



## Clinical trial results:

### A Phase IIa Randomized, Double-Blinded, Controlled With GARDASIL™ Clinical Trial to Study the Tolerability and Immunogenicity of V505 (a Multivalent Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] Vaccine) in Healthy 16- to 26-Year-Old Women

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-000108-42 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 16 May 2011    |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 10 March 2017 |
| First version publication date | 10 March 2017 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | v505-001 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00520598 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                              |
|------------------------------|----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.                                                                    |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.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                       | 16 May 2011 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 16 May 2011 |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 16 May 2011 |
| Was the trial ended prematurely?                     | No          |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and immunogenicity of V505 in comparison with GARDASIL™. The primary hypothesis of the study is that administration of a 3-dose regimen of at least 1 of 2 formulations of V505 generates anti-HPV 6, 11, 16, and 18 geometric mean antibody titers 4 weeks post dose 3 that are noninferior to those generated by GARDASIL™ in 16- to 26-year old adolescent and young adult women who are seronegative at Day 1 and polymerase chain reaction (PCR) negative Day 1 through Month 7 to the relevant HPV type(s) and the vaccines are well-tolerated.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 18 October 2007 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Australia: 212   |
| Country: Number of subjects enrolled | New Zealand: 299 |
| Worldwide total number of subjects   | 511              |
| EEA total number of subjects         | 0                |

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)                 | 65  |
| Adults (18-64 years)                      | 446 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Twelve clinical sites participated in this study in Australia and New Zealand.

### Pre-assignment

Screening details:

A total of 529 participants were screened for inclusion in this study and 511 participants were randomized. A total of 17 non-randomized participants did not meet inclusion/exclusion criteria.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Day 1 Through Month 7   |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | V505 Formulation 1 Vaccine [3 doses] |
|------------------|--------------------------------------|

Arm description:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | V505 Formulation 1 vaccine |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use          |

Dosage and administration details:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | V505 Formulation 2 Vaccine [3 doses] |
|------------------|--------------------------------------|

Arm description:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | V505 Formulation 2 vaccine |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use          |

Dosage and administration details:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | V505 Formulation 2 Vaccine [2 doses] |
|------------------|--------------------------------------|

Arm description:

V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)

|                                        |                          |
|----------------------------------------|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Placebo to vaccine       |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

|                                                                                          |                                      |
|------------------------------------------------------------------------------------------|--------------------------------------|
| Dosage and administration details:                                                       |                                      |
| Placebo vaccine [1 dose] intramuscular (Month 2)                                         |                                      |
| Investigational medicinal product name                                                   | V505 Formulation 2 vaccine           |
| Investigational medicinal product code                                                   |                                      |
| Other name                                                                               |                                      |
| Pharmaceutical forms                                                                     | Suspension for injection             |
| Routes of administration                                                                 | Intramuscular use                    |
| Dosage and administration details:                                                       |                                      |
| V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                 |                                      |
| <b>Arm title</b>                                                                         | V505 Formulation 3 Vaccine [2 doses] |
| Arm description:                                                                         |                                      |
| V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                 |                                      |
| Arm type                                                                                 | Experimental                         |
| Investigational medicinal product name                                                   | Placebo to vaccine                   |
| Investigational medicinal product code                                                   |                                      |
| Other name                                                                               |                                      |
| Pharmaceutical forms                                                                     | Suspension for injection             |
| Routes of administration                                                                 | Intramuscular use                    |
| Dosage and administration details:                                                       |                                      |
| Placebo vaccine [1 dose] intramuscular (Month 2)                                         |                                      |
| Investigational medicinal product name                                                   | V505 Formulation 3 vaccine           |
| Investigational medicinal product code                                                   |                                      |
| Other name                                                                               |                                      |
| Pharmaceutical forms                                                                     | Suspension for injection             |
| Routes of administration                                                                 | Intramuscular use                    |
| Dosage and administration details:                                                       |                                      |
| V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                 |                                      |
| <b>Arm title</b>                                                                         | qHPV Vaccine [3 doses]               |
| Arm description:                                                                         |                                      |
| HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)  |                                      |
| Arm type                                                                                 | Active comparator                    |
| Investigational medicinal product name                                                   | qHPV Vaccine                         |
| Investigational medicinal product code                                                   |                                      |
| Other name                                                                               | GARDASIL™                            |
| Pharmaceutical forms                                                                     | Suspension for injection             |
| Routes of administration                                                                 | Intramuscular use                    |
| Dosage and administration details:                                                       |                                      |
| HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™) [3 doses] (Day 1, Month 2, and Month 6) |                                      |

| <b>Number of subjects in period 1</b> | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 Vaccine [3 doses] | V505 Formulation 2 Vaccine [2 doses] |
|---------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Started                               | 101                                  | 105                                  | 103                                  |
| Vaccination 1                         | 101                                  | 105                                  | 103                                  |
| Vaccination 2                         | 99                                   | 102                                  | 102                                  |
| Vaccination 3                         | 98                                   | 101                                  | 99                                   |
| Completed                             | 97                                   | 101                                  | 97                                   |
| Not completed                         | 4                                    | 4                                    | 6                                    |

|                              |   |   |   |
|------------------------------|---|---|---|
| Consent withdrawn by subject | - | 3 | 2 |
| Lost to follow-up            | 4 | 1 | 4 |

| Number of subjects in period 1 | V505 Formulation 3 Vaccine [2 doses] | qHPV Vaccine [3 doses] |
|--------------------------------|--------------------------------------|------------------------|
| Started                        | 101                                  | 101                    |
| Vaccination 1                  | 101                                  | 101                    |
| Vaccination 2                  | 101                                  | 99                     |
| Vaccination 3                  | 100                                  | 96                     |
| Completed                      | 100                                  | 96                     |
| Not completed                  | 1                                    | 5                      |
| Consent withdrawn by subject   | 1                                    | 1                      |
| Lost to follow-up              | -                                    | 4                      |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Month 7 to Month 36     |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

## Arms

|                              |                                      |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes                                  |
| <b>Arm title</b>             | V505 Formulation 1 Vaccine [3 doses] |

Arm description:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | V505 Formulation 1 vaccine |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use          |

Dosage and administration details:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | V505 Formulation 2 Vaccine [3 doses] |
|------------------|--------------------------------------|

Arm description:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | V505 Formulation 2 vaccine |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use          |

Dosage and administration details:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                                                                                         |                                      |
|-----------------------------------------------------------------------------------------|--------------------------------------|
| <b>Arm title</b>                                                                        | V505 Formulation 2 Vaccine [2 doses] |
| Arm description:                                                                        |                                      |
| V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Arm type                                                                                | Experimental                         |
| Investigational medicinal product name                                                  | Placebo to vaccine                   |
| Investigational medicinal product code                                                  |                                      |
| Other name                                                                              |                                      |
| Pharmaceutical forms                                                                    | Suspension for injection             |
| Routes of administration                                                                | Intramuscular use                    |
| Dosage and administration details:                                                      |                                      |
| Placebo vaccine [1 dose] intramuscular (Month 2)                                        |                                      |
| Investigational medicinal product name                                                  | V505 Formulation 2 vaccine           |
| Investigational medicinal product code                                                  |                                      |
| Other name                                                                              |                                      |
| Pharmaceutical forms                                                                    | Suspension for injection             |
| Routes of administration                                                                | Intramuscular use                    |
| Dosage and administration details:                                                      |                                      |
| V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| <b>Arm title</b>                                                                        | V505 Formulation 3 Vaccine [2 doses] |
| Arm description:                                                                        |                                      |
| V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Arm type                                                                                | Experimental                         |
| Investigational medicinal product name                                                  | V505 Formulation 3 vaccine           |
| Investigational medicinal product code                                                  |                                      |
| Other name                                                                              |                                      |
| Pharmaceutical forms                                                                    | Suspension for injection             |
| Routes of administration                                                                | Intramuscular use                    |
| Dosage and administration details:                                                      |                                      |
| V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Investigational medicinal product name                                                  | Placebo to vaccine                   |
| Investigational medicinal product code                                                  |                                      |
| Other name                                                                              |                                      |
| Pharmaceutical forms                                                                    | Suspension for injection             |
| Routes of administration                                                                | Intramuscular use                    |
| Dosage and administration details:                                                      |                                      |
| Placebo vaccine [1 dose] intramuscular (Month 2)                                        |                                      |
| <b>Arm title</b>                                                                        | qHPV Vaccine [3 doses]               |
| Arm description:                                                                        |                                      |
| HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6) |                                      |
| Arm type                                                                                | Active comparator                    |
| Investigational medicinal product name                                                  | qHPV Vaccine                         |
| Investigational medicinal product code                                                  |                                      |
| Other name                                                                              | GARDASIL™                            |
| Pharmaceutical forms                                                                    | Suspension for injection             |
| Routes of administration                                                                | Intramuscular use                    |
| Dosage and administration details:                                                      |                                      |
| HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6) |                                      |

| <b>Number of subjects in period 2</b> | V505 Formulation 1<br>Vaccine [3 doses] | V505 Formulation 2<br>Vaccine [3 doses] | V505 Formulation 2<br>Vaccine [2 doses] |
|---------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Started                               | 97                                      | 101                                     | 97                                      |
| Completed                             | 92                                      | 95                                      | 91                                      |
| Not completed                         | 5                                       | 6                                       | 6                                       |
| Consent withdrawn by subject          | 3                                       | 1                                       | -                                       |
| Study Terminated By Sponsor           | -                                       | -                                       | -                                       |
| Lost to follow-up                     | 2                                       | 5                                       | 6                                       |

| <b>Number of subjects in period 2</b> | V505 Formulation 3<br>Vaccine [2 doses] | qHPV Vaccine [3<br>doses] |
|---------------------------------------|-----------------------------------------|---------------------------|
| Started                               | 100                                     | 96                        |
| Completed                             | 92                                      | 82                        |
| Not completed                         | 8                                       | 14                        |
| Consent withdrawn by subject          | 1                                       | 6                         |
| Study Terminated By Sponsor           | 1                                       | -                         |
| Lost to follow-up                     | 6                                       | 8                         |



## Baseline characteristics

### Reporting groups

|                              |                                                                                         |
|------------------------------|-----------------------------------------------------------------------------------------|
| Reporting group title        | V505 Formulation 1 Vaccine [3 doses]                                                    |
| Reporting group description: | V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |
| Reporting group title        | V505 Formulation 2 Vaccine [3 doses]                                                    |
| Reporting group description: | V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |
| Reporting group title        | V505 Formulation 2 Vaccine [2 doses]                                                    |
| Reporting group description: | V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                |
| Reporting group title        | V505 Formulation 3 Vaccine [2 doses]                                                    |
| Reporting group description: | V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                |
| Reporting group title        | qHPV Vaccine [3 doses]                                                                  |
| Reporting group description: | HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6) |

| Reporting group values                | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 Vaccine [3 doses] | V505 Formulation 2 Vaccine [2 doses] |
|---------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Number of subjects                    | 101                                  | 105                                  | 103                                  |
| Age Categorical<br>Units: Subjects    |                                      |                                      |                                      |
| Adolescents (12-17 years)             | 17                                   | 15                                   | 10                                   |
| Adults (18-64 years)                  | 84                                   | 90                                   | 93                                   |
| Age Continuous<br>Units: years        |                                      |                                      |                                      |
| arithmetic mean                       | 20.6                                 | 20.6                                 | 20.5                                 |
| standard deviation                    | ± 2.8                                | ± 2.6                                | ± 2.5                                |
| Gender Categorical<br>Units: Subjects |                                      |                                      |                                      |
| Female                                | 101                                  | 105                                  | 103                                  |
| Male                                  | 0                                    | 0                                    | 0                                    |

| Reporting group values                | V505 Formulation 3 Vaccine [2 doses] | qHPV Vaccine [3 doses] | Total |
|---------------------------------------|--------------------------------------|------------------------|-------|
| Number of subjects                    | 101                                  | 101                    | 511   |
| Age Categorical<br>Units: Subjects    |                                      |                        |       |
| Adolescents (12-17 years)             | 10                                   | 13                     | 65    |
| Adults (18-64 years)                  | 91                                   | 88                     | 446   |
| Age Continuous<br>Units: years        |                                      |                        |       |
| arithmetic mean                       | 21                                   | 20.4                   | -     |
| standard deviation                    | ± 2.5                                | ± 2.6                  | -     |
| Gender Categorical<br>Units: Subjects |                                      |                        |       |
| Female                                | 101                                  | 101                    | 511   |
| Male                                  | 0                                    | 0                      | 0     |



## End points

### End points reporting groups

|                                                                                                                         |                                      |
|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                   | V505 Formulation 1 Vaccine [3 doses] |
| Reporting group description:<br>V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |                                      |
| Reporting group title                                                                                                   | V505 Formulation 2 Vaccine [3 doses] |
| Reporting group description:<br>V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |                                      |
| Reporting group title                                                                                                   | V505 Formulation 2 Vaccine [2 doses] |
| Reporting group description:<br>V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Reporting group title                                                                                                   | V505 Formulation 3 Vaccine [2 doses] |
| Reporting group description:<br>V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Reporting group title                                                                                                   | qHPV Vaccine [3 doses]               |
| Reporting group description:<br>HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6) |                                      |
| Reporting group title                                                                                                   | V505 Formulation 1 Vaccine [3 doses] |
| Reporting group description:<br>V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |                                      |
| Reporting group title                                                                                                   | V505 Formulation 2 Vaccine [3 doses] |
| Reporting group description:<br>V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)                          |                                      |
| Reporting group title                                                                                                   | V505 Formulation 2 Vaccine [2 doses] |
| Reporting group description:<br>V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Reporting group title                                                                                                   | V505 Formulation 3 Vaccine [2 doses] |
| Reporting group description:<br>V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                                |                                      |
| Reporting group title                                                                                                   | qHPV Vaccine [3 doses]               |
| Reporting group description:<br>HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6) |                                      |
| Subject analysis set title                                                                                              | V505 Formulation 1 Vaccine [3 doses] |
| Subject analysis set type                                                                                               | Full analysis                        |
| Subject analysis set description:<br>V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)                     |                                      |
| Subject analysis set title                                                                                              | V505 Formulation 2 Vaccine [3 doses] |
| Subject analysis set type                                                                                               | Full analysis                        |
| Subject analysis set description:<br>V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)                     |                                      |
| Subject analysis set title                                                                                              | V505 Formulation 2 Vaccine [2 doses] |
| Subject analysis set type                                                                                               | Full analysis                        |
| Subject analysis set description:<br>V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)                           |                                      |
| Subject analysis set title                                                                                              | V505 Formulation 3 Vaccine [2 doses] |
| Subject analysis set type                                                                                               | Full analysis                        |
| Subject analysis set description:<br>V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)                           |                                      |
| Subject analysis set title                                                                                              | qHPV Vaccine [3 doses]               |

|                                                                                          |               |
|------------------------------------------------------------------------------------------|---------------|
| Subject analysis set type                                                                | Full analysis |
| Subject analysis set description:                                                        |               |
| HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™) [3 doses] (Day 1, Month 2, and Month 6) |               |

### Primary: Percentage of participants with injection-site adverse events

|                 |                                                                              |
|-----------------|------------------------------------------------------------------------------|
| End point title | Percentage of participants with injection-site adverse events <sup>[1]</sup> |
|-----------------|------------------------------------------------------------------------------|

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. Vaccination Report Cards were used to collect these AEs. The safety population included all participants who received at least 1 study vaccination and had follow-up data. Participants were summarized according to the clinical material received.

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

End point timeframe:

Day 1 to Day 5 following any vaccination

Notes:

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

Justification: No statistical analysis was planned or performed for this end point.

| End point values                  | V505<br>Formulation 1<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [2<br>doses] | V505<br>Formulation 3<br>Vaccine [2<br>doses] |
|-----------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Subject group type                | Subject analysis set                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set                          |
| Number of subjects analysed       | 101                                           | 105                                           | 102                                           | 100                                           |
| Units: Percentage of participants |                                               |                                               |                                               |                                               |
| number (not applicable)           | 97                                            | 100                                           | 98                                            | 100                                           |

| End point values                  | qHPV Vaccine<br>[3 doses] |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type                | Subject analysis set      |  |  |  |
| Number of subjects analysed       | 99                        |  |  |  |
| Units: Percentage of participants |                           |  |  |  |
| number (not applicable)           | 88.9                      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of participants with maximum temperatures (oral or oral equivalent $\geq 37.8$ °C [100.0 °F])

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Percentage of participants with maximum temperatures (oral or oral equivalent $\geq 37.8$ °C [100.0 °F]) |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

Multiple occurrences of maximum temperature were counted only once. Non-oral temperatures were converted to oral equivalent. Vaccination Report Cards were used to collect these AEs. The safety population included all participants who received at least 1 study vaccination and had follow-up data. Participants were summarized according to the clinical material received.

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

End point timeframe:

Day 1 to Day 5 following any vaccination.

| End point values                  | V505<br>Formulation 1<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [2<br>doses] | V505<br>Formulation 3<br>Vaccine [2<br>doses] |
|-----------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Subject group type                | Subject analysis set                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set                          |
| Number of subjects analysed       | 101                                           | 105                                           | 101                                           | 100                                           |
| Units: Percentage of participants |                                               |                                               |                                               |                                               |
| number (not applicable)           | 8.9                                           | 12.4                                          | 8.9                                           | 7                                             |

| End point values                  | qHPV Vaccine<br>[3 doses] |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type                | Subject analysis set      |  |  |  |
| Number of subjects analysed       | 99                        |  |  |  |
| Units: Percentage of participants |                           |  |  |  |
| number (not applicable)           | 6.1                       |  |  |  |

## Statistical analyses

| Statistical analysis title                                           | Difference in % vs qHPV Vaccine                               |
|----------------------------------------------------------------------|---------------------------------------------------------------|
| Statistical analysis description:<br>Difference in % vs qHPV Vaccine |                                                               |
| Comparison groups                                                    | V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                              | 200                                                           |
| Analysis specification                                               | Pre-specified                                                 |
| Analysis type                                                        | equivalence                                                   |
| P-value                                                              | = 0.445                                                       |
| Method                                                               | Miettinen & Nurminen method                                   |
| Parameter estimate                                                   | Difference in % vs qHPV Vaccine                               |
| Point estimate                                                       | 2.9                                                           |
| Confidence interval                                                  |                                                               |
| level                                                                | 95 %                                                          |
| sides                                                                | 2-sided                                                       |
| lower limit                                                          | -4.9                                                          |
| upper limit                                                          | 10.9                                                          |

| Statistical analysis title                                           | Difference in % vs qHPV Vaccine                        |
|----------------------------------------------------------------------|--------------------------------------------------------|
| Statistical analysis description:<br>Difference in % vs qHPV Vaccine |                                                        |
| Comparison groups                                                    | V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 |

|                                         |                                 |
|-----------------------------------------|---------------------------------|
|                                         | doses]                          |
| Number of subjects included in analysis | 204                             |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | equivalence                     |
| P-value                                 | = 0.121                         |
| Method                                  | Miettinen & Nurminen method     |
| Parameter estimate                      | Difference in % vs qHPV Vaccine |
| Point estimate                          | 6.3                             |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| sides                                   | 2-sided                         |
| lower limit                             | -1.8                            |
| upper limit                             | 14.8                            |

|                                                                      |                                                               |
|----------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                    | Difference in % vs qHPV Vaccine                               |
| Statistical analysis description:<br>Difference in % vs qHPV Vaccine |                                                               |
| Comparison groups                                                    | V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                              | 200                                                           |
| Analysis specification                                               | Pre-specified                                                 |
| Analysis type                                                        | equivalence                                                   |
| P-value                                                              | = 0.445                                                       |
| Method                                                               | Miettinen & Nurminen method                                   |
| Parameter estimate                                                   | Difference in % vs qHPV Vaccine                               |
| Point estimate                                                       | 2.9                                                           |
| Confidence interval                                                  |                                                               |
| level                                                                | 95 %                                                          |
| sides                                                                | 2-sided                                                       |
| lower limit                                                          | -4.9                                                          |
| upper limit                                                          | 10.9                                                          |

|                                                                      |                                                               |
|----------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                    | Difference in % vs qHPV Vaccine                               |
| Statistical analysis description:<br>Difference in % vs qHPV Vaccine |                                                               |
| Comparison groups                                                    | V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                              | 199                                                           |
| Analysis specification                                               | Pre-specified                                                 |
| Analysis type                                                        | equivalence                                                   |
| P-value                                                              | = 0.789                                                       |
| Method                                                               | Miettinen & Nurminen method                                   |
| Parameter estimate                                                   | Difference in % vs qHPV Vaccine                               |
| Point estimate                                                       | 0.9                                                           |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -6.6    |
| upper limit         | 8.5     |

### Primary: Geometric mean titers (GMTs) to HPV 6 in the vaccines administered in a 3-dose regimen

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Geometric mean titers (GMTs) to HPV 6 in the vaccines administered in a 3-dose regimen |
| End point description:<br>GMT (milli Merck Units/mL [mMU/mL]) for all participants who completed a 3-dose vaccination series. The per-protocol immunogenicity population (PPI) included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. |                                                                                        |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                                                |
| End point timeframe:<br>Month 7 (1 month post-dose 3)                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                        |

| End point values                         | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 Vaccine [3 doses] | qHPV Vaccine [3 doses] |  |
|------------------------------------------|--------------------------------------|--------------------------------------|------------------------|--|
| Subject group type                       | Subject analysis set                 | Subject analysis set                 | Subject analysis set   |  |
| Number of subjects analysed              | 68                                   | 70                                   | 65                     |  |
| Units: Milli Merck units (mMU)/mL        |                                      |                                      |                        |  |
| geometric mean (confidence interval 95%) | 2257 (1814 to 2808)                  | 3567 (2876 to 4423)                  | 856 (685 to 1070)      |  |

### Statistical analyses

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Statistical analysis title                                                                                             | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 133                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 2.64                                                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.97    |
| upper limit         | 3.53    |

|                                   |                                                    |
|-----------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b> | Estimated Fold Difference Exp./Comparator Vaccines |
|-----------------------------------|----------------------------------------------------|

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

|                                         |                                                               |
|-----------------------------------------|---------------------------------------------------------------|
| Comparison groups                       | V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis | 135                                                           |
| Analysis specification                  | Pre-specified                                                 |
| Analysis type                           | non-inferiority                                               |
| P-value                                 | < 0.001                                                       |
| Method                                  | ANOVA                                                         |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                          | 4.17                                                          |
| Confidence interval                     |                                                               |
| level                                   | 95 %                                                          |
| sides                                   | 2-sided                                                       |
| lower limit                             | 3.09                                                          |
| upper limit                             | 5.63                                                          |

### Primary: GMTs to HPV 11 in the vaccines administered in a 3-dose regimen

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | GMTs to HPV 11 in the vaccines administered in a 3-dose regimen |
|-----------------|-----------------------------------------------------------------|

End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                         | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 Vaccine [3 doses] | qHPV Vaccine [3 doses] |  |
|------------------------------------------|--------------------------------------|--------------------------------------|------------------------|--|
| Subject group type                       | Subject analysis set                 | Subject analysis set                 | Subject analysis set   |  |
| Number of subjects analysed              | 68                                   | 70                                   | 65                     |  |
| Units: mMU/mL                            |                                      |                                      |                        |  |
| geometric mean (confidence interval 95%) | 1551 (1236 to 1946)                  | 2714 (2170 to 3395)                  | 890 (705 to 1122)      |  |



## Statistical analyses

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                      | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 133                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 1.74                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 1.29                                                          |
| upper limit                                                                                                            | 2.35                                                          |

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                      | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 135                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 3.05                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 2.17                                                          |
| upper limit                                                                                                            | 4.29                                                          |

## Primary: GMTs to HPV 16 in the vaccines administered in a 3-dose regimen

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | GMTs to HPV 16 in the vaccines administered in a 3-dose regimen |
|-----------------|-----------------------------------------------------------------|

End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                            | V505<br>Formulation 1<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [3<br>doses] | qHPV Vaccine<br>[3 doses] |  |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------|--|
| Subject group type                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set      |  |
| Number of subjects analysed                 | 67                                            | 72                                            | 66                        |  |
| Units: mMU/mL                               |                                               |                                               |                           |  |
| geometric mean (confidence interval<br>95%) | 6665 (5607 to<br>7922)                        | 9911 (8389 to<br>11709)                       | 3126 (2627 to<br>3721)    |  |

## Statistical analyses

|                                   |                                                    |
|-----------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b> | Estimated Fold Difference Exp./Comparator Vaccines |
|-----------------------------------|----------------------------------------------------|

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

|                                         |                                                               |
|-----------------------------------------|---------------------------------------------------------------|
| Comparison groups                       | V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis | 133                                                           |
| Analysis specification                  | Pre-specified                                                 |
| Analysis type                           | non-inferiority                                               |
| P-value                                 | < 0.001                                                       |
| Method                                  | ANOVA                                                         |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                          | 2.13                                                          |
| Confidence interval                     |                                                               |
| level                                   | 95 %                                                          |
| sides                                   | 2-sided                                                       |
| lower limit                             | 1.73                                                          |
| upper limit                             | 2.62                                                          |

|                                   |                                                    |
|-----------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b> | Estimated Fold Difference Exp./Comparator Vaccines |
|-----------------------------------|----------------------------------------------------|

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

|                   |                                                               |
|-------------------|---------------------------------------------------------------|
| Comparison groups | V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
|-------------------|---------------------------------------------------------------|

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| Number of subjects included in analysis | 138                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | non-inferiority                          |
| P-value                                 | < 0.001                                  |
| Method                                  | ANOVA                                    |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines |
| Point estimate                          | 3.17                                     |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 2.5                                      |
| upper limit                             | 4.01                                     |

### Primary: GMTs to HPV 18 in the vaccines administered in a 3-dose regimen

|                        |                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | GMTs to HPV 18 in the vaccines administered in a 3-dose regimen                                                                                                                                                                                                                                                                                                                                     |
| End point description: | GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. |
| End point type         | Primary                                                                                                                                                                                                                                                                                                                                                                                             |
| End point timeframe:   | Month 7 (1 month post-dose 3)                                                                                                                                                                                                                                                                                                                                                                       |

| End point values                         | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 Vaccine [3 doses] | qHPV Vaccine [3 doses] |  |
|------------------------------------------|--------------------------------------|--------------------------------------|------------------------|--|
| Subject group type                       | Subject analysis set                 | Subject analysis set                 | Subject analysis set   |  |
| Number of subjects analysed              | 73                                   | 74                                   | 71                     |  |
| Units: mMU/mL                            |                                      |                                      |                        |  |
| geometric mean (confidence interval 95%) | 2112 (1629 to 2737)                  | 3620 (2798 to 4683)                  | 693 (533 to 901)       |  |

### Statistical analyses

|                                   |                                                                                   |
|-----------------------------------|-----------------------------------------------------------------------------------|
| Statistical analysis title        | Estimated Fold Difference Exp./Comparator Vaccines                                |
| Statistical analysis description: | Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |
| Comparison groups                 | V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]                     |

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| Number of subjects included in analysis | 144                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | non-inferiority                          |
| P-value                                 | < 0.001                                  |
| Method                                  | ANOVA                                    |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines |
| Point estimate                          | 3.05                                     |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 2.15                                     |
| upper limit                             | 4.32                                     |

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                      | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 145                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 5.23                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 3.66                                                          |
| upper limit                                                                                                            | 7.47                                                          |

### **Secondary: GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 3-dose regimen**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 3-dose regimen |
| End point description:<br>GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. Gardasil does not contain the following HPV types, HPV 31/33/45/52/58. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. A value of 99999 indicates a GMT that is less than quantifiable. |                                                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Secondary                                                                                 |
| End point timeframe:<br>Month 7 (1 month post-dose 3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                           |

| End point values                            | V505<br>Formulation 1<br>Vaccine [3<br>doses] | V505<br>Formulation 2<br>Vaccine [3<br>doses] | qHPV Vaccine<br>[3 doses] |  |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------|--|
| Subject group type                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set      |  |
| Number of subjects analysed                 | 101                                           | 105                                           | 101                       |  |
| Units: mMU/mL                               |                                               |                                               |                           |  |
| geometric mean (confidence interval<br>95%) |                                               |                                               |                           |  |
| Anti-HPV 31 (n=68, 77, 68)                  | 2265 (1752 to<br>2929)                        | 2632 (2067 to<br>3351)                        | 10 (8 to 13)              |  |
| Anti-HPV 33 (n=73, 76, 70)                  | 930 (749 to<br>1155)                          | 1244 (1006 to<br>1539)                        | 99999 (99999<br>to 99999) |  |
| Anti-HPV 45 (n=74, 78, 73)                  | 797 (624 to<br>1019)                          | 1136 (894 to<br>1443)                         | 99999 (99999<br>to 99999) |  |
| Anti-HPV 52 (n=74, 74, 71)                  | 1058 (826 to<br>1356)                         | 1814 (1415 to<br>2325)                        | 99999 (99999<br>to 99999) |  |
| Anti-HPV 58 (n=68, 74, 71)                  | 1940 (1460 to<br>2579)                        | 2642 (2011 to<br>3471)                        | 99999 (99999<br>to 99999) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: GMTs to HPV 6 in the vaccines administered in a 2-dose or 3-dose regimen

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | GMTs to HPV 6 in the vaccines administered in a 2-dose or 3-dose regimen |
|-----------------|--------------------------------------------------------------------------|

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                            | V505<br>Formulation 2<br>Vaccine [2<br>doses] | V505<br>Formulation 3<br>Vaccine [2<br>doses] | qHPV Vaccine<br>[3 doses] |  |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------|--|
| Subject group type                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set      |  |
| Number of subjects analysed                 | 60                                            | 62                                            | 65                        |  |
| Units: mMU/mL                               |                                               |                                               |                           |  |
| geometric mean (confidence interval<br>95%) | 3140 (2489 to<br>3962)                        | 3805 (3027 to<br>4783)                        | 856 (685 to<br>1070)      |  |

## Statistical analyses

|                                                                                   |                                                               |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                 | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:                                                 |                                                               |
| Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                 | V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                           | 125                                                           |
| Analysis specification                                                            | Pre-specified                                                 |
| Analysis type                                                                     | non-inferiority                                               |
| P-value                                                                           | < 0.001                                                       |
| Method                                                                            | ANOVA                                                         |
| Parameter estimate                                                                | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                    | 3.67                                                          |
| Confidence interval                                                               |                                                               |
| level                                                                             | 95 %                                                          |
| sides                                                                             | 2-sided                                                       |
| lower limit                                                                       | 2.72                                                          |
| upper limit                                                                       | 4.94                                                          |

|                                                                                   |                                                               |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                 | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:                                                 |                                                               |
| Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                 | V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                           | 127                                                           |
| Analysis specification                                                            | Pre-specified                                                 |
| Analysis type                                                                     | non-inferiority                                               |
| P-value                                                                           | < 0.001                                                       |
| Method                                                                            | ANOVA                                                         |
| Parameter estimate                                                                | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                    | 4.44                                                          |
| Confidence interval                                                               |                                                               |
| level                                                                             | 95 %                                                          |
| sides                                                                             | 2-sided                                                       |
| lower limit                                                                       | 3.22                                                          |
| upper limit                                                                       | 6.13                                                          |

## Secondary: GMTs to HPV 11 in the vaccines administered in a 2-dose or 3-dose regimen

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | GMTs to HPV 11 in the vaccines administered in a 2-dose or 3-dose regimen |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                           |
| GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. |                                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                                 |

End point timeframe:  
Month 7 (1 month post-dose 3)

| End point values                            | V505<br>Formulation 2<br>Vaccine [2<br>doses] | V505<br>Formulation 3<br>Vaccine [2<br>doses] | qHPV Vaccine<br>[3 doses] |  |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------|--|
| Subject group type                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set      |  |
| Number of subjects analysed                 | 60                                            | 62                                            | 65                        |  |
| Units: mMU/mL                               |                                               |                                               |                           |  |
| geometric mean (confidence interval<br>95%) | 2533 (1989 to<br>3225)                        | 2425 (1912 to<br>3075)                        | 890 (705 to<br>1122)      |  |

### Statistical analyses

| Statistical analysis title                                                                                             | Estimated Fold Difference Exp./Comparator Vaccines            |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 125                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 2.85                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 2.08                                                          |
| upper limit                                                                                                            | 3.89                                                          |

| Statistical analysis title                                                                                             | Estimated Fold Difference Exp./Comparator Vaccines            |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 127                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001 [2]                                                   |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 2.73                                                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.94    |
| upper limit         | 3.82    |

Notes:

[2] - Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

## Secondary: GMTs to HPV 16 in the vaccines administered in a 2-dose or 3-dose regimen

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | GMTs to HPV 16 in the vaccines administered in a 2-dose or 3-dose regimen |
|-----------------|---------------------------------------------------------------------------|

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                         | V505 Formulation 2 Vaccine [2 doses] | V505 Formulation 3 Vaccine [2 doses] | qHPV Vaccine [3 doses] |  |
|------------------------------------------|--------------------------------------|--------------------------------------|------------------------|--|
| Subject group type                       | Subject analysis set                 | Subject analysis set                 | Subject analysis set   |  |
| Number of subjects analysed              | 60                                   | 61                                   | 66                     |  |
| Units: mMU/mL                            |                                      |                                      |                        |  |
| geometric mean (confidence interval 95%) | 9717 (8095 to 11664)                 | 10561 (8811 to 12658)                | 3126 (2627 to 3721)    |  |

## Statistical analyses

|                            |                                                    |
|----------------------------|----------------------------------------------------|
| Statistical analysis title | Estimated Fold Difference Exp./Comparator Vaccines |
|----------------------------|----------------------------------------------------|

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

|                                         |                                                               |
|-----------------------------------------|---------------------------------------------------------------|
| Comparison groups                       | V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis | 126                                                           |
| Analysis specification                  | Pre-specified                                                 |
| Analysis type                           | non-inferiority                                               |
| P-value                                 | < 0.001                                                       |
| Method                                  | ANOVA                                                         |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                          | 3.11                                                          |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 2.37    |
| upper limit         | 4.08    |

|                                   |                                                    |
|-----------------------------------|----------------------------------------------------|
| <b>Statistical analysis title</b> | Estimated Fold Difference Exp./Comparator Vaccines |
|-----------------------------------|----------------------------------------------------|

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

|                                         |                                                               |
|-----------------------------------------|---------------------------------------------------------------|
| Comparison groups                       | V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis | 127                                                           |
| Analysis specification                  | Pre-specified                                                 |
| Analysis type                           | non-inferiority                                               |
| P-value                                 | < 0.001                                                       |
| Method                                  | ANOVA                                                         |
| Parameter estimate                      | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                          | 3.38                                                          |
| Confidence interval                     |                                                               |
| level                                   | 95 %                                                          |
| sides                                   | 2-sided                                                       |
| lower limit                             | 2.66                                                          |
| upper limit                             | 4.3                                                           |

## Secondary: GMTs to HPV 18 in the vaccines administered in a 2-dose or 3-dose regimen

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | GMTs to HPV 18 in the vaccines administered in a 2-dose or 3-dose regimen |
|-----------------|---------------------------------------------------------------------------|

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                         | V505 Formulation 2 Vaccine [2 doses] | V505 Formulation 3 Vaccine [2 doses] | qHPV Vaccine [3 doses] |  |
|------------------------------------------|--------------------------------------|--------------------------------------|------------------------|--|
| Subject group type                       | Subject analysis set                 | Subject analysis set                 | Subject analysis set   |  |
| Number of subjects analysed              | 65                                   | 69                                   | 71                     |  |
| Units: mMU/mL                            |                                      |                                      |                        |  |
| geometric mean (confidence interval 95%) | 1948 (1480 to 2564)                  | 3360 (2573 to 4387)                  | 693 (533 to 901)       |  |

## Statistical analyses

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                      | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 136                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 2.81                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 2.01                                                          |
| upper limit                                                                                                            | 3.93                                                          |

|                                                                                                                        |                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                      | Estimated Fold Difference Exp./Comparator Vaccines            |
| Statistical analysis description:<br>Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease. |                                                               |
| Comparison groups                                                                                                      | V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses] |
| Number of subjects included in analysis                                                                                | 140                                                           |
| Analysis specification                                                                                                 | Pre-specified                                                 |
| Analysis type                                                                                                          | non-inferiority                                               |
| P-value                                                                                                                | < 0.001                                                       |
| Method                                                                                                                 | ANOVA                                                         |
| Parameter estimate                                                                                                     | Estimated Difference Exp./Comp. Vaccines                      |
| Point estimate                                                                                                         | 4.85                                                          |
| Confidence interval                                                                                                    |                                                               |
| level                                                                                                                  | 95 %                                                          |
| sides                                                                                                                  | 2-sided                                                       |
| lower limit                                                                                                            | 3.36                                                          |
| upper limit                                                                                                            | 7                                                             |

## Secondary: GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 2-dose or 3-dose regimen

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines |
|-----------------|----------------------------------------------------------|

## End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. A value of 99999 indicates a GMT that is less than quantifiable.

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

End point timeframe:

Month 7 (1 month post-dose 3)

| End point values                            | V505<br>Formulation 2<br>Vaccine [2<br>doses] | V505<br>Formulation 3<br>Vaccine [2<br>doses] | qHPV Vaccine<br>[3 doses] |  |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------|--|
| Subject group type                          | Subject analysis set                          | Subject analysis set                          | Subject analysis set      |  |
| Number of subjects analysed                 | 103                                           | 101                                           | 101                       |  |
| Units: mMU/mL                               |                                               |                                               |                           |  |
| geometric mean (confidence interval<br>95%) |                                               |                                               |                           |  |
| Anti-HPV 31 (n=64, 68, 68)                  | 1938 (1487 to<br>2526)                        | 2265 (1751 to<br>2928)                        | 10 (8 to 13)              |  |
| Anti-HPV 33 (n=67, 68, 70)                  | 1723 (1374 to<br>2160)                        | 1692 (1352 to<br>2118)                        | 99999 (99999<br>to 99999) |  |
| Anti-HPV 45 (n=67, 70, 73)                  | 520 (402 to<br>673)                           | 740 (575 to<br>953)                           | 99999 (99999<br>to 99999) |  |
| Anti-HPV 52 (n=66, 70, 71)                  | 819 (630 to<br>1065)                          | 690 (535 to<br>891)                           | 99999 (99999<br>to 99999) |  |
| Anti-HPV 58 (n=68, 67, 71)                  | 1840 (1384 to<br>2445)                        | 2718 (2041 to<br>3621)                        | 99999 (99999<br>to 99999) |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 36 months

Adverse event reporting additional description:

For the present vaccine study, the number of participants with follow-up and not the actual count of participants who were randomized and vaccinated are displayed.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | V505 Formulation 1 Vaccine [3 doses] |
|-----------------------|--------------------------------------|

Reporting group description:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | V505 Formulation 2 [3 doses] |
|-----------------------|------------------------------|

Reporting group description:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | V505 Formulation 2 Vaccine [2 doses] |
|-----------------------|--------------------------------------|

Reporting group description:

V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | V505 Formulation 3 Vaccine [2 doses] |
|-----------------------|--------------------------------------|

Reporting group description:

V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | qHPV Vaccine [3 doses] |
|-----------------------|------------------------|

Reporting group description:

HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)

| Serious adverse events                            | V505 Formulation 1 Vaccine [3 doses] | V505 Formulation 2 [3 doses] | V505 Formulation 2 Vaccine [2 doses] |
|---------------------------------------------------|--------------------------------------|------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events |                                      |                              |                                      |
| subjects affected / exposed                       | 5 / 101 (4.95%)                      | 2 / 105 (1.90%)              | 3 / 102 (2.94%)                      |
| number of deaths (all causes)                     | 0                                    | 0                            | 0                                    |
| number of deaths resulting from adverse events    | 0                                    | 0                            | 0                                    |
| Surgical and medical procedures                   |                                      |                              |                                      |
| Abortion induced                                  |                                      |                              |                                      |
| subjects affected / exposed                       | 1 / 101 (0.99%)                      | 0 / 105 (0.00%)              | 1 / 102 (0.98%)                      |
| occurrences causally related to treatment / all   | 0 / 1                                | 0 / 0                        | 0 / 1                                |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                        | 0 / 0                                |
| Pregnancy, puerperium and perinatal conditions    |                                      |                              |                                      |
| Abortion spontaneous                              |                                      |                              |                                      |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 105 (0.95%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blighted ovum                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 105 (0.00%) | 0 / 102 (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           |
| Brow presentation                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 105 (0.00%) | 0 / 102 (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           |
| Foetal distress syndrome                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 105 (0.00%) | 0 / 102 (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           |
| Pre-eclampsia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 105 (0.95%) | 0 / 102 (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           |
| Premature separation of placenta                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 105 (0.95%) | 0 / 102 (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           |
| Prolonged labour                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 105 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Bartholin's abscess                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 105 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tonsillitis                                     |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 105 (0.00%) | 0 / 102 (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>                     | V505 Formulation 3 Vaccine [2 doses] | qHPV Vaccine [3 doses] |  |
|---------------------------------------------------|--------------------------------------|------------------------|--|
| Total subjects affected by serious adverse events |                                      |                        |  |
| subjects affected / exposed                       | 3 / 100 (3.00%)                      | 6 / 99 (6.06%)         |  |
| number of deaths (all causes)                     | 0                                    | 0                      |  |
| number of deaths resulting from adverse events    | 0                                    | 0                      |  |
| Surgical and medical procedures                   |                                      |                        |  |
| Abortion induced                                  |                                      |                        |  |
| subjects affected / exposed                       | 2 / 100 (2.00%)                      | 4 / 99 (4.04%)         |  |
| occurrences causally related to treatment / all   | 0 / 2                                | 0 / 4                  |  |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                  |  |
| Pregnancy, puerperium and perinatal conditions    |                                      |                        |  |
| Abortion spontaneous                              |                                      |                        |  |
| subjects affected / exposed                       | 1 / 100 (1.00%)                      | 1 / 99 (1.01%)         |  |
| occurrences causally related to treatment / all   | 0 / 1                                | 0 / 1                  |  |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                  |  |
| Blighted ovum                                     |                                      |                        |  |
| subjects affected / exposed                       | 0 / 100 (0.00%)                      | 0 / 99 (0.00%)         |  |
| occurrences causally related to treatment / all   | 0 / 0                                | 0 / 0                  |  |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                  |  |
| Brow presentation                                 |                                      |                        |  |
| subjects affected / exposed                       | 0 / 100 (0.00%)                      | 0 / 99 (0.00%)         |  |
| occurrences causally related to treatment / all   | 0 / 0                                | 0 / 0                  |  |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                  |  |
| Foetal distress syndrome                          |                                      |                        |  |
| subjects affected / exposed                       | 0 / 100 (0.00%)                      | 0 / 99 (0.00%)         |  |
| occurrences causally related to treatment / all   | 0 / 0                                | 0 / 0                  |  |
| deaths causally related to treatment / all        | 0 / 0                                | 0 / 0                  |  |
| Pre-eclampsia                                     |                                      |                        |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 99 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Premature separation of placenta                |                 |                |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 99 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Prolonged labour                                |                 |                |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 1 / 99 (1.01%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| Bartholin's abscess                             |                 |                |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 99 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tonsillitis                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 0 / 99 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | V505 Formulation 1<br>Vaccine [3 doses] | V505 Formulation 2<br>[3 doses] | V505 Formulation 2<br>Vaccine [2 doses] |
|-------------------------------------------------------|-----------------------------------------|---------------------------------|-----------------------------------------|
| Total subjects affected by non-serious adverse events |                                         |                                 |                                         |
| subjects affected / exposed                           | 100 / 101 (99.01%)                      | 105 / 105<br>(100.00%)          | 101 / 102 (99.02%)                      |
| Nervous system disorders                              |                                         |                                 |                                         |
| Dizziness                                             |                                         |                                 |                                         |
| subjects affected / exposed                           | 5 / 101 (4.95%)                         | 13 / 105 (12.38%)               | 8 / 102 (7.84%)                         |
| occurrences (all)                                     | 5                                       | 17                              | 9                                       |
| Headache                                              |                                         |                                 |                                         |
| subjects affected / exposed                           | 47 / 101 (46.53%)                       | 61 / 105 (58.10%)               | 48 / 102 (47.06%)                       |
| occurrences (all)                                     | 84                                      | 113                             | 74                                      |
| Lethargy                                              |                                         |                                 |                                         |

|                                                                                                                        |                          |                               |                           |
|------------------------------------------------------------------------------------------------------------------------|--------------------------|-------------------------------|---------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                       | 2 / 101 (1.98%)<br>2     | 6 / 105 (5.71%)<br>8          | 1 / 102 (0.98%)<br>1      |
| Blood and lymphatic system disorders<br>Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)            | 3 / 101 (2.97%)<br>3     | 5 / 105 (4.76%)<br>6          | 7 / 102 (6.86%)<br>7      |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 10 / 101 (9.90%)<br>11   | 13 / 105 (12.38%)<br>14       | 16 / 102 (15.69%)<br>17   |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)                                            | 50 / 101 (49.50%)<br>77  | 51 / 105 (48.57%)<br>75       | 35 / 102 (34.31%)<br>44   |
| Injection site haematoma<br>subjects affected / exposed<br>occurrences (all)                                           | 6 / 101 (5.94%)<br>7     | 8 / 105 (7.62%)<br>10         | 4 / 102 (3.92%)<br>4      |
| Injection site mass<br>subjects affected / exposed<br>occurrences (all)                                                | 3 / 101 (2.97%)<br>4     | 6 / 105 (5.71%)<br>7          | 3 / 102 (2.94%)<br>5      |
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)                                                | 99 / 101 (98.02%)<br>267 | 105 / 105<br>(100.00%)<br>289 | 100 / 102 (98.04%)<br>228 |
| Injection site pruritus<br>subjects affected / exposed<br>occurrences (all)                                            | 8 / 101 (7.92%)<br>12    | 11 / 105 (10.48%)<br>14       | 2 / 102 (1.96%)<br>3      |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)                                            | 60 / 101 (59.41%)<br>106 | 68 / 105 (64.76%)<br>124      | 49 / 102 (48.04%)<br>74   |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                               | 2 / 101 (1.98%)<br>4     | 12 / 105 (11.43%)<br>14       | 5 / 102 (4.90%)<br>5      |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                            | 9 / 101 (8.91%)<br>9     | 12 / 105 (11.43%)<br>18       | 11 / 102 (10.78%)<br>13   |
| Gastrointestinal disorders                                                                                             |                          |                               |                           |



|                                                                                                                           |                         |                         |                         |
|---------------------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------|-------------------------|
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                                        | 4 / 101 (3.96%)<br>4    | 0 / 105 (0.00%)<br>0    | 3 / 102 (2.94%)<br>3    |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                             | 4 / 101 (3.96%)<br>4    | 3 / 105 (2.86%)<br>3    | 3 / 102 (2.94%)<br>3    |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                                                | 13 / 101 (12.87%)<br>14 | 14 / 105 (13.33%)<br>18 | 19 / 102 (18.63%)<br>26 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                              | 3 / 101 (2.97%)<br>4    | 6 / 105 (5.71%)<br>6    | 7 / 102 (6.86%)<br>7    |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all)             | 8 / 101 (7.92%)<br>9    | 3 / 105 (2.86%)<br>4    | 4 / 102 (3.92%)<br>4    |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 10 / 101 (9.90%)<br>11  | 8 / 105 (7.62%)<br>10   | 7 / 102 (6.86%)<br>7    |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 101 (0.00%)<br>0    | 4 / 105 (3.81%)<br>5    | 2 / 102 (1.96%)<br>2    |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                                                             | 3 / 101 (2.97%)<br>4    | 8 / 105 (7.62%)<br>10   | 3 / 102 (2.94%)<br>3    |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                                                               | 4 / 101 (3.96%)<br>5    | 10 / 105 (9.52%)<br>10  | 6 / 102 (5.88%)<br>8    |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                        | 8 / 101 (7.92%)<br>8    | 5 / 105 (4.76%)<br>5    | 10 / 102 (9.80%)<br>12  |

|                                   |                                         |                           |  |
|-----------------------------------|-----------------------------------------|---------------------------|--|
| <b>Non-serious adverse events</b> | V505 Formulation 3<br>Vaccine [2 doses] | qHPV Vaccine [3<br>doses] |  |
|-----------------------------------|-----------------------------------------|---------------------------|--|

|                                                       |                        |                  |  |
|-------------------------------------------------------|------------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                        |                  |  |
| subjects affected / exposed                           | 100 / 100<br>(100.00%) | 94 / 99 (94.95%) |  |
| Nervous system disorders                              |                        |                  |  |
| Dizziness                                             |                        |                  |  |
| subjects affected / exposed                           | 4 / 100 (4.00%)        | 4 / 99 (4.04%)   |  |
| occurrences (all)                                     | 4                      | 5                |  |
| Headache                                              |                        |                  |  |
| subjects affected / exposed                           | 57 / 100 (57.00%)      | 39 / 99 (39.39%) |  |
| occurrences (all)                                     | 103                    | 61               |  |
| Lethargy                                              |                        |                  |  |
| subjects affected / exposed                           | 5 / 100 (5.00%)        | 3 / 99 (3.03%)   |  |
| occurrences (all)                                     | 6                      | 5                |  |
| Blood and lymphatic system disorders                  |                        |                  |  |
| Lymphadenopathy                                       |                        |                  |  |
| subjects affected / exposed                           | 2 / 100 (2.00%)        | 2 / 99 (2.02%)   |  |
| occurrences (all)                                     | 2                      | 2                |  |
| General disorders and administration site conditions  |                        |                  |  |
| Fatigue                                               |                        |                  |  |
| subjects affected / exposed                           | 10 / 100 (10.00%)      | 11 / 99 (11.11%) |  |
| occurrences (all)                                     | 11                     | 14               |  |
| Injection site erythema                               |                        |                  |  |
| subjects affected / exposed                           | 46 / 100 (46.00%)      | 24 / 99 (24.24%) |  |
| occurrences (all)                                     | 62                     | 35               |  |
| Injection site haematoma                              |                        |                  |  |
| subjects affected / exposed                           | 9 / 100 (9.00%)        | 6 / 99 (6.06%)   |  |
| occurrences (all)                                     | 11                     | 7                |  |
| Injection site mass                                   |                        |                  |  |
| subjects affected / exposed                           | 2 / 100 (2.00%)        | 2 / 99 (2.02%)   |  |
| occurrences (all)                                     | 2                      | 2                |  |
| Injection site pain                                   |                        |                  |  |
| subjects affected / exposed                           | 100 / 100<br>(100.00%) | 87 / 99 (87.88%) |  |
| occurrences (all)                                     | 231                    | 181              |  |
| Injection site pruritus                               |                        |                  |  |
| subjects affected / exposed                           | 1 / 100 (1.00%)        | 4 / 99 (4.04%)   |  |
| occurrences (all)                                     | 1                      | 4                |  |
| Injection site swelling                               |                        |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 60 / 100 (60.00%) | 24 / 99 (24.24%) |  |
| occurrences (all)                               | 88                | 38               |  |
| Pain                                            |                   |                  |  |
| subjects affected / exposed                     | 8 / 100 (8.00%)   | 3 / 99 (3.03%)   |  |
| occurrences (all)                               | 10                | 4                |  |
| Pyrexia                                         |                   |                  |  |
| subjects affected / exposed                     | 11 / 100 (11.00%) | 7 / 99 (7.07%)   |  |
| occurrences (all)                               | 12                | 7                |  |
| Gastrointestinal disorders                      |                   |                  |  |
| Abdominal pain                                  |                   |                  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%)   | 6 / 99 (6.06%)   |  |
| occurrences (all)                               | 3                 | 6                |  |
| Diarrhoea                                       |                   |                  |  |
| subjects affected / exposed                     | 5 / 100 (5.00%)   | 6 / 99 (6.06%)   |  |
| occurrences (all)                               | 5                 | 7                |  |
| Nausea                                          |                   |                  |  |
| subjects affected / exposed                     | 14 / 100 (14.00%) | 12 / 99 (12.12%) |  |
| occurrences (all)                               | 18                | 13               |  |
| Vomiting                                        |                   |                  |  |
| subjects affected / exposed                     | 5 / 100 (5.00%)   | 4 / 99 (4.04%)   |  |
| occurrences (all)                               | 5                 | 4                |  |
| Reproductive system and breast disorders        |                   |                  |  |
| Dysmenorrhoea                                   |                   |                  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%)   | 4 / 99 (4.04%)   |  |
| occurrences (all)                               | 3                 | 4                |  |
| Respiratory, thoracic and mediastinal disorders |                   |                  |  |
| Oropharyngeal pain                              |                   |                  |  |
| subjects affected / exposed                     | 10 / 100 (10.00%) | 7 / 99 (7.07%)   |  |
| occurrences (all)                               | 10                | 7                |  |
| Musculoskeletal and connective tissue disorders |                   |                  |  |
| Arthralgia                                      |                   |                  |  |
| subjects affected / exposed                     | 6 / 100 (6.00%)   | 0 / 99 (0.00%)   |  |
| occurrences (all)                               | 6                 | 0                |  |
| Back pain                                       |                   |                  |  |

|                                                                                                    |                      |                     |  |
|----------------------------------------------------------------------------------------------------|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                   | 6 / 100 (6.00%)<br>6 | 5 / 99 (5.05%)<br>5 |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                                        | 8 / 100 (8.00%)<br>8 | 4 / 99 (4.04%)<br>4 |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 7 / 100 (7.00%)<br>7 | 6 / 99 (6.06%)<br>6 |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported