# Clinical trial results:
# Immunogenicity of DTaP-IPV-Hep B-PRP-T Combined Vaccine Compared with PENTAXIM and ENGERIX B® at 2, 3, and 4 Months Primary Schedule in Healthy Turkish Infants

## Summary

| | |
|---|---|
| EudraCT number | 2011-004454-26 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 18 June 2007 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 February 2016 |
| First version publication date | 12 September 2014 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | A3L10 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00315055 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Sanofi Pasteur SA |
| Sponsor organisation address | 1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280 |
| Public contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com |
| Scientific contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-001201-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 30 June 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 June 2007 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 June 2007 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the immune response to Hep B antigen of the DTaP-IPV-Hep B-PRP-T is non-inferior to that of the association of PENTAXIM™ + ENGERIX B® 1 month after a three-dose primary series at 2, 3, and 4 months of age.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy:

All subjects participating in the study were to have received the DTaP-IPV-Hep B-PRP-T vaccine at 2, 3, and 4 months of age which is in agreement with the national immunization program in Turkey.

Evidence for comparator:

PENTAXIM + ENGERIX B® vaccines were chosen as the control vaccines for this trial as they are part of the standard range of vaccines currently used in Turkey. In addition, PENTAXIM contains the same D, T, aP, IPV, and PRP-T antigens as the investigational vaccine while ENGERIX B® contains the same amount of HBsAg as the investigational vaccine.

| | |
|---|---|
| Actual start date of recruitment | 01 June 2006 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Turkey: 310 |
| Worldwide total number of subjects | 310 |
| 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) | 310 |

| | |
|---|---|
| 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:

Subjects were enrolled and treated from 01 June 2006 to 18 June 2007 in 1 clinical center in Turkey.

### Pre-assignment

Screening details:

A total of 310 subjects who met the inclusion but non of the exclusion criteria were enrolled and vaccinated.

### Period 1

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

Blinding implementation details:

Not applicable.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | DTaP-IPV-Hep B-PRP~T |

Arm description:

Participants received 3 vaccinations with Diphtheria (D) and tetanus (T) toxoids, acellular pertussis (2-component) (aP), recombinant Hepatitis B surface antigen (HBsAg), inactivated poliomyelitis virus (IPV), and Hemophilus influenzae type b (Hib) polysaccharide conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Hexaxim |
| Investigational medicinal product code | DTaP-IPV-HepB-PRP-T vaccine |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, one dose each at 2, 3, and 4 months of age.

| | |
|---|---|
| **Arm title** | PENTAXIM™ and ENGERIX® |

Arm description:

Participants received 3 vaccinations with DTaP-IPV-PRP~T (PENTAXIM™ ) and recombinant Hepatitis B (ENGERIX® PEDIATRIC) vaccines, with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Pentaxim |
| Investigational medicinal product code | DTaP-IPV-PRP-T vaccine |
| Other name | |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, one dose at 2, 3, and 4 months of age.

| | |
|---|---|
| Investigational medicinal product name | ENGERIX B |
| Investigational medicinal product code | Recombinant Hep B vaccine |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:
0.5 mL, intramuscular, one dose each at 2, 3, and 4 months of age.

| **Number of subjects in period 1** | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® |
|---|---|---|
| Started | 155 | 155 |
| Completed | 152 | 150 |
| Not completed | 3 | 5 |
| Lost to follow-up | 1 | 1 |
| Protocol deviation | 2 | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | DTaP-IPV-Hep B-PRP~T |
| Reporting group description: | |
| Participants received 3 vaccinations with Diphtheria (D) and tetanus (T) toxoids, acellular pertussis (2-component) (aP), recombinant Hepatitis B surface antigen (HBsAg), inactivated poliomyelitis virus (IPV), and Hemophilus influenzae type b (Hib) polysaccharide conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60). | |
| Reporting group title | PENTAXIM™ and ENGERIX® |
| Reporting group description: | |
| Participants received 3 vaccinations with DTaP-IPV-PRP~T (PENTAXIM™ ) and recombinant Hepatitis B (ENGERIX® PEDIATRIC) vaccines, with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60). | |

| Reporting group values | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | Total |
|---|---|---|---|
| Number of subjects | 155 | 155 | 310 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 155 | 155 | 310 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: months | | | |
| arithmetic mean | 2.08 | 2.08 | |
| standard deviation | ± 0.09 | ± 0.102 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 67 | 72 | 139 |
| Male | 88 | 83 | 171 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | DTaP-IPV-Hep B-PRP~T |

Reporting group description:

Participants received 3 vaccinations with Diphtheria (D) and tetanus (T) toxoids, acellular pertussis (2-component) (aP), recombinant Hepatitis B surface antigen (HBsAg), inactivated poliomyelitis virus (IPV), and Hemophilus influenzae type b (Hib) polysaccharide conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

| | |
|---|---|
| Reporting group title | PENTAXIM™ and ENGERIX® |

Reporting group description:

Participants received 3 vaccinations with DTaP-IPV-PRP~T (PENTAXIM™ ) and recombinant Hepatitis B (ENGERIX® PEDIATRIC) vaccines, with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

### Primary: Percentage of Subjects With Anti HBs Seroprotection After the 3 Dose Primary Vaccination Series With Either DTaP-IPV-Hep B-PRP~T or PENTAXIM™ + ENGERIX B® Vaccines

| | |
|---|---|
| End point title | Percentage of Subjects With Anti HBs Seroprotection After the 3 Dose Primary Vaccination Series With Either DTaP-IPV-Hep B-PRP~T or PENTAXIM™ + ENGERIX B® Vaccines[1] |

End point description:

Antibodies to hepatitis B surface antigen (HBs) were measured by means of automated enhanced chemoluminescence assay. Seroprotection was defined as a titer ≥ 10 mIU/mL.

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

End point timeframe:

Day 90 post first dose

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 groups / study vaccine administered for this outcome.

| End point values | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 134 | 128 | | |
| Units: Percentage of subjects | | | | |
| Percentage of Subjects With Seroprotection | 94 | 96 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Seroprotection Against Hepatitis B Surface Antigen, Polyribosyl Ribitol Phosphate, Diptheria, and Tetanus After the 3 Dose Primary Series With Either DTaP-IPV-Hep B-PRP~T or PENTAXIM™ + ENGERIX B®

| | |
|---|---|
| End point title | Percentage of Subjects With Seroprotection Against Hepatitis B Surface Antigen, Polyribosyl Ribitol Phosphate, Diptheria, and Tetanus After the 3 Dose Primary Series With Either DTaP-IPV- |

| | |
|---|---|
| | Hep B-PRP~T or PENTAXIM™ + ENGERIX B® |

End point description:

Antibodies to hepatitis B surface antigen (HBs) were measured by means of automated enhanced chemoluminescence assay. Antibodies to Polyribosyl ribitol phosphate and tetanus were measured by enzyme linked immunosorbent assay (ELISA), and antibodies to diphtheria were measured by a neutralization test using crystal violet. Seroprotection was defined as: titers ≥ 100 mIU/mL for HBs; ≥ 0.01 and ≥ 0.1 IU/mL for anti-Tetanus and anti-diphtheria, and ≥ 0.15 µg/mL and ≥ 1.0 µg/mL for anti-PRP.

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

End point timeframe:

Day 90 post first dose

| **End point values** | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 145 | 141 | | |
| Units: Percentage of subjects | | | | |
| Anti-HBs (≥ 100 mIU/mL) | 65 | 78 | | |
| Anti-PRP (≥ 0.15 µg/mL) | 91 | 98 | | |
| Anti-PRP (≥ 1.0 µg/mL) | 73 | 77 | | |
| Anti-Diphtheria (≥0.01 IU/mL) | 99 | 97 | | |
| Anti-Diphtheria (≥0.1 IU/mL) | 34 | 44 | | |
| Anti-Tetanus (≥0.01 IU/mL) | 100 | 100 | | |
| Anti-Tetanus (≥0.1 IU/mL) | 100 | 99 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Seroprotection Against Poliovirus Antigens After the 3 Dose Primary Series Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B®

| | |
|---|---|
| End point title | Percentage of Subjects With Seroprotection Against Poliovirus Antigens After the 3 Dose Primary Series Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B® |

End point description:

Antibodies to poliovirus types 1, 2, and 3 were measured by microneutralization on Vero cell culture. Seroprotection was defined as titers ≥8 1/dil.

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

End point timeframe:

Day 90 post first dose

| End point values | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 145 | 141 | | |
| Units: Percentage of subjects | | | | |
| Anti-Polio 1 | 98 | 98 | | |
| Anti-Polio 2 | 95 | 94 | | |
| Anti-Polio 3 | 97 | 100 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Anti-Pertussis Seroconversion After the 3 Dose Primary Series Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B®

| End point title | Percentage of Subjects With Anti-Pertussis Seroconversion After the 3 Dose Primary Series Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B® |
|---|---|

End point description:

Antibodies to pertussis toxoid (PT) and filamentous hemagglutinin (FHA) were measured by means of enzyme linked immunosorbent assay (ELISA). Seroconversion was defined as a ≥ 4-fold increase in titer between baseline (Day 0 pre-vaccination and Day 30 post-dose 3 (Day 90).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-dose 3

| End point values | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 145 | 141 | | |
| Units: Percentage of subjects | | | | |
| Anti-PT (Pre-dose 1) | 55 | 48 | | |
| Anti-PT (Post-dose 3) | 100 | 100 | | |
| Anti-FHA (Pre-dose 1) | 65 | 62 | | |
| Anti-FHA (Post-dose 3) | 100 | 100 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titers of Antibodies After the 3 Dose Primary Series With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B®

| End point title | Geometric Mean Titers of Antibodies After the 3 Dose Primary Series With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B® |
|---|---|

End point description:

Antibodies to hepatitis B surface antigen (HBs) were measured by means of automated enhanced chemoluminescence assay. Antibodies to PRP, tetanus, pertussis toxoid (PT), and filamentous hemagglutinin (FHA) were measured by enzyme linked immunosorbent assay (ELISA), and antibodies to diphtheria were measured by a neutralization test using crystal violet.

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

End point timeframe:

Day 90 (30 Days post-dose 3)

| **End point values** | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 145 | 141 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs | 149 (115 to 191) | 265 (205 to 342) | | |
| Anti-PRP | 2.12 (1.62 to 2.77) | 2.37 (1.91 to 2.94) | | |
| Anti-Diphtheria | 0.071 (0.06 to 0.084) | 0.091 (0.075 to 0.11) | | |
| Anti-Tetanus | 0.839 (0.731 to 0.962) | 0.709 (0.625 to 0.804) | | |
| Anti-Polio 1 | 102 (74.9 to 138) | 112 (85.4 to 147) | | |
| Anti-Polio 2 | 73.5 (52.9 to 102) | 78.2 (58.2 to 105) | | |
| Anti-Polio 3 | 133 (93 to 190) | 214 (159 to 288) | | |
| Anti-PT | 123 (109 to 139) | 138 (122 to 155) | | |
| Anti-FHA | 102 (90.4 to 114) | 69.3 (62 to 77.6) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With at Least a Solicited Injection Site or Systemic Reaction After Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B®

| End point title | Number of Subjects With at Least a Solicited Injection Site or Systemic Reaction After Vaccination With Either DTaP-IPV-HB-PRP~T or PENTAXIM™ + ENGERIX B® |
|---|---|

End point description:

Solicited Injection Site Reactions: Pain, Erythema, Swelling. Solicited Systemic Reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia, Irritability

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

End point timeframe:

Day 0 to Day 7 post any dose

| End point values | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 152 | | |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain Post-dose 1 | 70 | 55 | | |
| Injection site Pain Post-dose 2 | 66 | 58 | | |
| Injection site Pain Post-dose 3 | 57 | 48 | | |
| Injection site Erythema Post-dose 1 | 23 | 17 | | |
| Injection site Erythema Post-dose 2 | 25 | 17 | | |
| Injection site Erythema Post-dose 3 | 30 | 17 | | |
| Injection site Swelling Post-dose 1 | 21 | 16 | | |
| Injection site Swelling Post Dose 2 | 21 | 12 | | |
| Injection site Sweling Post Dose 3 | 17 | 11 | | |
| Pyrexia Post-dose 1 | 15 | 12 | | |
| Pyrexia Post-dose 2 | 33 | 23 | | |
| Pyrexia Post-dose 3 | 41 | 24 | | |
| Vomiting Post-dose 1 | 57 | 44 | | |
| Vomiting Post-dose 2 | 55 | 48 | | |
| Vomiting Post-dose 3 | 44 | 40 | | |
| Crying Post-dose 1 | 51 | 41 | | |
| Crying Post-dose 2 | 54 | 38 | | |
| Crying Post-dose 3 | 45 | 30 | | |
| Somnolence Post-dose 1 | 51 | 45 | | |
| Somnolence Post-dose 2 | 35 | 38 | | |
| Somnolence Post-dose 3 | 26 | 36 | | |
| Anorexia Post-dose 1 | 43 | 27 | | |
| Anorexia Post-dose 2 | 48 | 35 | | |
| Anorexia Post-dose 3 | 42 | 40 | | |
| Irritability Post-dose 1 | 83 | 67 | | |
| Irritability Post-dose 2 | 81 | 74 | | |
| Irritability Post-dose 3 | 71 | 64 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed following the administration first dose of study vaccine (Day 0) through 6 months after the last dose.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 9.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | DTaP-IPV-Hep B-PRP~T |

Reporting group description:

Participants received 3 vaccinations with Diphtheria (D) and tetanus (T) toxoids, acellular pertussis (2-component) (aP), recombinant Hepatitis B surface antigen (HBsAg), inactivated poliomyelitis virus (IPV), and Hemophilus influenzae type b (Hib) polysaccharide conjugated to tetanus protein (DTaP-IPV-Hep B-PRP~T), with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

| | |
|---|---|
| Reporting group title | PENTAXIM™ and ENGERIX® |

Reporting group description:

Participants received 3 vaccinations with DTaP-IPV-PRP~T (PENTAXIM™ ) and recombinant Hepatitis B (ENGERIX® PEDIATRIC) vaccines, with one dose each at 2, 3, and 4 months of age (Days 0, 30, and 60).

| Serious adverse events | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 153 (1.31%) | 3 / 152 (1.97%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 152 (0.66%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 152 (0.66%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 153 (0.65%) | 1 / 152 (0.66%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 152 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | DTaP-IPV-Hep B-PRP~T | PENTAXIM™ and ENGERIX® | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 83 / 153 (54.25%) | 74 / 152 (48.68%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 51 / 153 (33.33%) | 45 / 152 (29.61%) | |
| occurrences (all) | 51 | 45 | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 70 / 153 (45.75%) | 58 / 152 (38.16%) | |
| occurrences (all) | 70 | 58 | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 30 / 153 (19.61%) | 17 / 152 (11.18%) | |
| occurrences (all) | 30 | 17 | |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 21 / 153 (13.73%) | 16 / 152 (10.53%) | |
| occurrences (all) | 21 | 16 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 83 / 153 (54.25%) | 74 / 152 (48.68%) | |
| occurrences (all) | 83 | 74 | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 41 / 153 (26.80%) | 24 / 152 (15.79%) | |
| occurrences (all) | 41 | 24 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 57 / 153 (37.25%) | 48 / 152 (31.58%) | |
| occurrences (all) | 57 | 48 | |
| Psychiatric disorders | | | |
| Crying | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 54 / 153 (35.29%) | 41 / 152 (26.97%) | |
| occurrences (all) | 54 | 41 | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 48 / 153 (31.37%) | 40 / 152 (26.32%) | |
| occurrences (all) | 48 | 40 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 16 January 2006 | Prior to the enrollment of subjects in the study, the protocol was updated to include (i) the incorporation of an Independent Data Monitoring Committee (ii) the requirements for collection of baseline, immunogenicity, and safety data and analysis. |
| 16 April 2007 | A modification to remove all study procedures related to the booster vaccination, include another secondary immunogenicity assessment, and a change to the type of assays used to detect antibody levels at qualified contract laboratories. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported