# Clinical trial results:
# One-, Three-, Five-, Eight- and Ten-Year Data on the Long- Term Immunogenicity of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) in Adults and Adolescents

## Summary

| | |
|---|---|
| EudraCT number | 2015-005843-15 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 19 February 2008 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 April 2016 |
| First version publication date | 16 April 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | TC9704-LT |

### Additional study identifiers

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

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Sanofi Pasteur Limited |
| Sponsor organisation address | 1755 Steeles Ave. West, Toronto, Canada, M2R 3T4 |
| Public contact | Clinical Team Leader, Sanofi Pasteur Limited, 416 667-2273, antigona.tomovici@sanofipasteur.com |
| Scientific contact | Clinical Team Leader, Sanofi Pasteur Limited, 416 667-2273, antigona.tomovici@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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 19 February 2008 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 19 February 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To describe the antibody levels for tetanus, diphtheria and pertussis at 1 year, 3 years, 5 years, 8 years and 10 years after vaccination with Tdap Vaccine.

Protection of trial subjects:

Subjects were vaccinated in the main TC9704 study. No vaccination was administered as part of this long-term immunogenicity follow-up study.

Background therapy:

Subjects in the original TC9704 study were randomized to 1 of 5 groups: 2 groups received Tetanus and Diphtheria Toxoids Adsorbed Vaccine and Acellular Pertussis Vaccine Adsorbed administered separately and 3 groups received Tdap vaccine (ADACEL®; Lots 21-11, 22-11, 23-11). For the follow-up studies, only subjects from the 2 British Columbia sites, who received Tdap vaccine were invited to participate in the long-term immunogenicity follow-up visits to provide blood samples at 1, 3, 5, 8 and 10 years post-vaccination.

Evidence for comparator:

Not applicable

| | |
|---|---|
| Actual start date of recruitment | 07 October 1998 |
| 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 | Canada: 449 |
| Worldwide total number of subjects | 449 |
| 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) | 0 |

| | |
|---|---|
| Adults (18-64 years) | 449 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study subjects were enrolled from 07 October 1998 (1-year follow up) to 19 February 2008 (10-year follow up) at 2 clinic centers in Canada.

### Pre-assignment

Screening details:

A total of 449 subjects who met all of the inclusion and none of the exclusion criteria were included in the long-term immunogenicity analysis.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (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** | Tdap Vaccine (Lot 21-11) |

Arm description:

Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 21-11 on Day 0.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle, 1 injection on Day 0.

| | |
|---|---|
| **Arm title** | Tdap Vaccine (Lot 22-11) |

Arm description:

Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 22-11 on Day 0.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle, 1 injection on Day 0.

| | |
|---|---|
| **Arm title** | Tdap Vaccine (Lot 23-11) |

Arm description:

Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 23-11 on Day 0.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the deltoid muscle, 1 injection on Day 0.

| **Number of subjects in period 1** | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) |
|---|---|---|---|
| Started | 151 | 149 | 149 |
| Completed | 51 | 43 | 50 |
| Not completed | 100 | 106 | 99 |
| Lost to follow-up | 100 | 106 | 99 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Tdap Vaccine (Lot 21-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 21-11 on Day 0. | |
| Reporting group title | Tdap Vaccine (Lot 22-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 22-11 on Day 0. | |
| Reporting group title | Tdap Vaccine (Lot 23-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 23-11 on Day 0. | |

| Reporting group values | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) |
|---|---|---|---|
| Number of subjects | 151 | 149 | 149 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 151 | 149 | 149 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 34.1 | 33.7 | 33.6 |
| standard deviation | ± 10.4 | ± 10.6 | ± 10 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 108 | 104 | 92 |
| Male | 43 | 45 | 57 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 449 | | |
| 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) | 449 | | |

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

| | | | |
|---|---|---|---|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 304 | | |
| Male | 145 | | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Combined Tdap Vaccine |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Subjects who received 1 of 3 lots of Tdap Vaccine on Day 0 and returned for the long-term immunogenicity follow-up visits to provide blood samples at 1, 3, 5, 8, and 10 years post-vaccination.

| **Reporting group values** | Combined Tdap Vaccine | | |
|---|---|---|---|
| Number of subjects | 449 | | |
| Age categorical | | | |
| 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) | 449 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 33.8 | | |
| standard deviation | ± 10.3 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 304 | | |
| Male | 145 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Tdap Vaccine (Lot 21-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 21-11 on Day 0. | |
| Reporting group title | Tdap Vaccine (Lot 22-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 22-11 on Day 0. | |
| Reporting group title | Tdap Vaccine (Lot 23-11) |
| Reporting group description: | |
| Subjects received 1 dose of Tdap vaccine (ADACEL®) Lot 23-11 on Day 0. | |
| Subject analysis set title | Combined Tdap Vaccine |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Subjects who received 1 of 3 lots of Tdap Vaccine on Day 0 and returned for the long-term immunogenicity follow-up visits to provide blood samples at 1, 3, 5, 8, and 10 years post-vaccination. | |

### Primary: Percentage of Subjects with Seroprotection to Tetanus and Diphtheria Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL®

| | |
|---|---|
| End point title | Percentage of Subjects with Seroprotection to Tetanus and Diphtheria Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL®[1] |
| End point description: | |
| Anti-Diphtheria antibody responses were assessed using the micro metabolic inhibition test (MIT). Anti-Tetanus antibody responses were assessed using enzyme-linked immunosorbent assay (ELISA). Seroprotection for diphtheria was defined as titers ≥ 0.01 IU/mL and ≥ 0.1 IU/mL. Seroprotection for tetanus was defined as titers ≥ 0.01 EU/mL and ≥ 0.1 EU/mL. | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 (pre-vaccination) and 1 month and 1, 3, 5, 8, and 10 years 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 vaccine groups from the primary series for the long term follow-up period.

| End point values | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) | Combined Tdap Vaccine |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 151 | 149 | 149 | 449 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Diphtheria; ≥ 0.01 IU/mL; Pre-injection | 84.1 | 79.2 | 79.9 | 81.1 |
| Diphtheria; ≥ 0.01 IU/mL; 1 month Post-injection | 98.7 | 97.3 | 98 | 98 |
| Diphtheria; ≥ 0.01 IU/mL; 1 year Post-injection | 95.5 | 96.9 | 98.5 | 97 |
| Diphtheria; ≥ 0.01 IU/mL; 3 year Post-injection | 97 | 98.5 | 95.7 | 97 |
| Diphtheria; ≥ 0.01 IU/mL; 5 year Post-injection | 90 | 96.4 | 93.5 | 93.3 |

| | | | | |
|---|---|---|---|---|
| Diphtheria; ≥ 0.01 IU/mL; 8 year Post-injection | 92 | 96 | 96.1 | 94.7 |
| Diphtheria; ≥ 0.01 IU/mL; 10 year Post-injection | 85.1 | 97.5 | 95.8 | 92.6 |
| Tetanus; ≥ 0.01 EU/mL; Pre-injection | 98.7 | 98.6 | 99.3 | 98.9 |
| Tetanus; ≥ 0.01 EU/mL; 1 month Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.01 EU/mL; 1 year Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.01 EU/mL; 3 year Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.01 EU/mL; 5 year Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.01 EU/mL; 8 year Post-injection | 100 | 100 | 98 | 99.3 |
| Tetanus; ≥ 0.01 EU/mL; 10 year Post-injection | 100 | 100 | 97.8 | 99.2 |
| Diphtheria; ≥ 0.1 IU/mL; Pre-injection | 31.8 | 26.8 | 26.2 | 28.3 |
| Diphtheria; ≥ 0.1 IU/mL; 1 month Post-injection | 84.8 | 85.7 | 84.5 | 85 |
| Diphtheria; ≥ 0.1 IU/mL; 1 year Post-injection | 63.6 | 71.9 | 67.6 | 67.7 |
| Diphtheria; ≥ 0.1 IU/mL; 3 year Post-injection | 59.7 | 59.1 | 61.4 | 60.1 |
| Diphtheria; ≥ 0.1 IU/mL; 5 year Post-injection | 61.7 | 44.6 | 50 | 52.2 |
| Diphtheria; ≥ 0.1 IU/mL; 8 year Post-injection | 56 | 48 | 54.9 | 53 |
| Diphtheria; ≥ 0.1 IU/mL; 10 year Post-injection | 51.1 | 40 | 54.2 | 48.9 |
| Tetanus; ≥ 0.1 EU/mL; Pre-injection | 97.4 | 95.9 | 97.3 | 96.9 |
| Tetanus; ≥ 0.1 EU/mL; 1 month Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.1 EU/mL; 1 year Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.1 EU/mL; 3 year Post-injection | 100 | 100 | 100 | 100 |
| Tetanus; ≥ 0.1 EU/mL; 5 year Post-injection | 100 | 100 | 98.4 | 99.4 |
| Tetanus; ≥ 0.1 EU/mL; 8 year Post-injection | 98 | 100 | 98 | 98.6 |
| Tetanus; ≥ 0.1 EU/mL; 10 year Post-injection | 100 | 100 | 97.8 | 99.2 |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Summary of Geometric Mean Titers of Anti-Tetanus and Anti-Diphtheria Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL®

| | |
|---|---|
| End point title | Summary of Geometric Mean Titers of Anti-Tetanus and Anti-Diphtheria Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL® |

End point description:

Anti-Diphtheria antibody responses were assessed using the micro metabolic inhibition test (MIT). Anti-

Tetanus antibody responses were assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and 1 month and 1, 3, 5, 8, and 10 years post-vaccination

| **End point values** | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) | Combined Tdap Vaccine |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 151 | 149 | 149 | 449 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Diphtheria; Pre-injection | 0.05 (0.04 to 0.07) | 0.04 (0.03 to 0.05) | 0.03 (0.02 to 0.04) | 0.04 (0.03 to 0.05) |
| Diphtheria; 1 month Post-injection | 0.93 (0.67 to 1.29) | 0.84 (0.59 to 1.2) | 0.83 (0.59 to 1.17) | 0.86 (0.71 to 1.05) |
| Diphtheria; 1 year Post-injection | 0.22 (0.14 to 0.33) | 0.25 (0.17 to 0.36) | 0.27 (0.18 to 0.4) | 0.24 (0.19 to 0.31) |
| Diphtheria; 3 year Post-injection | 0.15 (0.1 to 0.23) | 0.15 (0.11 to 0.21) | 0.16 (0.11 to 0.24) | 0.16 (0.13 to 0.19) |
| Diphtheria; 5 year Post-injection | 0.12 (0.07 to 0.19) | 0.1 (0.07 to 0.15) | 0.1 (0.07 to 0.16) | 0.11 (0.08 to 0.14) |
| Diphtheria; 8 year Post-injection | 0.13 (0.07 to 0.25) | 0.12 (0.08 to 0.17) | 0.13 (0.08 to 0.2) | 0.13 (0.1 to 0.17) |
| Diphtheria; 10 year Post-injection | 0.11 (0.06 to 0.2) | 0.1 (0.06 to 0.16) | 0.09 (0.06 to 0.14) | 0.1 (0.07 to 0.13) |
| Tetanus; Pre-injection | 1.11 (0.92 to 1.34) | 1.1 (0.88 to 1.37) | 1.08 (0.9 to 1.31) | 1.1 (0.98 to 1.23) |
| Tetanus; 1 month Post-injection | 16.78 (14.84 to 18.97) | 16.67 (14.58 to 19.06) | 14.82 (12.76 to 17.21) | 16.07 (14.86 to 17.37) |
| Tetanus; 1 year Post-injection | 4.61 (3.8 to 5.59) | 4.26 (3.52 to 5.17) | 3.83 (3.14 to 4.66) | 4.22 (3.77 to 4.71) |
| Tetanus; 3 year Post-injection | 2.38 (1.98 to 2.86) | 2.48 (2.03 to 3.02) | 2.3 (1.87 to 2.83) | 2.38 (2.13 to 2.67) |
| Tetanus; 5 year Post-injection | 2.56 (1.95 to 3.36) | 2.95 (2.35 to 3.7) | 2.5 (1.88 to 3.34) | 2.65 (2.28 to 3.09) |
| Tetanus; 8 year Post-injection | 2.73 (1.93 to 3.85) | 3.54 (2.69 to 4.66) | 2.46 (1.63 to 3.7) | 2.86 (2.35 to 3.49) |
| Tetanus; 10 year Post-injection | 1.93 (1.41 to 2.66) | 3.06 (2.13 to 4.4) | 1.47 (0.98 to 2.22) | 2.01 (1.63 to 2.49) |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Summary of Geometric Mean Titers of Anti-Pertussis Antibodies Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL®

| End point title | Summary of Geometric Mean Titers of Anti-Pertussis Antibodies Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL® |
|---|---|

End point description:

Anti-Pertussis (Pertussis toxoid, Filamentous Hemagglutinin, Pertactin, and Fimbriae types 2 and 3) antibody responses were assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and 1 month and 1, 3, 5, 8, and 10 years post-vaccination

| **End point values** | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) | Combined Tdap Vaccine |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 151 | 149 | 149 | 449 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Pertussis toxoid; Pre-injection | 8.82 (7.07 to 11) | 7.66 (6.11 to 9.59) | 10.5 (8.49 to 12.99) | 8.92 (7.86 to 10.12) |
| Pertussis toxoid; 1 month Post-injection | 147.08 (126.85 to 170.54) | 168.29 (145.32 to 194.88) | 120.63 (105.17 to 138.35) | 144.02 (132.48 to 156.57) |
| Pertussis toxoid; 1 year Post-injection | 51.52 (41.07 to 64.62) | 63.41 (49.94 to 80.52) | 51.58 (41.74 to 63.74) | 55.14 (48.48 to 62.71) |
| Pertussis toxoid; 3 year Post-injection | 49.11 (37.66 to 64.06) | 57.92 (43.88 to 76.46) | 41.65 (32.19 to 53.89) | 49.12 (42.16 to 57.23) |
| Pertussis toxoid; 5 year Post-injection | 39.84 (31.41 to 50.54) | 56.72 (44.55 to 72.21) | 37.8 (30.24 to 47.25) | 43.85 (38.31 to 50.19) |
| Pertussis toxoid; 8 year Post-injection | 25.15 (19.32 to 32.74) | 21.66 (16.18 to 28.98) | 23.82 (17.7 to 32.06) | 23.47 (19.97 to 27.57) |
| Pertussis toxoid; 10 year Post-injection | 25.91 (19.56 to 34.32) | 18.56 (12.84 to 26.83) | 18.07 (13.01 to 25.1) | 20.6 (17.12 to 24.78) |
| Filamentous hemagglutinin; Pre-injection | 22.64 (18.29 to 28.03) | 23.59 (19.63 to 28.36) | 24.87 (20.06 to 30.84) | 23.68 (21.06 to 26.63) |
| Filamentous hemagglutinin; 1 month Post-injection | 311.86 (271.8 to 357.82) | 327.8 (286.94 to 374.48) | 360.42 (311.29 to 417.3) | 332.62 (307.07 to 360.3) |
| Filamentous hemagglutinin; 1 year Post-injection | 105.55 (84.49 to 131.87) | 101.41 (81.01 to 126.94) | 132.09 (109.61 to 159.18) | 112.44 (99.62 to 126.92) |
| Filamentous hemagglutinin; 3 year Post-injection | 59.06 (47.57 to 73.32) | 58.25 (47.58 to 71.32) | 74.96 (59.46 to 94.51) | 63.7 (56.25 to 72.13) |
| Filamentous hemagglutinin; 5 year Post-injection | 40.5 (32.44 to 50.56) | 50.75 (41.27 to 62.41) | 51.96 (41.68 to 64.78) | 47.46 (41.92 to 53.72) |
| Filamentous hemagglutinin; 8 year Post-injection | 52.91 (41.2 to 67.95) | 55.33 (45.25 to 67.65) | 75.04 (58.92 to 95.58) | 60.37 (52.83 to 68.99) |
| Filamentous hemagglutinin; 10 year Post-injection | 38.35 (29.7 to 49.52) | 37.31 (29.6 to 47.04) | 43.07 (32.33 to 57.38) | 39.63 (34.16 to 45.96) |
| Pertactin; Pre-injection | 5.83 (4.38 to 7.76) | 4.27 (3.26 to 5.59) | 5.27 (3.92 to 7.1) | 5.09 (4.32 to 5.99) |
| Pertactin; 1 month Post-injection | 286.16 (225.87 to 362.54) | 347.4 (273.86 to 440.7) | 217.67 (165.67 to 285.99) | 278.58 (241.19 to 321.76) |
| Pertactin; 1 year Post-injection | 81.07 (54.69 to 120.17) | 87.04 (60.08 to 126.08) | 68.78 (48.5 to 97.56) | 78.45 (63.52 to 96.91) |
| Pertactin; 3 year Post-injection | 79.99 (57.27 to 111.74) | 76.76 (55.72 to 105.76) | 79.01 (55.21 to 113.08) | 78.56 (64.85 to 95.18) |
| Pertactin; 5 year Post-injection | 36.56 (24.54 to 54.47) | 45.05 (30.44 to 66.67) | 34.07 (22.44 to 51.73) | 38.17 (30.35 to 48.01) |

| | | | | |
|---|---|---|---|---|
| Pertactin; 8 year Post-injection | 37.41 (25.94 to 53.94) | 47.27 (32.63 to 68.46) | 43.88 (28.51 to 67.52) | 42.59 (34.15 to 53.12) |
| Pertactin; 10 year Post-injection | 43.18 (29.25 to 63.74) | 35.91 (23.55 to 54.75) | 41.72 (26.88 to 64.75) | 40.38 (31.9 to 51.11) |
| Fimbriae types 2 and 3; Pre-injection | 22.31 (17.43 to 28.55) | 18.76 (14.01 to 25.12) | 19.35 (14.26 to 26.27) | 20.09 (17.09 to 23.62) |
| Fimbriae types 2 and 3; 1 month Post-injection | 1314.62 (1097.33 to 1574.94) | 1048.31 (844.83 to 1300.81) | 690.27 (557.86 to 854.1) | 985.27 (874.58 to 1109.97) |
| Fimbriae types 2 and 3; 1 year Post-injection | 319.3 (247.19 to 412.43) | 338.34 (248.93 to 459.85) | 251.7 (188.03 to 336.92) | 300.08 (254.99 to 353.15) |
| Fimbriae types 2 and 3; 3 year Post-injection | 249.23 (194.9 to 318.69) | 249.68 (183.89 to 399.01) | 194.11 (141.26 to 266.73) | 229.44 (194.23 to 271.04) |
| Fimbriae types 2 and 3; 5 year Post-injection | 205.51 (153.54 to 275.06) | 226.5 (159.48 to 321.69) | 160.79 (114.47 to 225.84) | 194.9 (161.63 to 235.02) |
| Fimbriae types 2 and 3; 8 year Post-injection | 147.85 (113.86 to 191.97) | 180.23 (129.37 to 251.08) | 133.39 (95.38 to 186.54) | 152.45 (127.76 to 181.92) |
| Fimbriae types 2 and 3; 10 year Post-injection | 130.67 (97.63 to 174.9) | 145.36 (98.48 to 214.55) | 113.72 (81.71 to 158.26) | 128.43 (106.32 to 155.13) |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects with Seropositivity to Pertussis antigens Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL®

| | |
|---|---|
| End point title | Percentage of Subjects with Seropositivity to Pertussis antigens Following Vaccination with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) - ADACEL® |

End point description:

Anti-Pertussis (Pertussis toxoid, Filamentous Hemagglutinin, Pertactin, and Fimbriae types 2 and 3) antibody responses were assessed using enzyme-linked immunosorbent assay (ELISA). Seropositivity was defined as subjects with titers ≥ 5 EU/mL for Pertussis Toxoid, ≥ 3 EU/mL for Filamentous Hemagglutinin, ≥ 17 EU/mL for Fimbriae types 2 and 3, and ≥ 3 EU/mL for Pertactin at 1 month and 1, 3, 5 years post-vaccination; and with titers ≥ 4 EU/mL for Pertussis Toxoid, ≥ 3 EU/mL for Filamentous Hemagglutinin, ≥ 4 EU/mL for Fimbriae types 2 and 3 and Pertactin at 8 and 10 years post-vaccination.

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

End point timeframe:

Day 0 (pre-vaccination) and 1 month and 1, 3, 5, 8, and 10 years post-vaccination

| **End point values** | Tdap Vaccine (Lot 21-11) | Tdap Vaccine (Lot 22-11) | Tdap Vaccine (Lot 23-11) | Combined Tdap Vaccine |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 151 | 149 | 149 | 449 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Pertussis toxoid; Pre-injection | 68.5 | 62.3 | 77.6 | 69.5 |

| | | | | |
|---|---|---|---|---|
| Pertussis toxoid; 1 month Post-injection | 100 | 100 | 100 | 100 |
| Pertussis toxoid; 1 year Post-injection | 98.5 | 100 | 98.5 | 99 |
| Pertussis toxoid; 3 year Post-injection | 97.1 | 97.1 | 94.3 | 96.2 |
| Pertussis toxoid; 5 year Post-injection | 96.8 | 100 | 98.5 | 98.4 |
| Pertussis toxoid; 8 year Post-injection | 97.9 | 92.2 | 92.2 | 94 |
| Pertussis toxoid; 10 year Post-injection | 97.6 | 88.9 | 86.7 | 91.1 |
| Filamentous hemagglutinin; Pre-injection | 92.1 | 95.3 | 93.3 | 93.5 |
| Filamentous hemagglutinin; 1 month Post-injection | 100 | 100 | 100 | 100 |
| Filamentous hemagglutinin; 1 year Post-injection | 100 | 98.5 | 100 | 99.5 |
| Filamentous hemagglutinin; 3 year Post-injection | 100 | 100 | 100 | 100 |
| Filamentous hemagglutinin; 5 year Post-injection | 100 | 100 | 100 | 100 |
| Filamentous hemagglutinin; 8 year Post-injection | 100 | 100 | 100 | 100 |
| Filamentous hemagglutinin; 10 year Post-injection | 100 | 100 | 100 | 100 |
| Pertactin; Pre-injection | 63.6 | 57.7 | 64.4 | 61.9 |
| Pertactin; 1 month Post-injection | 99.3 | 100 | 98.6 | 99.3 |
| Pertactin; 1 year Post-injection | 95.5 | 100 | 98.5 | 98 |
| Pertactin; 3 year Post-injection | 100 | 100 | 98.6 | 99.5 |
| Pertactin; 5 year Post-injection | 95.2 | 98.4 | 90.8 | 94.7 |
| Pertactin; 8 year Post-injection | 92.6 | 100 | 90.6 | 94.3 |
| Pertactin; 10 year Post-injection | 94.1 | 100 | 90 | 94.4 |
| Fimbriae types 2 and 3; Pre-injection | 57.6 | 54.4 | 60.4 | 57.5 |
| Fimbriae types 2 and 3; 1 month Post-injection | 100 | 99.3 | 99.3 | 99.6 |
| Fimbriae types 2 and 3; 1 year Post-injection | 100 | 95.4 | 97.1 | 97.5 |
| Fimbriae types 2 and 3; 3 year Post-injection | 98.5 | 94.3 | 92.8 | 95.2 |
| Fimbriae types 2 and 3; 5 year Post-injection | 98.4 | 93.4 | 92.3 | 94.7 |
| Fimbriae types 2 and 3; 8 year Post-injection | 100 | 100 | 98.1 | 99.4 |
| Fimbriae types 2 and 3; 10 year Post-injection | 100 | 97.6 | 98 | 98.6 |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information[1] | |
|---|---|
| Timeframe for reporting adverse events: Safety was not assessed in this 10-year immunogenicity follow-up study. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 10 |

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 end points were not assessed in the 10-year follow-up study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 23 May 2001 | Allowed for the collection of additional blood samples for long-term follow-up serology studies. |
| 23 June 2005 | The major changes included adding the 8-year follow-up study, including details of collection, storage, and and shipment of long-term follow up blood samples and sera, providing details of the study population for the long-term follow-up studies (including inclusion/exclusion criteria), and clarified the statistical analysis for the long-term follow-up studies. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported