Clinical trial results:
Comparison of the immunogenicity and safety of a combined adsorbed low dose diphtheria, tetanus and inactivated poliomyelitis vaccine (REVAXIS®) with a combined diphtheria, tetanus and inactivated poliomyelitis vaccine (DT Polio®) when given as a booster dose at 6 years of age.

Summary

EudraCT number	2005-001446-16
Trial protocol	FR
Global end of trial date	16 January 2008

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	29 May 2015

Trial information

Trial identification

Sponsor protocol code	F05-TdI-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00447525
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur MSD S.N.C.
Sponsor organisation address	162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367
Public contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C, ClinicalTrialsDisclosure@spmsd.com
Scientific contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C, ClinicalTrialsDisclosure@spmsd.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	16 January 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the Diphtheria seroprotection response (defined as anti-diphtheria antibody titre (SN) ≥0.1 IU/mL), the Tetanus seroprotection response (defined as an anti-tetanus antibody titre (EIA) ≥0.1 IU/mL), and the Poliomyelitis type 1, 2 & 3 seroprotection responses (defined as an anti-poliovirus antibody type 1, 2 & 3 titre (SN) ≥8 (1/dil)) 1 month (28 to 35 days) after a single dose of REVAXIS® (dT-IPV vaccine) is non inferior to the Diphtheria, Tetanus and Poliomyelitis type 1, 2 & 3 seroprotection responses 1 month after a single dose of DT Polio® (DT-IPV vaccine) when given as a second booster to healthy 6 year-old children who received 3-dose primary series within the first 6 months of life and a first booster at 16-18 months of life (+/-2 months) including DT-IPV vaccine.

Protection of trial subjects:

Subjects in the study received a single dose of the study vaccine or comparator vaccine supplied in a pre-filled 0.5 mL syringe that was administered by qualified study personnel.
Subjects with allergy to any of the vaccine components were not vaccinated.
After each vaccination, subjects were also kept under observation for 20 minutes to ensure their safety.
Appropriate equipment were also available on site in case of any immediate allergic reactions.

Background therapy:

Children were previously vaccinated with 3 doses of a diphtheria, tetanus and poliomyelitis containing vaccine given alone or in combination within the first 6 months of life and a booster dose of a diphtheria, tetanus and poliomyelitis containing vaccine given alone or in combination at 16-18 months of life (+/-2 months).

Evidence for comparator:

The comparator group (DT Polio Group) was added in order to answer the study objective.
Indeed, this study was designed to provide comparative data of the immunogenicity and the safety of REVAXIS versus DT Polio when given as a booster dose at 6 years of age.
DT Polio was a reference vaccine licensed and recommended as diphtheria, tetanus and poliovirus booster at 6 years of age in France.

Actual start date of recruitment	24 January 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	France: 760
Worldwide total number of subjects	760
EEA total number of subjects	760

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)	760
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:

Study participants were recruited for the study between 24 January 2007 and 10 December 2007 in 71 active centres in France.

Pre-assignment

Screening details:

788 subjects were screened in this study.
760 subjects were randomised.
759 subjects met all inclusion criteria and none of the non-inclusion criteria.
758 subjects were vaccinated and completed the study.

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:

Blinding is not applicable as this study was an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	REVAXIS Group

Arm description:

Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).

Arm type	Experimental
Investigational medicinal product name	REVAXIS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose (intramuscular, deltoid) at 6 years of age.

Arm title	DT Polio Group

Arm description:

Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).

Arm type	Active comparator
Investigational medicinal product name	DT Polio®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose (intramuscular, deltoid) at 6 years of age.

Number of subjects in period 1	REVAXIS Group	DT Polio Group
Started	384	376
Vaccinated	383	375
Completed	383	375
Not completed	1	1
Consent withdrawn by subject	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	REVAXIS Group
Reporting group description:	
Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).	
Reporting group title	DT Polio Group
Reporting group description:	
Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).	

Reporting group values	REVAXIS Group	DT Polio Group	Total
Number of subjects	384	376	760
Age categorical			
Units: Subjects			
Children (2-11 years)	384	376	760
Age continuous			
Age in years at vaccination (1 missing value in the REVAXIS group)			
Units: years			
arithmetic mean	6.4	6.4	
standard deviation	± 0.3	± 0.3	-
Gender categorical			
Female and male			
Units: Subjects			
Female	182	180	362
Male	202	196	398
Weight continuous			
Weight in kg at vaccination			
Units: kg			
arithmetic mean	22.4	22.6	
standard deviation	± 3.6	± 3.8	-
Height continuous			
Height in cm at vaccination			
Units: cm			
arithmetic mean	119	119.2	
standard deviation	± 5.3	± 5.5	-

End points

End points reporting groups

Reporting group title	REVAXIS Group
Reporting group description:	
Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).	
Reporting group title	DT Polio Group
Reporting group description:	
Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).	

Primary: Seroprotection against diphtheria (SN), tetanus (EIA), and polio 1, 2 & 3 (SN) one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Seroprotection against diphtheria (SN), tetanus (EIA), and polio 1, 2 & 3 (SN) one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (i.e., 28 to 35 days post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus.
Seroprotection was defined as a titre ≥0.10 IU/mL for diphtheria (SN), ≥0.10 IU/mL for tetanus (EIA), ≥8 (1/dil) for polio 1, 2 & 3 (SN).
Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

End point type	Primary

End point timeframe:

One month (28 to 35 days) after vaccination.

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	283		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Diphtheria ≥0.10 IU/mL (SN) (N=284, 283)	98.6 (96.4 to 99.6)	99.3 (97.5 to 99.9)		
Anti-Tetanus ≥0.10 IU/mL (EIA) (N=284, 283)	99.6 (98.1 to 100)	100 (98.7 to 100)		
Anti-Polio 1 ≥8 (1/dil) (SN) (N=284, 283)	100 (98.7 to 100)	100 (98.7 to 100)		
Anti-Polio 2 ≥8 (1/dil) (SN) (N=284, 283)	100 (98.7 to 100)	100 (98.7 to 100)		
Anti-Polio 3 ≥8 (1/dil) (SN) (N=284, 282)	100 (98.7 to 100)	100 (98.7 to 100)		

Statistical analyses

Statistical analysis title	Non-inferiority analysis for diphtheria (SN)

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

Comparison groups	REVAXIS Group v DT Polio Group
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Wilson score method without CC
Parameter estimate	Difference in percentages of subjects
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.3

Notes:

[1] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥0.10 IU/mL for diphtheria (SN) was greater than -5%.
CI was based on the Wilson score method without continuity correction (CC).

Statistical analysis title	Non inferiority analysis for tetanus (EIA)

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

Comparison groups	REVAXIS Group v DT Polio Group
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	Wilson score method without CC
Parameter estimate	Difference in percentages of subjects
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1

Notes:

[2] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥0.10 IU/mL for tetanus (EIA) was greater than -5%.
CI was based on the Wilson score method without continuity correction (CC).

Statistical analysis title	Non inferiority analysis for Polio 1 (SN)

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was

concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

Comparison groups	REVAXIS Group v DT Polio Group
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	Wilson score method without CC
Parameter estimate	Difference in percentages of subjects
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Notes:

[3] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥8 (1/dil for polio 1 (SN) was greater than -5%.
CI was based on the Wilson score method without continuity correction (CC).

Statistical analysis title	Non inferiority analysis for Polio 2 (SN)

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

Comparison groups	REVAXIS Group v DT Polio Group
Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	Wilson score method without CC
Parameter estimate	Difference in percentages of subjects
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Notes:

[4] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥8 (1/dil) for polio 2 (SN) was greater than -5%.
CI was based on the Wilson score method without continuity correction (CC).

Statistical analysis title	Non inferiority analysis for Polio 3 (SN)

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

Comparison groups	REVAXIS Group v DT Polio Group

Number of subjects included in analysis	567
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	Wilson score method without CC
Parameter estimate	Difference in percentages of subjects
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Notes:

[5] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥8 (1/dil) for polio 3 (SN) was greater than -5%.
CI was based on the Wilson score method without continuity correction (CC).

Secondary: Geometric Mean Titres of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Geometric Mean Titres of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus. Antibody titres are expressed in IU/mL for diphtheria (SN), for diphtheria (EIA), and for tetanus (EIA), and 1/dil for polio 1, 2 & 3 (SN).
Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination.

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	283		
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-Diphtheria (SN) (N=284, 283)	3.71 (3.14 to 4.38)	23.32 (19.52 to 27.85)		
Anti-Diphtheria (EIA) (N=284, 281)	1.9 (1.65 to 2.19)	8.31 (7.24 to 9.54)		
Anti-Tetanus (EIA) (N=284, 283)	9.38 (8.33 to 10.56)	13.87 (12.21 to 15.76)		
Anti-Polio 1 (SN) (N=284, 283)	4776.77 (4093.41 to 5574.21)	7705.41 (6681.88 to 8885.73)		
Anti-Polio 2 (SN) (N=284, 283)	5715.35 (4919.35 to 6640.16)	4534.24 (3931.99 to 5228.73)		

Anti-Polio 3 (SN) (N=284, 282)	6015.97 (5138.41 to 7043.41)	2248.5 (1906.62 to 2651.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Response rates for diphtheria (SN & EIA) and tetanus (EIA) one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Response rates for diphtheria (SN & EIA) and tetanus (EIA) one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus.
Thresholds were defined as titres ≥1.0 IU/mL for diphtheria (SN), ≥0.10 IU/mL and ≥1.0 IU/mL for diphtheria (EIA), ≥1.0 IU/mL for tetanus (EIA).
Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination.

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	283		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Diphtheria ≥1.0 IU/mL (SN) (N=284, 283)	85.9 (81.3 to 89.7)	98.6 (96.4 to 99.6)		
Anti-Diphtheria ≥0.1 IU/mL (EIA) (N=284, 281)	98.6 (96.4 to 99.6)	99.6 (98 to 100)		
Anti-Diphtheria ≥1.0 IU/mL (EIA) (N=284, 281)	71.1 (65.5 to 76.3)	95 (91.8 to 97.2)		
Anti-Tetanus ≥1.0 IU/mL (EIA) (N=284, 283)	98.6 (96.4 to 99.6)	97.5 (95 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean of (individual) Titres Ratios of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Geometric Mean of (individual) Titres Ratios of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus.
Individual post (D28) / pre (D0) antibody titre ratios were measured for diphtheria, tetanus and polio 1, 2 & 3.
Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination.

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	283		
Units: Not applicable				
geometric mean (confidence interval 95%)				
Anti-Diphtheria (SN) (N=284, 283)	58.62 (47.59 to 72.2)	307.62 (247.53 to 382.31)		
Anti-Diphtheria (EIA) (N=284, 280)	27.79 (23.75 to 32.52)	112.23 (97.28 to 129.47)		
Anti-Tetanus (EIA) (N=284, 283)	38.7 (33.37 to 44.89)	58.95 (51.61 to 67.32)		
Anti-Polio 1 (SN) (N=283, 282)	63.52 (49.07 to 82.23)	121.98 (93.58 to 159.02)		
Anti-Polio 2 (SN) (N=284, 283)	56.92 (44.28 to 73.17)	54.11 (42 to 69.71)		
Anti-Polio 3 (SN) (N=284, 282)	51.51 (40.26 to 65.89)	23.68 (18.88 to 29.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of safety (D0-D28)

End point title	Summary of safety (D0-D28)

End point description:

Adverse events (AEs) were reported onto the diary card by the parent(s) or legal representative:
- From day 0 (D0) to D7 for solicited injection-site adverse reactions (ISRs: injection site pain, erythema, and swelling) and solicited systemic AEs (headache, myalgia, pyrexia);
- From D0 to Visit 2 for unsolicited (spontaneously reported) ISRs and systemic AEs.
AEs at injection sites were always considered as related to vaccine (Injection-Site Reactions (ISRs)). The investigator had to assess whether systemic AEs were related or not to the vaccine. All (related and unrelated) are displayed here.
Descriptive analysis was done on the Safety Analysis set.

One subject was randomised in the DT Polio Group but received REVAXIS vaccine. The subject was thus included in the REVAXIS Group in the Safety Analysis set, which therefore included 384 subjects in the REVAXIS group, and 374 subjects in the DT Polio Group.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination.

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	374		
Units: Percentage of subjects				
number (not applicable)				
D0 to D28, any AE	83.1	85.6		
D0 to D7, any AE	82.6	84.2		
D0 to D7, ISR	76	78.6		
D0 to D7, solicited ISR	76	78.6		
D0 to D7, unsolicited ISR	3.4	5.6		
D0 to D7, systemic AE	42.4	40.9		
D0 to D7, solicited systemic AE	35.4	36.4		
D0 to D7, unsolicited systemic AE	12.2	12.3		
D0 to D7, vaccine-related systemic AE	33.3	34		
D0 to D7, vaccine-related solicited systemic AE	31.3	32.9		
D0 to D7, vaccine-related unsolicited systemic AE	3.1	2.9		
D8 to D28, any AE	10.7	11		
D8 to D28, ISR	0	0		
D8 to D28, systemic AE	10.7	11		
D8 to D28, vaccine-related systemic AE	1.3	0.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects reporting solicited injection-site reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Proportion of subjects reporting solicited injection-site reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

Solicited injection-site adverse reactions (ISRs: injection-site pain, injection-site erythema, and injection-site swelling) were reported onto the diary card by the parent(s) or legal representative from day 0 (D0) to D7.
AEs at injection sites were always considered as related to vaccine (Injection-Site Reactions (ISRs)).
Descriptive analysis was done on the Safety Analysis set.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	374		
Units: Percentage of subjects				
number (not applicable)				
Injection site erythema	40.9	47.1		
Injection site pain	69.8	69.8		
Injection site swelling	32.3	37.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects reporting solicited systemic adverse events and reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

End point title	Proportion of subjects reporting solicited systemic adverse events and reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

End point description:

Solicited systemic adverse events (AEs: headache, myalgia, pyrexia) were reported onto the diary card by the parent(s) or legal representative from day 0 (D0) to D7.
The investigator had to assess whether systemic AEs were related or not to the vaccine. All (related and unrelated) are displayed here.

Pyrexia was defined in this study as an oral temperature of 37.5°C or over. From D0 to D7, temperature values were captured in the diary card. In case of an oral temperature of 37.5°C or over at D7, the maximum temperature value of the event was also captured. From D0 to D7, temperature had to be measured once daily at the same time every day, preferably in the evening, and at the time of any apparent fever. At any time during the study, the highest observed temperature of the day had to be recorded in the diary card.

Descriptive analysis was done on the Safety Analysis set.

End point type	Secondary

End point timeframe:

One month (28 to 35 days) after vaccination

End point values	REVAXIS Group	DT Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384	374		
Units: Percentage of subjects				
number (not applicable)				
Headache (all)	15.1	19.3		
Headache (related)	12.2	16.6		
Myalgia (all)	21.4	17.9		
Myalgia (related)	19.3	17.1		

Pyrexia (all)	11.2	14.4		
Pyrexia (related)	9.6	11.2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from Day 0 (D0) to Visit 2 (D28 to D35).
Solicited AEs (collected from D0 to D7) are detailed in the "End points" section.
Unsolicited AEs (collected from D0 to D28) are detailed in this section.

Adverse event reporting additional description:

One subject was randomised in the DT Polio Group but received REVAXIS vaccine. The subject was thus included in the REVAXIS Group in the Safety Analysis set, which therefore included 384 subjects in the REVAXIS group, and 374 subjects in the DT Polio Group.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	REVAXIS Group

Reporting group description:

Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).

The number of subjects reporting at least 1 unsolicited ISR or AE with incidence ≥1% are presented hereafter. If each unsolicited ISR or AE with incidence ≥1% was reported by a different subject, the number of subjects reporting at least 1 unsolicited ISR or AE with incidence ≥1% would have been 67.

Reporting group title	DT Polio Group

Reporting group description:

Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).

The number of subjects reporting at least 1 unsolicited ISR or AE with incidence ≥1% are presented hereafter. If each unsolicited ISR or AE with incidence ≥1% was reported by a different subject, the number of subjects reporting at least 1 unsolicited ISR or AE with incidence ≥1% would have been 59.

Serious adverse events	REVAXIS Group	DT Polio Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 384 (0.00%)	1 / 374 (0.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Nose fracture	Additional description: Subject 9500002 experienced accidental severe nose fracture 14 days after receiving one dose of DT Polio vaccine. He was hospitalised to treat the fracture by surgery. SAE assessed as unrelated with the study vaccine.		
subjects affected / exposed	0 / 384 (0.00%)	1 / 374 (0.27%)	
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: 1 %

Non-serious adverse events	REVAXIS Group	DT Polio Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 384 (17.45%)	59 / 374 (15.78%)	
Nervous system disorders			
D8-D28, Headache			
subjects affected / exposed	5 / 384 (1.30%)	2 / 374 (0.53%)	
occurrences (all)	6	2	
General disorders and administration site conditions			
D8-D28, Pyrexia			
subjects affected / exposed	6 / 384 (1.56%)	4 / 374 (1.07%)	
occurrences (all)	7	4	
D0-D7, Pruritus			
subjects affected / exposed	5 / 384 (1.30%)	11 / 374 (2.94%)	
occurrences (all)	5	11	
Gastrointestinal disorders			
D0-D7, Abdominal pain			
subjects affected / exposed	4 / 384 (1.04%)	8 / 374 (2.14%)	
occurrences (all)	4	8	
D0-D7, Vomiting			
subjects affected / exposed	4 / 384 (1.04%)	4 / 374 (1.07%)	
occurrences (all)	4	4	
Respiratory, thoracic and mediastinal disorders			
D0-D7, Cough			
subjects affected / exposed	8 / 384 (2.08%)	6 / 374 (1.60%)	
occurrences (all)	8	6	
D8-D28, Cough			
subjects affected / exposed	6 / 384 (1.56%)	3 / 374 (0.80%)	
occurrences (all)	7	3	
Infections and infestations			
D8-D28, Ear infection			
subjects affected / exposed	3 / 384 (0.78%)	7 / 374 (1.87%)	
occurrences (all)	3	7	
D8-D28, Gastroenteritis			
subjects affected / exposed	1 / 384 (0.26%)	4 / 374 (1.07%)	
occurrences (all)	1	4	
D8-D28, Nasopharyngitis			

subjects affected / exposed	5 / 384 (1.30%)	0 / 374 (0.00%)	
occurrences (all)	5	0	
D0-D7, Rhinitis			
subjects affected / exposed	7 / 384 (1.82%)	5 / 374 (1.34%)	
occurrences (all)	7	5	
D8-D28, Pharyngitis			
subjects affected / exposed	5 / 384 (1.30%)	2 / 374 (0.53%)	
occurrences (all)	5	2	
D0-D7, Tonsillitis			
subjects affected / exposed	4 / 384 (1.04%)	1 / 374 (0.27%)	
occurrences (all)	4	1	
D8-D28, Tonsillitis			
subjects affected / exposed	4 / 384 (1.04%)	2 / 374 (0.53%)	
occurrences (all)	4	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2007	Administrative changes
31 May 2007	Extension of the recruitment period for 4 additional months
13 July 2007	Opening of 6 new sites and closure of 6 inactive sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported