# Clinical trial results:
# Regulatory Post-Marketing Surveillance (PMS) Study for AVAXIM 160U (Hepatitis A Vaccine)

## Summary

| | |
|---|---|
| EudraCT number | 2016-001964-13 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 03 November 2015 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 20 October 2017 |
| First version publication date | 20 October 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | HAF85 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01838070 |
| WHO universal trial number (UTN) | U1111-1127-7211 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Sanofi Pasteur Korea Ltd |
| Sponsor organisation address | 11 fl, 235, Banpo-daero, Seocho-gu Seoul, Korea, Republic of, 137-804 |
| Public contact | Global Medical Affairs Rep., Sanofi Pasteur Korea Ltd, 82 22136 9533, RegistryContactUS@sanofipasteur.com |
| Scientific contact | Global Medical Affairs Rep., Sanofi Pasteur Korea Ltd, 82 22136 9533, RegistryContactUS@sanofipasteur.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 | 03 November 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 03 November 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety of AVAXIM 160U (Hepatitis A vaccine) administered under the routine practice, according to Korea Food and Drug Administration "Basic standard for reexamination of new drug" based on the pharmaceutical law in Korea.

Protection of trial subjects:

No vaccination was administered during this trial. Subjects in this trial previously received AVAXIM 160U (Hepatitis A vaccine) and safety events occurring within 30 days after vaccination under the routine practice during the 4-year surveillance period is reported here.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|---|---|
| Actual start date of recruitment | 04 November 2011 |
| 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 | Korea, Republic of: 614 |
| Worldwide total number of subjects | 614 |
| 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) | 14 |
| Adults (18-64 years) | 596 |
| From 65 to 84 years | 4 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled for a 4-year surveillance period (04 November 2011 to 03 November 2015) at 16 clinic centers in South Korea.

### Pre-assignment

Screening details:

A total of 614 subjects whose case report forms were retrieved were included in the safety evaluation.

### Period 1

| | |
|---|---|
| Period 1 title | 4-year surveillance period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Not applicable

### Arms

| | |
|---|---|
| **Arm title** | All subjects |

Arm description:

Subjects who were 16 to 84 years old who previously received Avaxim 160U for 16 years old and older (Hepatitis A vaccine) injection once, were enrolled during the 4-year surveillance period, and whose Case Report forms were retrieved.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Avaxim® 160U Injection (Hepatitis A Vaccine) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, single injection on Day 0.

| **Number of subjects in period 1** | All subjects |
|---|---|
| Started | 614 |
| Completed | 614 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | All subjects |

Reporting group description:

Subjects who were 16 to 84 years old who previously received Avaxim 160U for 16 years old and older (Hepatitis A vaccine) injection once, were enrolled during the 4-year surveillance period, and whose Case Report forms were retrieved.

| Reporting group values | All subjects | Total | |
|---|---|---|---|
| Number of subjects | 614 | 614 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 14 | 14 | |
| Adults (18-64 years) | 596 | 596 | |
| From 65-84 years | 4 | 4 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 32.19 | | |
| standard deviation | ± 8.25 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 386 | 386 | |
| Male | 228 | 228 | |

## End points

### End points reporting groups

| Reporting group title | All subjects |
|---|---|

Reporting group description:

Subjects who were 16 to 84 years old who previously received Avaxim 160U for 16 years old and older (Hepatitis A vaccine) injection once, were enrolled during the 4-year surveillance period, and whose Case Report forms were retrieved.

### Primary: Number of Subjects Reporting Solicited Injection-Site and Systemic Events Following A Single Dose of Avaxim 160U Injection (Hepatitis A Vaccine)

| End point title | Number of Subjects Reporting Solicited Injection-Site and Systemic Events Following A Single Dose of Avaxim 160U Injection (Hepatitis A Vaccine)[1] |
|---|---|

End point description:

1. Solicited injection site reaction (Pain and Erythema) occurring during 7 days after the AVAXIM 160U administration during the 4-year surveillance period. Grade 3: Pain, Significant, prevents daily activity and Erythema, >100 mm.
2. Solicited systemic adverse reactions (Fever [Temperature], Headache, Myalgia or Arthralgia, Asthenia and Gastro-intestinal disorders) occurring during 7 days after the AVAXIM 160U administration during the 4-year surveillance period. Grade 3: Fever, ≥39.0°C; Headache, Myalgia, Arthralgia, Asthenia, and Gastro-intestinal disorders, Significant, prevents daily activity.

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

End point timeframe:

7 days after the AVAXIM 160U administration during the 4-year surveillance period.

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: Descriptive analyses were performed based on the study group and the study vaccine previously administered for this outcome.

| End point values | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 614 | | | |
| Units: Number of subjects | | | | |
| number (not applicable) | | | | |
| Any Injection site Pain | 9 | | | |
| Grade 3 Injection site Pain | 0 | | | |
| Any Injection site Erythema | 3 | | | |
| Grade 3 Injection site Erythema | 0 | | | |
| Any Fever | 3 | | | |
| Grade 3 Fever | 0 | | | |
| Any Headache | 4 | | | |
| Grade 3 Headache | 0 | | | |
| Any Myalgia | 2 | | | |
| Grade 3 Myalgia | 0 | | | |
| Any Arthralgia | 0 | | | |
| Grade 3 Arthralgia | 0 | | | |
| Any Asthenia | 0 | | | |
| Grade 3 Asthenia | 0 | | | |
| Any Gastro-intestinal disorders | 1 | | | |
| Grade 3 Gastro-intestinal disorders | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects Reporting Unexpected Adverse Events Following A Single Dose of Avaxim 160U Injection (Hepatitis A Vaccine)

| End point title | Number of Subjects Reporting Unexpected Adverse Events Following A Single Dose of Avaxim 160U Injection (Hepatitis A Vaccine) |
|---|---|

End point description:

The number subjects with unsolicited adverse events following a single dose of Avaxim 160 U Injection (Hepatitis A Vaccine) are reported.

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

End point timeframe:

30 days after the AVAXIM 160U administration during the 4-year surveillance period.

| **End point values** | All subjects | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 614 | | | |
| Units: Number of subjects | | | | |
| number (not applicable) | | | | |
| Bronchitis | 4 | | | |
| Pharyngitis | 4 | | | |
| Nasopharyngitis | 3 | | | |
| Influenza | 1 | | | |
| Laryngitis | 1 | | | |
| Vaginal infection | 1 | | | |
| Vulvovaginal candidiasis | 1 | | | |
| Stomatitis | 1 | | | |
| Vomiting | 1 | | | |
| Chest pain | 1 | | | |
| Inflammation | 1 | | | |
| Cough | 2 | | | |
| Conjunctival disorder | 1 | | | |
| Back pain | 1 | | | |
| Dizziness | 1 | | | |
| Ectropion of cervix | 1 | | | |
| Uterine cervical erosion | 1 | | | |
| Vulvovaginal pruritus | 1 | | | |
| Dermatitis contact | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Adverse event data were collected throughout the 4-year surveillance period. | |
| Assessment type | Non-systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |
| **Reporting groups** | |
| Reporting group title | All subjects |
| Reporting group description: | |
| Subjects who were 16 to 84 years old who previously received Avaxim 160U for 16 years old and older (Hepatitis A vaccine) injection once, were enrolled during the 4-year surveillance period, and whose Case Report forms were retrieved. | |

| Serious adverse events | All subjects | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 614 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 0.1 %

| Non-serious adverse events | All subjects | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 614 (2.28%) | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| Inflammation | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Eye disorders<br>Conjunctival disorder<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 614 (0.16%)<br>1 | | |
| Gastrointestinal disorders<br>Dyspepsia<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastrointestinal inflammation<br>subjects affected / exposed<br>occurrences (all)<br><br>Stomatitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | <br><br>2 / 614 (0.33%)<br>2<br><br><br>1 / 614 (0.16%)<br>1<br><br><br>1 / 614 (0.16%)<br>1<br><br><br>1 / 614 (0.16%)<br>1 | | |
| Reproductive system and breast disorders<br>Ectropion of cervix<br>subjects affected / exposed<br>occurrences (all)<br><br>Uterine cervical erosion<br>subjects affected / exposed<br>occurrences (all)<br><br>Vulvovaginal pruritus<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 614 (0.16%)<br>1<br><br><br>1 / 614 (0.16%)<br>1<br><br><br>1 / 614 (0.16%)<br>1 | | |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | <br><br>2 / 614 (0.33%)<br>2 | | |
| Skin and subcutaneous tissue disorders<br>Dermatitis contact<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 614 (0.16%)<br>1 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Back pain | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 614 (0.65%) | | |
| occurrences (all) | 4 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 4 / 614 (0.65%) | | |
| occurrences (all) | 4 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 614 (0.49%) | | |
| occurrences (all) | 3 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| Vaginal infection | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |
| Vulvovaginal candidiasis | | | |
| subjects affected / exposed | 1 / 614 (0.16%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 August 2013 | Updated inclusion criteria, methods of recruitment, and informed consent forms. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported