# Clinical trial results:
# Comparison of Pertussis Specific Cellular and Humoral Immunity Before and After a Acellular Pertussis Booster-Vaccination in Combination With a Diphtheria-Tetanus-Polio-Vaccine Between Three Groups of Adolescents 10-14 Years of Age That Have Previously Either Received 4 or 5 Doses of Acellular Pertussis Vaccine or 4 Doses of Whole-Cell Pertussis Vaccine

## Summary

| | |
|---|---|
| EudraCT number | 2005-005532-27 |
| Trial protocol | DE |
| Global end of trial date | 31 October 2006 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 February 2016 |
| First version publication date | 27 March 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | PERTIMMUN06 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Sanofi Pasteur |
| Sponsor organisation address | 1 Discovery Drive, Swiftwater, United States, 18370 |
| Public contact | Vice President and Global Medical Expert, Sanofi Pasteur, +1 5709571506, Dr.Johnson@sanofipasteur.com |
| Scientific contact | Vice President and Global Medical Expert, Sanofi Pasteur, +1 5709571506, Dr.Johnson@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? | 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 | 13 September 2007 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 31 October 2006 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the pertussis-specific humoral and cellular immunity after vaccination with REPEVAX® or COVAXiS® + IPV Merieux® among 3 groups:
Group A: Adolescents 10-14 years of age who had received five doses of acellular pertussis vaccine and who simultaneously participated in the TRI05 study in which they received either REPEVAX® or COVAXiS® + IPV Merieux® based on on their randomization group.
Group B: Adolescents 10-14 years of age who previously received four doses of acellular pertussis vaccine. Subjects of group B could not participate in the TRI05 study, and in this study received either REPEVAX® or COVAXiS® + IPV Merieux® as recommended by their physician.
Group C: Adolescents 10-14 years of age who previously received four doses of whole-cell pertussis vaccine and had not yet received acellular pertussis vaccine and who simultaneously participated in the TRI05 study in which they had received either REPEVAX® or COVAXiS® + IPV Merieux® based on their randomization group.

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:

Subjects may have received a 5th consecutive aP immunization at 4 - 6 years of age (which became part of the official German recommendations in March 2006) or have received only 4 consecutive aP or wP immunizations (last dose at 18-24 months).

Evidence for comparator:

Not applicable

| | |
|---|---|
| Actual start date of recruitment | 01 February 2006 |
| 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 | Germany: 78 |
| Worldwide total number of subjects | 78 |
| EEA total number of subjects | 78 |

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) | 22 |
| Adolescents (12-17 years) | 56 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled from 01 February 2006 to 16 August 2006 at 17 clinical centers in Germany.

### Pre-assignment

Screening details:

A total of 78 subjects who met the inclusion, but none of the exclusion criteria were enrolled and vaccinated.

### Period 1

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

Blinding implementation details:

Not applicable

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Study Group A |

Arm description:

Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years).

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

Dosage and administration details:

A single 0.5 ml dose

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

Dosage and administration details:

A single 0.5 mL dose

| | |
|---|---|
| **Arm title** | Study Group B |

Arm description:

Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months).

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

| | |
|---|---|
| Dosage and administration details:<br>A single 0.5 ml dose | |
| Investigational medicinal product name | COVAXiS |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>A single 0.5 mL dose | |
| **Arm title** | Study Group C |
| Arm description:<br>Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine. | |
| Arm type | Experimental |
| Investigational medicinal product name | REPEVAX |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>A single 0.5 ml dose | |
| Investigational medicinal product name | COVAXiS |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>A single 0.5 mL dose | |

| **Number of subjects in period 1** | Study Group A | Study Group B | Study Group C |
|---|---|---|---|
| Started | 37 | 23 | 18 |
| Completed | 37 | 23 | 18 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Study Group A |
| Reporting group description: | |
| Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years). | |
| Reporting group title | Study Group B |
| Reporting group description: | |
| Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months). | |
| Reporting group title | Study Group C |
| Reporting group description: | |
| Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine. | |

| Reporting group values | Study Group A | Study Group B | Study Group C |
|---|---|---|---|
| Number of subjects | 37 | 23 | 18 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 17 | 5 | 0 |
| Adolescents (12-17 years) | 20 | 18 | 18 |
| 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: years | | | |
| arithmetic mean | 12.2 | 12 | 13.3 |
| standard deviation | ± 0.2 | ± 0.5 | ± 0.3 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 12 | 6 |
| Male | 22 | 11 | 12 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 78 | | |
| 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) | 22 | | |
| Adolescents (12-17 years) | 56 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 33 | | |
| Male | 45 | | |

## End points

### End points reporting groups

| Reporting group title | Study Group A |
|---|---|
| Reporting group description: | |
| Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years). | |
| Reporting group title | Study Group B |
| Reporting group description: | |
| Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months). | |
| Reporting group title | Study Group C |
| Reporting group description: | |
| Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine. | |

### Primary: Summary of Geometric Mean Titers (GMTs) of Pertussis Antibodies Before and After a Acellular Pertussis Booster Vaccination

| End point title | Summary of Geometric Mean Titers (GMTs) of Pertussis Antibodies Before and After a Acellular Pertussis Booster Vaccination[1] |
|---|---|
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 (pre-vaccination) and 1 month post-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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | Study Group A | Study Group B | Study Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 23 | 18 | |
| Units: EU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IgG-Pertussis toxoid (pre-vaccination) | 4.22 (3.24 to 5.48) | 3.85 (2.83 to 5.25) | 9.7 (4.18 to 22.47) | |
| IgG-Pertussis toxoid (post-vaccination) | 16.35 (11.35 to 23.55) | 17.06 (9.66 to 30.14) | 50.33 (26.13 to 96.96) | |
| IgG-Filamentous hemagglutinin (pre-vaccination) | 25.19 (16.78 to 37.82) | 14.98 (9.39 to 23.9) | 10.67 (5.21 to 21.89) | |
| igG-Filamentous hemagglutinin (post-vaccination) | 160.97 (122.34 to 211.81) | 127.04 (89.09 to 181.15) | 135.57 (98.94 to 191.28) | |
| igG-Pertactin (pre-vaccination) | 18.78 (12.5 to 28.21) | 13.33 (6.34 to 28.02) | 13.95 (6.3 to 30.87) | |
| igG-Pertactin (post-vaccination) | 600.72 (449.61 to 802.63) | 407.34 (260.6 to 636.7) | 638.95 (370.02 to 1103.33) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with positive cell mediated immunity-response against Pertussis Toxoid (PT) Before and After Acellular Pertussis Booster Vaccination.

| End point title | Percentage of Subjects with positive cell mediated immunity-response against Pertussis Toxoid (PT) Before and After Acellular Pertussis Booster Vaccination. |
|---|---|

End point description:

A positive cell mediated immunity-response against PT is defined as a simulation index of ≥ 4.

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

End point timeframe:

Pre-vaccination (Day 0) and Day 28 to 36 post-vaccination

| End point values | Study Group A | Study Group B | Study Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 21 | 17 | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Pre-vaccination | 38 | 43 | 53 | |
| Post-vaccination | 62 | 81 | 77 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Filamentous Hemagglutinin Before and After Acellular Pertussis Booster Vaccination.

| End point title | Percentage of Subjects with positive Cell mediated immunity-response against Filamentous Hemagglutinin Before and After Acellular Pertussis Booster Vaccination. |
|---|---|

End point description:

A positive cell mediated immunity-response against Filamentous Hemagglutinin was defined as a stimulation index (SI) of ≥4.

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

End point timeframe:

Pre-vaccination (Day 0) and Day 28-36 Post-vaccination

| End point values | Study Group A | Study Group B | Study Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 21 | 17 | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Pre-vaccination | 78 | 62 | 65 | |
| Post-vaccination | 87 | 95 | 94 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Pertactin Before and After Acellular Pertussis Booster Vaccination.

| End point title | Percentage of Subjects with positive Cell mediated immunity-response against Pertactin Before and After Acellular Pertussis Booster Vaccination. |
|---|---|

End point description:

A positive cell mediated immunity-response against Pertactin was defined as a stimulation index (SI) of ≥4.

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

End point timeframe:

Pre-vaccination (Day 0) and Day 28-36 Post-vaccination

| End point values | Study Group A | Study Group B | Study Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 21 | 17 | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Pre-vaccination | 35 | 62 | 53 | |
| Post-vaccination | 68 | 71 | 82 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Fimbriae type 2/3 Before and After Acellular Pertussis Booster Vaccination.

| End point title | Percentage of Subjects with positive Cell mediated immunity-response against Fimbriae type 2/3 Before and After Acellular Pertussis Booster Vaccination. |
|---|---|

End point description:

A positive cell mediated immunity-response against Fimbriae type 2/3 (FIM) was defined as a stimulation index (SI) of ≥4.

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

End point timeframe:

Pre-vaccination (Day 0) and Day 28 to 36 Post-vaccination

| **End point values** | Study Group A | Study Group B | Study Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37 | 21 | 17 | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Pre-vaccination | 60 | 52 | 53 | |
| Post-vaccination | 73 | 76 | 82 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

Safety outcomes including adverse events information were not part of this protocol and were not solicited during the study.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 6.0 |

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Safety outcomes including adverse events information were not part of this protocol and were not solicited during the study.

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Not applicable |

Notes: