



## Clinical trial results:

**Phase II, double blind, randomized, comparative study of the immunogenicity and safety of GlaxoSmithKline Biologicals' modified formulation varicella vaccine and Varilrix™ given as a 2 dose course in the second year of life**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2007-000683-24 |
| Trial protocol           | CZ HU          |
| Global end of trial date | 29 April 2008  |

### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 31 March 2021  |
| First version publication date | 31 July 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Minor corrections in safety section.</li></ul> |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 109705 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00568334 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 15 October 2008 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 18 March 2008   |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 29 April 2008   |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of Varilrix HSA-free vaccine as compared to Varilrix vaccine in terms of geometric mean titer (GMT) of varicella zoster virus (VZV) antibodies 43-57 days after the first dose vaccination.

Criterion for non-inferiority: The lower limit of the 95% confidence interval (CI) for the GMT ratio (derived from immunofluorescence assay [IFA]) between Group Varilrix HSA free and (divided by) Group Varilrix is equal to or above the pre-defined clinical limit of 0.5.

If this first criterion was met, an additional criterion was to be tested.

Additional criterion of non-inferiority: The lower limit of the 95% CI for the GMC ratio (derived from ELISA) between Group Varilrix HSA-free and (divided by) Group Varilrix is equal to or above the pre-defined clinical limit of 0.67

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 13 November 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 | Czech Republic: 114 |
| Country: Number of subjects enrolled | Hungary: 130        |
| Worldwide total number of subjects   | 244                 |
| EEA total number of subjects         | 244                 |

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)  | 244 |

|                           |   |
|---------------------------|---|
| Children (2-11 years)     | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years)      | 0 |
| From 65 to 84 years       | 0 |
| 85 years and over         | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall study (overall period)         |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

|                              |                         |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | Yes                     |
| <b>Arm title</b>             | Varilrix HSA-Free Group |

Arm description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine produced without human serum albumin (HSA-Free), administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Varilrix HSA-free                               |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Subcutaneous use                                |

Dosage and administration details:

Two doses of OKAH HSA-free vaccine administered subcutaneously into the left upper arm (deltoid region) on Day 0 and Week 6 (Day 43-57).

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

Arm description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine, administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Varilrix  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Subcutaneous use                                |

Dosage and administration details:

Two doses of OKAH vaccine administered subcutaneously into the left upper arm (deltoid region) on Day 0 and Week 6 (Day 43-57).

| <b>Number of subjects in period 1</b> | Varilrix HSA-Free Group | Varilrix Group |
|---------------------------------------|-------------------------|----------------|
| Started                               | 122                     | 122            |
| Completed                             | 121                     | 121            |
| Not completed                         | 1                       | 1              |
| Consent withdrawn by subject          | -                       | 1              |
| Lost to follow-up                     | 1                       | -              |

## Baseline characteristics

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Varilrix HSA-Free Group |
|-----------------------|-------------------------|

Reporting group description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine produced without human serum albumin (HSA-Free), administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

|                       |                |
|-----------------------|----------------|
| Reporting group title | Varilrix Group |
|-----------------------|----------------|

Reporting group description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine, administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

| Reporting group values                             | Varilrix HSA-Free Group | Varilrix Group | Total |
|--|-------------------------|----------------|-------|
| Number of subjects                                 | 122                     | 122            | 244   |
| Age categorical<br>Units: Subjects                 |                         |                |       |
| In utero   |                         |                | 0     |
| Preterm newborn infants (gestational age < 37 wks) |                         |                | 0     |
| Newborns (0-27 days)                               |                         |                | 0     |
| Infants and toddlers (28 days-23 months)           |                         |                | 0     |
| Children (2-11 years)                              |                         |                | 0     |
| Adolescents (12-17 years)                          |                         |                | 0     |
| Adults (18-64 years)                               |                         |                | 0     |
| From 65-84 years                                   |                         |                | 0     |
| 85 years and over                                  |                         |                | 0     |
| Age continuous<br>Units: months                    |                         |                |       |
| arithmetic mean                                    | 15.6                    | 14.8           |       |
| standard deviation                                 | ± 3.34                  | ± 3.08         | -     |
| Gender categorical<br>Units: Subjects              |                         |                |       |
| Female   | 59                      | 60             | 119   |
| Male   | 63                      | 62             | 125   |

## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Varilrix HSA-Free Group |
| Reporting group description:<br>Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine produced without human serum albumin (HSA-Free), administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6). |                         |
| Reporting group title   | Varilrix Group          |
| Reporting group description:<br>Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine, administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).   |                         |

### Primary: Antibody Titers Against Varicella Zoster Virus (VZV)

|  |  |
|--|--|
| End point title  | Antibody Titers Against Varicella Zoster Virus (VZV) |
| End point description:<br>Antibody titers have been assessed by immunofluorescence assay (IFA) and presented as geometric mean titers (GMTs), for initially seronegative subjects [with anti-VZV titer below (<) 1:4]. |  |
| End point type   | Primary  |
| End point timeframe:<br>At 43-57 days after the first vaccination dose (Week 6).   |  |

| End point values                         | Varilrix HSA-Free Group | Varilrix Group       |  |  |
|--|-------------------------|----------------------|--|--|
| Subject group type                       | Reporting group         | Reporting group      |  |  |
| Number of subjects analysed              | 116                     | 115                  |  |  |
| Units: Titer                             |                         |                      |  |  |
| geometric mean (confidence interval 95%) |                         |                      |  |  |
| anti-VZV                                 | 172.6 (141.6 to 210.3)  | 154.3 (128.7 to 185) |  |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | Non-inferiority of HSAFREEcompared to OKAH vaccine |
| Statistical analysis description:<br>Non-inferiority of Varilrix™ HSA-Free vaccine as compared to Varilrix™ vaccine in terms of geometric mean titers (GMTs) of varicella zoster virus (VZV) antibodies 43-57 days after the first vaccine dose. |  |
| Comparison groups  | Varilrix HSA-Free Group v Varilrix Group           |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 231                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| Parameter estimate                      | GMT Ratio                      |
| Point estimate                          | 1.12                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.86                           |
| upper limit                             | 1.46                           |

Notes:

[1] - The lower limit (LL) of the 95% confidence interval (CI) for the GMT ratio (derived from IFA) between Group Varilrix HSA-Free and (divided by) Group Varilrix is equal to or above ( $\geq$ ) the pre-defined clinical limit of 0.5.

### Primary: Antibody Concentrations Against Varicella Zoster Virus (VZV)

|                        |   |
|------------------------|---|
| End point title        | Antibody Concentrations Against Varicella Zoster Virus (VZV)  |
| End point description: | Antibody concentrations have been assessed by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in milli-international units per milliliter (mIU/mL), for initially seronegative subjects [with anti-VZV concentration below (<) 25 mIU/mL]. |
| End point type         | Primary   |
| End point timeframe:   | At 43-57 days after the first vaccine dose (Week 6)   |

| End point values                         | Varilrix HSA-Free Group | Varilrix Group        |  |  |
|--|-------------------------|-----------------------|--|--|
| Subject group type                       | Reporting group         | Reporting group       |  |  |
| Number of subjects analysed              | 116                     | 115                   |  |  |
| Units: mIU/mL                            |                         |                       |  |  |
| geometric mean (confidence interval 95%) |                         |                       |  |  |
| anti-VZV                                 | 123.5 (107.9 to 141.4)  | 110.7 (98.4 to 124.6) |  |  |

### Statistical analyses

|                                   |   |
|-----------------------------------|---|
| Statistical analysis title        | Non-inferiority of HSAFREE compared to OKAH vaccine   |
| Statistical analysis description: | Non-inferiority of Varilrix™ HSA-Free vaccine as compared to Varilrix™ vaccine in terms of geometric mean concentrations (GMCs) of varicella zoster virus (VZV) antibodies 43-57 days after the first vaccine dose. |
| Comparison groups                 | Varilrix HSA-Free Group v Varilrix Group  |



|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 231                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[2]</sup> |
| Parameter estimate                      | GMC Ratio                      |
| Point estimate                          | 1.12                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.93                           |
| upper limit                             | 1.33                           |

Notes:

[2] - The lower limit (LL) of the 95% confidence interval (CI) for the GMC ratio (derived from ELISA) between Group Varilrix HSA-Free and (divided by) Group Varilrix is equal to or above ( $\geq$ ) the pre-defined clinical limit of 0.67.

### Secondary: Number of Seroconverted Subjects for Varicella Antibodies

|                        |   |
|------------------------|---|
| End point title        | Number of Seroconverted Subjects for Varicella Antibodies   |
| End point description: | Seroconversion/seroresponse (considering the IFA data) was defined as the appearance of anti-VZV antibodies [i.e. titer/concentration greater than or equal to ( $\geq$ ) the assay cut-off value of 1:4] in the sera of subjects who were seronegative before vaccination. |
| End point type         | Secondary   |
| End point timeframe:   | At 43-57 days post-Dose 1 (Week 6) and 86-114 days post-Dose 2 (Week 12)  |

| End point values                         | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|--|-------------------------|-----------------|--|--|
| Subject group type                       | Reporting group         | Reporting group |  |  |
| Number of subjects analysed              | 116                     | 115             |  |  |
| Units: Subjects                          |                         |                 |  |  |
| anti-VZV $\geq$ 1:4 [N=116,115]; Week 6  | 114                     | 114             |  |  |
| anti-VZV $\geq$ 1:4 [N=115,112]; Week 12 | 115                     | 112             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Anti-VZV Antibody Concentrations Above Cut-off Values

|                        |   |
|------------------------|---|
| End point title        | Number of Subjects With Anti-VZV Antibody Concentrations Above Cut-off Values   |
| End point description: | Anti-VZV antibody concentrations greater than or equal to ( $\geq$ ) the assay cut-off values of: 25 mIU/mL, 50 mIU/mL and 75 mIU/mL have been assessed by ELISA, in the sera of subjects who were seronegative before vaccination. |
| End point type         | Secondary   |
| End point timeframe:   | At 43-57 days post-Dose 1 (Week 6) and 86-114 days post-Dose 2 (Week 12)  |

| End point values                                  | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|---|-------------------------|-----------------|--|--|
| Subject group type                                | Reporting group         | Reporting group |  |  |
| Number of subjects analysed                       | 116                     | 115             |  |  |
| Units: Subjects                                   |                         |                 |  |  |
| anti-VZV $\geq$ 25 mIU/mL [N=116,115];<br>Week 6  | 114                     | 113             |  |  |
| anti-VZV $\geq$ 25 mIU/mL [N=116,114];<br>Week 12 | 116                     | 114             |  |  |
| anti-VZV $\geq$ 50 mIU/mL [N=116,115];<br>Week 6  | 105                     | 103             |  |  |
| anti-VZV $\geq$ 50 mIU/mL [N=116,114];<br>Week 12 | 116                     | 114             |  |  |
| anti-VZV $\geq$ 75 mIU/mL [N=116,115];<br>Week 6  | 89                      | 89              |  |  |
| anti-VZV $\geq$ 75 mIU/mL [N=116,114];<br>Week 12 | 116                     | 114             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]

|                        |  |
|------------------------|--|
| End point title        | Antibody titers against the varicella zoster virus (VZV) by Immunofluorescence Assay [IFA]   |
| End point description: | Antibody titers have been assessed by immunofluorescence assay (IFA) and presented as geometric mean titers (GMTs), for initially seronegative subjects [with anti-VZV titer below (<) 1:4]. |
| End point type         | Secondary  |
| End point timeframe:   | At 86-114 days after the second vaccination dose (Week 12).  |

| End point values                         | Varilrix HSA-Free Group   | Varilrix Group          |  |  |
|--|---------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group         |  |  |
| Number of subjects analysed              | 115                       | 112                     |  |  |
| Units: Titers                            |                           |                         |  |  |
| geometric mean (confidence interval 95%) |                           |                         |  |  |
| anti-VZV                                 | 1452.5 (1240.7 to 1700.5) | 1395.4 (1183 to 1645.9) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA]

|                 |   |
|-----------------|---|
| End point title | Antibody titers against the varicella zoster virus (VZV) by enzyme-linked immunosorbent assay [ELISA] |
|-----------------|---|

End point description:

Antibody concentrations have been assessed by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in milli-international units per milliliter (mIU/mL), for initially seronegative subjects [with anti-VZV concentration below (<) 25 mIU/mL].

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

End point timeframe:

At 86-114 days after the second vaccination dose (Week 12).

| End point values                         | Varilrix HSA-Free Group  | Varilrix Group          |  |  |
|--|--------------------------|-------------------------|--|--|
| Subject group type                       | Reporting group          | Reporting group         |  |  |
| Number of subjects analysed              | 116                      | 114                     |  |  |
| Units: mIU/mL                            |                          |                         |  |  |
| geometric mean (confidence interval 95%) |                          |                         |  |  |
| anti-VZV                                 | 1013.6 (880.9 to 1166.4) | 999.2 (877.3 to 1138.1) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting any and grade 3 solicited local symptoms |
|-----------------|---|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose (Dose 1 and Dose 2)

| End point values            | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|-----------------------------|-------------------------|-----------------|--|--|
| Subject group type          | Reporting group         | Reporting group |  |  |
| Number of subjects analysed | 121                     | 122             |  |  |
| Units: Subjects             |                         |                 |  |  |
| Any Pain; Dose 1            | 13                      | 15              |  |  |
| Grade 3 Pain; Dose 1        | 0                       | 0               |  |  |
| Any Redness; Dose 1         | 33                      | 34              |  |  |
| Grade 3 Redness; Dose 1     | 0                       | 0               |  |  |
| Any Swelling; Dose 1        | 5                       | 7               |  |  |
| Grade 3 Swelling; Dose 1    | 0                       | 0               |  |  |
| Any Pain; Dose 2            | 23                      | 18              |  |  |
| Grade 3 Pain; Dose 2        | 0                       | 0               |  |  |
| Any Redness; Dose 2         | 44                      | 46              |  |  |
| Grade 3 Redness; Dose 2     | 6                       | 3               |  |  |
| Any Swelling; Dose 2        | 18                      | 14              |  |  |
| Grade 3 Swelling; Dose 2    | 2                       | 2               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

|                 |  |
|-----------------|--|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms |
|-----------------|--|

End point description:

Assessed solicited general symptoms were fever and rash. Any = occurrence of the symptom regardless of intensity grade and relationship to vaccination. Any fever was defined as axillary fever  $\geq 37.5^{\circ}\text{C}$  and grade 3 fever  $> 39.0^{\circ}\text{C}$  after vaccination. Grade 3 rash =  $> 150$  lesions. Related = considered by the investigator to be causally related to the study vaccination.

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

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period following each dose (Dose 1 and Dose 2)

| End point values            | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|-----------------------------|-------------------------|-----------------|--|--|
| Subject group type          | Reporting group         | Reporting group |  |  |
| Number of subjects analysed | 121                     | 122             |  |  |
| Units: Subjects             |                         |                 |  |  |
| Any temperature; Dose 1     | 64                      | 52              |  |  |
| Grade 3 temperature; Dose 1 | 13                      | 11              |  |  |
| Any rash; Dose 1            | 2                       | 2               |  |  |
| Grade 3 rash; Dose 1        | 1                       | 0               |  |  |
| Any temperature; Dose 2     | 54                      | 53              |  |  |
| Grade 3 temperature; Dose 2 | 6                       | 12              |  |  |
| Any rash; Dose 2            | 3                       | 3               |  |  |
| Grade 3 rash; Dose 2        | 1                       | 0               |  |  |

|                             |    |    |  |  |
|-----------------------------|----|----|--|--|
| Related temperature; Dose 1 | 31 | 18 |  |  |
| Related rash; Dose 1        | 0  | 0  |  |  |
| Related temperature; Dose 2 | 31 | 23 |  |  |
| Related rash; Dose 2        | 1  | 0  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Any Unsolicited Adverse Event (AE)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Any Unsolicited Adverse Event (AE) |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

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

End point timeframe:

Within the 43-day (Days 0-42) post-vaccination period following each dose

| End point values              | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|-------------------------------|-------------------------|-----------------|--|--|
| Subject group type            | Reporting group         | Reporting group |  |  |
| Number of subjects analysed   | 122                     | 122             |  |  |
| Units: Subjects               |                         |                 |  |  |
| Any AE(s), Dose 1 [N=122;122] | 56                      | 45              |  |  |
| Any AE(s), Dose 2 [N=121;121] | 35                      | 42              |  |  |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that results in death, are life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

From Day 0 up to study end (Day 86-114)

| <b>End point values</b>     | Varilrix HSA-Free Group | Varilrix Group  |  |  |
|-----------------------------|-------------------------|-----------------|--|--|
| Subject group type          | Reporting group         | Reporting group |  |  |
| Number of subjects analysed | 122                     | 121             |  |  |
| Units: Subjects             |                         |                 |  |  |
| any SAE(s)                  | 2                       | 5               |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local symptoms were collected during the 4-day (Days 0-3) post each dose. Solicited general symptoms and unsolicited AEs during the 43-day (Days 0-42) post each dose. SAEs were collected during the entire study period (Day 0 to Day 86/114).

Adverse event reporting additional description:

The number of occurrences reported for serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Varilrix HSA-Free Group |
|-----------------------|-------------------------|

Reporting group description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine produced without human serum albumin (HSA-Free), administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

|                       |                |
|-----------------------|----------------|
| Reporting group title | Varilrix Group |
|-----------------------|----------------|

Reporting group description:

Healthy male or female children between, and including, 11 and 21 months of age, who received 2 doses of Varilrix™ vaccine, administered subcutaneously into the deltoid region of the left upper arm, at Day 0 and Day 43-57 (Week 6).

| Serious adverse events                            | Varilrix HSA-Free Group | Varilrix Group  |  |
|---|-------------------------|-----------------|--|
| Total subjects affected by serious adverse events |                         |                 |  |
| subjects affected / exposed                       | 2 / 122 (1.64%)         | 5 / 122 (4.10%) |  |
| number of deaths (all causes)                     | 0                       | 0               |  |
| number of deaths resulting from adverse events    |                         |                 |  |
| Injury, poisoning and procedural complications    |                         |                 |  |
| Concussion  |                         |                 |  |
| alternative assessment type: Non-systematic       |                         |                 |  |
| subjects affected / exposed                       | 0 / 122 (0.00%)         | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all   | 0 / 0                   | 0 / 1           |  |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0           |  |
| Psychiatric disorders                             |                         |                 |  |
| Breath holding                                    |                         |                 |  |
| alternative assessment type: Non-systematic       |                         |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 122 (0.00%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Otitis media                                    |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 1 / 122 (0.82%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 122 (0.00%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 1 / 122 (0.82%) | 0 / 122 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Laryngitis                                      |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 122 (0.00%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mastoiditis                                     |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 122 (0.00%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sinusitis                                       |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 122 (0.00%) | 1 / 122 (0.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Varilrix HSA-Free Group | Varilrix Group     |  |
|---|-------------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                         |                    |  |
| subjects affected / exposed                           | 103 / 122 (84.43%)      | 100 / 122 (81.97%) |  |
| General disorders and administration site conditions  |                         |                    |  |
| Pain; Dose 1  |                         |                    |  |
| subjects affected / exposed <sup>[1]</sup>            | 13 / 121 (10.74%)       | 15 / 122 (12.30%)  |  |
| occurrences (all)                                     | 13                      | 15                 |  |
| Redness; Dose 1                                       |                         |                    |  |
| subjects affected / exposed <sup>[2]</sup>            | 33 / 121 (27.27%)       | 34 / 122 (27.87%)  |  |
| occurrences (all)                                     | 33                      | 34                 |  |
| Swelling; Dose 1                                      |                         |                    |  |
| subjects affected / exposed <sup>[3]</sup>            | 5 / 121 (4.13%)         | 7 / 122 (5.74%)    |  |
| occurrences (all)                                     | 5                       | 7                  |  |
| Pain; Dose 2  |                         |                    |  |
| subjects affected / exposed <sup>[4]</sup>            | 23 / 121 (19.01%)       | 18 / 121 (14.88%)  |  |
| occurrences (all)                                     | 23                      | 18                 |  |
| Redness; Dose 2                                       |                         |                    |  |
| subjects affected / exposed <sup>[5]</sup>            | 44 / 121 (36.36%)       | 46 / 121 (38.02%)  |  |
| occurrences (all)                                     | 44                      | 46                 |  |
| Swelling; Dose 2                                      |                         |                    |  |
| subjects affected / exposed <sup>[6]</sup>            | 18 / 121 (14.88%)       | 14 / 121 (11.57%)  |  |
| occurrences (all)                                     | 18                      | 14                 |  |
| Fever; Dose 1   |                         |                    |  |
| subjects affected / exposed <sup>[7]</sup>            | 64 / 121 (52.89%)       | 52 / 122 (42.62%)  |  |
| occurrences (all)                                     | 64                      | 52                 |  |
| Fever; Dose 2   |                         |                    |  |
| subjects affected / exposed <sup>[8]</sup>            | 54 / 121 (44.63%)       | 53 / 121 (43.80%)  |  |
| occurrences (all)                                     | 54                      | 53                 |  |
| Infections and infestations                           |                         |                    |  |

|  |                         |                         |  |
|--|-------------------------|-------------------------|--|
| Bronchitis; Dose 1<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                      | 15 / 122 (12.30%)<br>15 | 8 / 122 (6.56%)<br>8    |  |
| Viral infection; Dose 1<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                 | 11 / 122 (9.02%)<br>11  | 11 / 122 (9.02%)<br>11  |  |
| Rhinitis; Dose 1<br>subjects affected / exposed<br>occurrences (all)   | 6 / 122 (4.92%)<br>6    | 8 / 122 (6.56%)<br>8    |  |
| Bronchitis; Dose 2<br>alternative assessment type: Non-systematic<br>subjects affected / exposed <sup>[9]</sup><br>occurrences (all)       | 8 / 121 (6.61%)<br>8    | 11 / 121 (9.09%)<br>11  |  |
| Viral infection; Dose 2<br>alternative assessment type: Non-systematic<br>subjects affected / exposed <sup>[10]</sup><br>occurrences (all) | 6 / 121 (4.96%)<br>6    | 13 / 121 (10.74%)<br>13 |  |
| Rhinitis; Dose 2<br>alternative assessment type: Non-systematic<br>subjects affected / exposed <sup>[11]</sup><br>occurrences (all)        | 7 / 121 (5.79%)<br>7    | 1 / 121 (0.83%)<br>1    |  |

Notes:

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of solicited symptoms, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects/doses with documented safety data (i.e. symptom screen/sheet completed).

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

Justification: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

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

Justification: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

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

Justification: For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported