                     |                  |
| NOCDs reported up to Month 48 | 8                        | 11                                  | 13                                  | 6                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with New Onset of Chronic Diseases (NOCDs) |
|-----------------|---|

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

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

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| (NOCDS)                     | 8                        | 11                                  | 14                                  | 7                |

## Statistical analyses

No statistical analyses for this end point

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

|  |  |
|--|--|
| End point title  | Number of subjects with serious adverse events (SAEs). |
| End point description:   |  |
| SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity, or are a congenital anomaly/birth defect in the offspring of a study subject. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| From Month 0 to Month 7.   |  |

| End point values            | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| SAE(s) up to Month 7        | 4                        | 4                                   | 4                                   | 2                |

## Statistical analyses

No statistical analyses for this end point

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

|   |  |
|---|--|
| End point title   | Number of subjects with serious adverse events (SAEs). |
| End point description:  |  |
| SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| From Month 0 to Month 48.   |  |

| <b>End point values</b>     | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| SAEs up to Month 48         | 10                       | 13                                  | 19                                  | 13               |

### Statistical analyses

No statistical analyses for this end point

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

|   |   |
|---|---|
| End point title   | Number of subjects with serious adverse events (SAEs) |
| End point description:<br>SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Throughout the study period, from Month 0 to Month 60.  |   |

| <b>End point values</b>     | Cervarix 1/Placebo Group | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|-----------------------------|--------------------------|-------------------------------------|-------------------------------------|------------------|
| Subject group type          | Reporting group          | Reporting group                     | Reporting group                     | Reporting group  |
| Number of subjects analysed | 240                      | 241                                 | 240                                 | 239              |
| Units: Subjects             |                          |                                     |                                     |                  |
| (SAEs)                      | 14                       | 16                                  | 19                                  | 15               |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events: From Month 0 to Month 60. Unsolicited adverse events: Within the 30-day (Days 0-29) follow-up period after vaccination. Solicited symptoms: Within the 7-day (Days 0-6) follow-up period after vaccination.

Adverse event reporting additional description:

3 among the serious adverse events (SAEs) listed below are SAEs reported for the subject's offsprings (Spina bifida, Foetal distress syndrome and Premature baby).

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 10 |
|--------------------|----|

### Reporting groups

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Cervarix 1/Placebo/Cervarix 1 Group |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Cervarix 2/Placebo/Cervarix 2 Group |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Cervarix 2 Group |
|-----------------------|------------------|

Reporting group description:

Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Cervarix 1/Placebo Group |
|-----------------------|--------------------------|

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

| Serious adverse events  | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group |
|---|-------------------------------------|-------------------------------------|------------------|
| Total subjects affected by serious adverse events                   |                                     |                                     |                  |
| subjects affected / exposed   | 16 / 241 (6.64%)                    | 19 / 240 (7.92%)                    | 15 / 239 (6.28%) |
| number of deaths (all causes)                                       | 0                                   | 0                                   | 0                |
| number of deaths resulting from adverse events                      | 0                                   | 0                                   | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                                     |                  |
| Fibroma   |                                     |                                     |                  |
| alternative assessment type: Non-systematic                         |                                     |                                     |                  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Fibrosarcoma                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Malignant melanoma stage IV                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine leiomyoma                               |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Benign hydatidiform mole                        |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Vascular disorders                              |                 |                 |                 |
| Circulatory collapse                            |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Pregnancy, puerperium and perinatal conditions  |                 |                 |                 |
| Abortion spontaneous                            |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Abortion spontaneous incomplete<br>alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 2 / 240 (0.83%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all                                | 0 / 0           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all                                     | 0 / 0           | 0 / 0           | 0 / 0           |
| Ectopic pregnancy<br>alternative assessment type: Non-systematic               |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Foetal distress syndrome<br>alternative assessment type: Non-systematic        |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Pre-eclampsia<br>alternative assessment type: Non-systematic                   |                 |                 |                 |
| subjects affected / exposed  | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Premature baby<br>alternative assessment type: Non-systematic                  |                 |                 |                 |
| subjects affected / exposed  | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Abortion missed<br>alternative assessment type: Non-systematic                 |                 |                 |                 |
| subjects affected / exposed  | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Reproductive system and breast disorders        |                 |                 |                 |
| Adenomyosis                                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Ovarian cyst                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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, thoracic and mediastinal disorders |                 |                 |                 |
| Hyperventilation                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Psychiatric disorders                           |                 |                 |                 |
| Abnormal behaviour                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Anorexia nervosa                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Bulimia nervosa                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Depression<br>alternative assessment type: Non-systematic         |                 |                 |                 |
| subjects affected / exposed                                       | 1 / 241 (0.41%) | 1 / 240 (0.42%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all                   | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all                        | 0 / 0           | 0 / 0           | 0 / 0           |
| Major depression<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed                                       | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Psychotic disorder<br>alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                                       | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Suicide attempt<br>alternative assessment type: Non-systematic    |                 |                 |                 |
| subjects affected / exposed                                       | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Injury, poisoning and procedural complications                    |                 |                 |                 |
| Concussion<br>alternative assessment type: Non-systematic         |                 |                 |                 |
| subjects affected / exposed                                       | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Humerus fracture<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed                                       | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Ligament rupture<br>alternative assessment type: Non-systematic   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Multiple injuries                               |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Road traffic accident                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Tibia fracture                                  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Upper limb fracture                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Contusion                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Fall  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |

|   |                                   |                                   |                                   |
|---|-----------------------------------|-----------------------------------|-----------------------------------|
| Stab wound<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 240 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 239 (0.00%)<br>0 / 0<br>0 / 0 |
| Congenital, familial and genetic disorders<br>Atrial septal defect<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 240 (0.42%)<br>0 / 1<br>0 / 0 | 0 / 239 (0.00%)<br>0 / 0<br>0 / 0 |
| Spina bifida<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 240 (0.42%)<br>0 / 1<br>0 / 0 | 0 / 239 (0.00%)<br>0 / 0<br>0 / 0 |
| Nervous system disorders<br>Basilar artery thrombosis<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all              | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 240 (0.42%)<br>0 / 1<br>0 / 0 | 0 / 239 (0.00%)<br>0 / 0<br>0 / 0 |
| Cerebrovascular accident<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 240 (0.42%)<br>0 / 1<br>0 / 0 | 0 / 239 (0.00%)<br>0 / 0<br>0 / 0 |
| Migraine with aura<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 241 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 240 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 239 (0.42%)<br>0 / 1<br>0 / 0 |
| Gastrointestinal disorders  |                                   |                                   |                                   |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Abdominal pain<br>alternative assessment type: Non-systematic                             |                 |                 |                 |
| subjects affected / exposed   | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Appendix disorder<br>alternative assessment type: Non-systematic                          |                 |                 |                 |
| subjects affected / exposed   | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Umbilical hernia, obstructive<br>alternative assessment type: Non-systematic              |                 |                 |                 |
| subjects affected / exposed   | 2 / 241 (0.83%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Vomiting<br>alternative assessment type: Non-systematic                                   |                 |                 |                 |
| subjects affected / exposed   | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastroenteritis<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastroenteritis viral<br>alternative assessment type: Non-systematic                      |                 |                 |                 |
| subjects affected / exposed   | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Hepatobiliary disorders<br>Bile duct stone<br>alternative assessment type: Non-systematic |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Cholecystitis acute<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed  | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Hepatomegaly<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Skin and subcutaneous tissue disorders<br>Erythema multiforme<br>alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders<br>Cystitis haemorrhagic<br>alternative assessment type: Non-systematic          |                 |                 |                 |
| subjects affected / exposed  | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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 colic<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed  | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal disorder<br>alternative assessment type: Non-systematic  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Basedow's disease                               |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Coccydynia                                      |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Ligament laxity                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Polyarthritis                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| 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                     |                 |                 |                 |
| Acute tonsillitis                               |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Appendicitis                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 2 / 241 (0.83%) | 4 / 240 (1.67%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 4           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endometritis decidual                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Pharyngitis streptococcal                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pilonidal cyst                                  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 0 / 239 (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           |
| Tonsillitis                                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 2 / 239 (0.84%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tonsillitis bacterial                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 1 / 240 (0.42%) | 0 / 239 (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           |
| Urinary tract infection                         |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 241 (0.00%) | 0 / 240 (0.00%) | 1 / 239 (0.42%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Vestibular neuronitis                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 241 (0.41%) | 0 / 240 (0.00%) | 0 / 239 (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>Serious adverse events</b>                                       | Cervarix 1/Placebo Group |  |  |
|---|--------------------------|--|--|
| Total subjects affected by serious adverse events                   |                          |  |  |
| subjects affected / exposed   | 14 / 240 (5.83%)         |  |  |
| number of deaths (all causes)                                       | 0                        |  |  |
| number of deaths resulting from adverse events                      | 0                        |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                          |  |  |
| Fibroma   |                          |  |  |
| alternative assessment type: Non-systematic                         |                          |  |  |
| subjects affected / exposed   | 0 / 240 (0.00%)          |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                    |  |  |
| deaths causally related to treatment / all                          | 0 / 0                    |  |  |
| Fibrosarcoma  |                          |  |  |
| alternative assessment type: Non-systematic                         |                          |  |  |
| subjects affected / exposed   | 0 / 240 (0.00%)          |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                    |  |  |
| deaths causally related to treatment / all                          | 0 / 0                    |  |  |
| Malignant melanoma stage IV   |                          |  |  |
| alternative assessment type: Non-systematic                         |                          |  |  |
| subjects affected / exposed   | 0 / 240 (0.00%)          |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                    |  |  |
| deaths causally related to treatment / all                          | 0 / 0                    |  |  |
| Uterine leiomyoma   |                          |  |  |
| alternative assessment type: Non-systematic                         |                          |  |  |
| subjects affected / exposed   | 1 / 240 (0.42%)          |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                    |  |  |
| deaths causally related to treatment / all                          | 0 / 0                    |  |  |
| Benign hydatidiform mole  |                          |  |  |
| alternative assessment type: Non-systematic                         |                          |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vascular disorders                              |                 |  |  |
| Circulatory collapse                            |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pregnancy, puerperium and perinatal conditions  |                 |  |  |
| Abortion spontaneous                            |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Abortion spontaneous incomplete                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ectopic pregnancy                               |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Foetal distress syndrome                        |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pre-eclampsia                                   |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Premature baby                                  |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Abortion missed                                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Adenomyosis                                     |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ovarian cyst                                    |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Hyperventilation                                |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Abnormal behaviour                              |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Anorexia nervosa                                |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Bulimia nervosa                                 |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Depression                                      |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Major depression                                |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Psychotic disorder                              |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Suicide attempt                                 |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Injury, poisoning and procedural complications  |                 |  |  |
| Concussion                                      |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Humerus fracture                                |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ligament rupture                                |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Multiple injuries                               |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Road traffic accident                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Tibia fracture                                  |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Upper limb fracture                             |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Contusion                                       |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Fall  |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Stab wound                                      |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Congenital, familial and genetic disorders      |                 |  |  |
| Atrial septal defect                            |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Spina bifida                                    |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Basilar artery thrombosis                       |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Cerebrovascular accident                        |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Migraine with aura                              |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Gastrointestinal disorders                      |                 |  |  |  |
| Abdominal pain                                  |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 3 / 240 (1.25%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Appendix disorder                               |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Umbilical hernia, obstructive                   |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Vomiting  |                 |  |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastroenteritis                                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastroenteritis viral                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Bile duct stone                                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cholecystitis acute                             |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatomegaly                                    |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Erythema multiforme                             |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Cystitis haemorrhagic                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal colic                                     |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal disorder                                  |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endocrine disorders                             |                 |  |  |
| Basedow's disease                               |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Coccydynia                                      |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ligament laxity                                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Polyarthrititis                                 |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Acute tonsillitis                               |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Appendicitis                                    |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endometritis decidual                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pharyngitis streptococcal                       |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pilonidal cyst                                  |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Tonsillitis                                     |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Tonsillitis bacterial                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 0 / 240 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary tract infection                         |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vestibular neuronitis                           |                 |  |  |
| alternative assessment type: Non-systematic     |                 |  |  |
| subjects affected / exposed                     | 1 / 240 (0.42%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Cervarix 1/Placebo/Cervarix 1 Group | Cervarix 2/Placebo/Cervarix 2 Group | Cervarix 2 Group   |
|---|-------------------------------------|-------------------------------------|--------------------|
| Total subjects affected by non-serious adverse events |                                     |                                     |                    |
| subjects affected / exposed                           | 233 / 241 (96.68%)                  | 228 / 240 (95.00%)                  | 233 / 239 (97.49%) |
| General disorders and administration site conditions  |                                     |                                     |                    |
| Pain  |                                     |                                     |                    |

|   |                    |                    |                    |
|---|--------------------|--------------------|--------------------|
| subjects affected / exposed                 | 225 / 241 (93.36%) | 222 / 240 (92.50%) | 225 / 239 (94.14%) |
| occurrences (all)                           | 225                | 222                | 225                |
| Redness                                     |                    |                    |                    |
| subjects affected / exposed                 | 112 / 241 (46.47%) | 123 / 240 (51.25%) | 145 / 239 (60.67%) |
| occurrences (all)                           | 112                | 123                | 145                |
| Swelling                                    |                    |                    |                    |
| subjects affected / exposed                 | 88 / 241 (36.51%)  | 83 / 240 (34.58%)  | 118 / 239 (49.37%) |
| occurrences (all)                           | 88                 | 83                 | 118                |
| Arthralgia                                  |                    |                    |                    |
| subjects affected / exposed                 | 57 / 241 (23.65%)  | 39 / 240 (16.25%)  | 43 / 239 (17.99%)  |
| occurrences (all)                           | 57                 | 39                 | 43                 |
| Fatigue                                     |                    |                    |                    |
| alternative assessment type: Non-systematic |                    |                    |                    |
| subjects affected / exposed                 | 109 / 241 (45.23%) | 104 / 240 (43.33%) | 107 / 239 (44.77%) |
| occurrences (all)                           | 109                | 104                | 107                |
| Fever                                       |                    |                    |                    |
| subjects affected / exposed                 | 20 / 241 (8.30%)   | 22 / 240 (9.17%)   | 39 / 239 (16.32%)  |
| occurrences (all)                           | 20                 | 22                 | 39                 |
| Gastrointestinal                            |                    |                    |                    |
| subjects affected / exposed                 | 48 / 241 (19.92%)  | 36 / 240 (15.00%)  | 68 / 239 (28.45%)  |
| occurrences (all)                           | 48                 | 36                 | 68                 |
| Headache                                    |                    |                    |                    |
| subjects affected / exposed                 | 116 / 241 (48.13%) | 112 / 240 (46.67%) | 125 / 239 (52.30%) |
| occurrences (all)                           | 116                | 112                | 125                |
| Rash  |                    |                    |                    |
| alternative assessment type: Non-systematic |                    |                    |                    |
| subjects affected / exposed                 | 12 / 241 (4.98%)   | 10 / 240 (4.17%)   | 15 / 239 (6.28%)   |
| occurrences (all)                           | 12                 | 10                 | 15                 |
| Gastrointestinal disorders                  |                    |                    |                    |
| Myalgia                                     |                    |                    |                    |
| subjects affected / exposed                 | 109 / 241 (45.23%) | 98 / 240 (40.83%)  | 99 / 239 (41.42%)  |
| occurrences (all)                           | 109                | 98                 | 99                 |
| Infections and infestations                 |                    |                    |                    |
| Nasopharyngitis                             |                    |                    |                    |
| alternative assessment type: Non-systematic |                    |                    |                    |

|                             |                  |                 |                  |
|-----------------------------|------------------|-----------------|------------------|
| subjects affected / exposed | 11 / 241 (4.56%) | 9 / 240 (3.75%) | 15 / 239 (6.28%) |
| occurrences (all)           | 11               | 9               | 15               |

| <b>Non-serious adverse events</b>                     | Cervarix 1/Placebo Group |  |  |
|---|--------------------------|--|--|
| Total subjects affected by non-serious adverse events |                          |  |  |
| subjects affected / exposed                           | 229 / 240 (95.42%)       |  |  |
| General disorders and administration site conditions  |                          |  |  |
| Pain  |                          |  |  |
| subjects affected / exposed                           | 222 / 240 (92.50%)       |  |  |
| occurrences (all)                                     | 222                      |  |  |
| Redness   |                          |  |  |
| subjects affected / exposed                           | 109 / 240 (45.42%)       |  |  |
| occurrences (all)                                     | 109                      |  |  |
| Swelling  |                          |  |  |
| subjects affected / exposed                           | 92 / 240 (38.33%)        |  |  |
| occurrences (all)                                     | 92                       |  |  |
| Arthralgia  |                          |  |  |
| subjects affected / exposed                           | 45 / 240 (18.75%)        |  |  |
| occurrences (all)                                     | 45                       |  |  |
| Fatigue   |                          |  |  |
| alternative assessment type: Non-systematic           |                          |  |  |
| subjects affected / exposed                           | 100 / 240 (41.67%)       |  |  |
| occurrences (all)                                     | 100                      |  |  |
| Fever   |                          |  |  |
| subjects affected / exposed                           | 23 / 240 (9.58%)         |  |  |
| occurrences (all)                                     | 23                       |  |  |
| Gastrointestinal                                      |                          |  |  |
| subjects affected / exposed                           | 48 / 240 (20.00%)        |  |  |
| occurrences (all)                                     | 48                       |  |  |
| Headache  |                          |  |  |
| subjects affected / exposed                           | 101 / 240 (42.08%)       |  |  |
| occurrences (all)                                     | 101                      |  |  |
| Rash  |                          |  |  |
| alternative assessment type: Non-systematic           |                          |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)  | 12 / 240 (5.00%)<br>12  |  |  |
| Gastrointestinal disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 79 / 240 (32.92%)<br>79 |  |  |
| Infections and infestations<br>Nasopharyngitis<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 10 / 240 (4.17%)<br>10  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 22 June 2009 | <p>Amendment 1</p> <ul style="list-style-type: none"><li>• In the purpose of collecting long-term immunogenicity and safety data for the HPV-16/18 L1 VLP AS04 vaccine in an alternative 2-dose schedule versus the 3-dose schedule, the study was extended by three years to include three additional visits planned for Months 36, 48 and 60.</li><li>• The protocol was amended to allow subjects who miss one or more follow-up study visits to be invited to attend the next visit.</li><li>• Administrative changes were made.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported