Clinical trial results:
A phase IIIb, open-label, randomised, multicentre study to evaluate the immunogenicity and safety of a booster dose of GlaxoSmithKline Biologicals' dTpa-IPV vaccine (Boostrix Polio) compared with Sanofi-Pasteur-MSD's DTPa-IPV (Tetravac), when co-administered with MMRV (Priorix Tetra) in 5 to 6-year-old healthy children.

Summary

EudraCT number	2008-006124-64
Trial protocol	IT
Global end of trial date	18 November 2009

Results information

Result version number	v3
This version publication date	13 May 2018
First version publication date	20 February 2015
Version creation reason	• Correction of full data set Minor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	111815

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00871000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000500-PIP01-08
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	29 June 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 November 2009
Global end of trial reached?	Yes
Global end of trial date	18 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that GSK Biologicals' dTpa-IPV vaccine is non-inferior to Sanofi-Pasteur-MSD's DTPa-IPV vaccine, in terms of seroprotection rates against diphtheria, tetanus and poliovirus types 1, 2 and 3, one month after vaccination.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccinee remained under medical supervision for 30 minutes after vaccination

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2009
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	Italy: 303
Worldwide total number of subjects	303
EEA total number of subjects	303

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)	303
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Boostrix Polio Group

Arm description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Boostrix Polio vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Boostrix Polio vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm

Arm type	Experimental
Investigational medicinal product name	Boostrix Polio
Investigational medicinal product code	
Other name	dTpa-IPV, GSK Biologicals' combined reduced-antigen-content diphteria, tetanus, acellular pertussis and inactivated poliovirus vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscular administration in the deltoid region of the left upper arm at Day 0.

Investigational medicinal product name	Priorix Tetra
Investigational medicinal product code	
Other name	MMRV, GSK Biologicals' live attenuated measles-mumps-rubella-varicella vaccine
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose, subcutaneous administration in the deltoid region of the right upper arm at Day 0.

Arm title	Tetravac Group

Arm description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Tetravac vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Tetravac vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm.

Arm type	Active comparator

Investigational medicinal product name	Priorix Tetra
Investigational medicinal product code	
Other name	MMRV, GSK Biologicals' live attenuated measles-mumps-rubella-varicella vaccine
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose, subcutaneous administration in the deltoid region of the right upper arm at Day 0.

Investigational medicinal product name	Tetravac
Investigational medicinal product code	
Other name	dTpa-IPV, GSK Biologicals' combined reduced-antigen-content diphteria, tetanus, acellular pertussis and inactivated poliovirus vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscular administration in the deltoid region of the left upper arm at Day 0.

Number of subjects in period 1	Boostrix Polio Group	Tetravac Group
Started	151	152
Completed	150	152
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Boostrix Polio Group
Reporting group description:	
Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Boostrix Polio vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Boostrix Polio vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm	
Reporting group title	Tetravac Group
Reporting group description:	
Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Tetravac vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Tetravac vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm.	

Reporting group values	Boostrix Polio Group	Tetravac Group	Total
Number of subjects	151	152	303
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
geometric mean	5	5	
standard deviation	± 0.14	± 0.14	-
Gender categorical Units: Subjects			
Female	81	68	149
Male	70	84	154
Race/Ethnicity Units: Subjects			
African heritage/African American	1	0	1
Asian-Central/South Asian heritage	1	4	5
White-Arabic/North African heritage	2	0	2
White-Caucasian/European heritage	147	147	294
Not specified	0	1	1

End points

End points reporting groups

Reporting group title	Boostrix Polio Group

Reporting group description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Boostrix Polio vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Boostrix Polio vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm

Reporting group title	Tetravac Group

Reporting group description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Tetravac vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Tetravac vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm.

Primary: Anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations

End point title	Anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations[1]

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in international units per milliliter (IU/mL). The reference cut-off value was greater than or equal to (≥) 0.1 IU/mL.

End point type	Primary

End point timeframe:

At 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	9.207 (8.057 to 10.522)	21.393 (19.165 to 23.88)		
Anti-T	12.527 (10.957 to 14.323)	11.07 (9.872 to 12.413)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-poliovirus types 1, 2 and 3 antibody titres

End point title	Anti-poliovirus types 1, 2 and 3 antibody titres[2]

End point description:

Antibody titers were presented as geometric mean titers (GMTs) for the assay cut-off ≥ the value of 8.

End point type	Primary

End point timeframe:

At 1 Month post-vaccination

Notes:

[2] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 [N=139;144]	1145.6 (978.7 to 1340.9)	948 (817.5 to 1099.4)		
Anti-Polio 2 [N=139;144]	1076.4 (908.7 to 1274.9)	1315.3 (1123.1 to 1540.3)		
Anti-Polio 3 [N=138;144]	1937.8 (1631.4 to 2301.8)	1657.3 (1385.5 to 1982.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-D and anti-T antibodies

End point title	Number of seropositive subjects for anti-D and anti-T antibodies

End point description:

A seropositive subject was defined as a subject with anti-D and anti-T concentrations ≥ 0.1 IU/mL. Antibody concentrations have been assessed by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-D	139	144		
Anti-T	139	144		

Statistical analyses

Statistical analysis title	Seroprotection in terms of anti-D antibodies

Statistical analysis description:

To demonstrate that GSK Biologicals' Boostrix Polio™ vaccine is non-inferior to Sanofi-Pasteur-MSD's Tetravac™ vaccine, in terms of seroprotection rates against diphtheria, one month after vaccination.

Comparison groups	Boostrix Polio Group v Tetravac Group
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.7

Notes:

[3] - Non-inferiority in terms of seroprotection rates against diphtheria was demonstrated if the upper limit of the standardised asymptotic 95% confidence interval (CI) on the group difference [Tetravac Group minus Boostrix Polio Group] in the percentage of subjects with anti-diphtheria antibody concentrations ≥ 0.1 IU/mL was ≤ 10%.

Statistical analysis title	Seroprotection in terms of anti-T antibodies

Statistical analysis description:

To demonstrate that GSK Biologicals' Boostrix Polio™ vaccine is non-inferior to Sanofi-Pasteur-MSD's Tetravac™ vaccine, in terms of seroprotection rates against tetanus, one month after vaccination.

Comparison groups	Boostrix Polio Group v Tetravac Group
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.7

Notes:

[4] - Non-inferiority in terms of seroprotection rates against tetanus was demonstrated if the upper limit of the standardised asymptotic 95% confidence interval (CI) on the group difference [Tetravac Group minus Boostrix Polio Group] in the percentage of subjects with anti-tetanus antibody concentrations ≥ 0.1 IU/mL was ≤ 10%.

Primary: Number of seroprotected subjects against polio types 1, 2 and 3	
End point title	Number of seroprotected subjects against polio types 1, 2 and 3

End point description:

A seroprotected subject was defined as a subject with anti-polio types 1, 2 and 3 titers ≥ the value of 8. Antibody titers have been assessed by neutralization assay.

End point type	Primary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-Polio 1 [N=139;144]	139	144		
Anti-Polio 2 [N=139;144]	139	144		
Anti-Polio 3 [N=138;144]	138	144		

Statistical analyses

Statistical analysis title	Seroprotection in terms of anti-Polio 1 antibodies

Statistical analysis description:

To demonstrate that GSK Biologicals' Boostrix Polio™ vaccine is non-inferior to Sanofi-Pasteur-MSD's Tetravac™ vaccine, in terms of seroprotection rates against poliovirus type 1, one month after vaccination.

Comparison groups	Boostrix Polio Group v Tetravac Group
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.7

Notes:

[5] - Non-inferiority in terms of seroprotection rates against poliovirus type 1 was demonstrated if the upper limit of the standardised asymptotic 95% confidence interval (CI) on the group difference [Tetravac Group minus Boostrix Polio Group] in the percentage of subjects with anti-poliovirus type 1 antibody titers ≥ 8 was ≤ 10%.

Statistical analysis title	Seroprotection in terms of anti-Polio 2 antibodies

Statistical analysis description:

To demonstrate that GSK Biologicals' Boostrix Polio™ vaccine is non-inferior to Sanofi-Pasteur-MSD's Tetravac™ vaccine, in terms of seroprotection rates against poliovirus type 2, one month after vaccination

Comparison groups	Boostrix Polio Group v Tetravac Group
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.7

Statistical analysis title	Seroprotection in terms of anti-Polio 3 antibodies

Statistical analysis description:

To demonstrate that GSK Biologicals' Boostrix Polio™ vaccine is non-inferior to Sanofi-Pasteur-MSD's Tetravac™ vaccine, in terms of seroprotection rates against poliovirus type 3, one month after vaccination

Comparison groups	Boostrix Polio Group v Tetravac Group
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.72

Notes:

[6] - Non-inferiority in terms of seroprotection rates against poliovirus type 1 was demonstrated if the upper limit of the standardised asymptotic 95% confidence interval (CI) on the group difference [Tetravac Group minus Boostrix Polio Group] in the percentage of subjects with anti-poliovirus type 3 antibody titers ≥ 8 was ≤ 10%.

Secondary: Anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

End point description:

Antibody concentrations were presented as geometric mean concentrations, expressed in ELISA units per milliliter (EL.U/mL). The reference cut-off value was ≥ 5 EL.U/mL.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	59.8 (52.2 to 68.5)	75.9 (65.7 to 87.7)		
Anti-FHA	556.2 (491.4 to 629.5)	613.5 (547 to 688.2)		
Anti-PRN	354.8 (280.2 to 449.4)	7.8 (6.5 to 9.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against diphteria (D) and tetanus (T) antigens

End point title	Number of seroprotected subjects against diphteria (D) and tetanus (T) antigens

End point description:

A seroprotected subject was defined as a subject with anti-D and anti-T concentrations ≥ 1.0 IU/mL. Antibody concentrations have been assessed by ELISA.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-D	138	144		
Anti-T	137	143		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-measles, anti-mumps, anti-rubella and anti-varicella.

End point title	Number of seropositive subjects for anti-measles, anti-mumps, anti-rubella and anti-varicella.

End point description:

Seropositivity was defined as subjects with antibody concentrations: ≥ 150 milli-international units per milliliter (mIU/mL), ≥ 231 units per milliliter (U/mL), ≥ 4 international units per milliliter (IU/mL) and ≥ 50 mIU/mL for anti-measles, anti-mumps, anti-rubella and anti-varicella antibodies, respectively.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: Subjects				
Anti- measles	139	146		
Anti-mumps	139	144		
Anti-rubella	139	145		
Anti- varicella	135	140		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles and anti-varicella antibody concentrations.

End point title	Anti-measles and anti-varicella antibody concentrations.

End point description:

Antibody concentrations were assessed by ELISA, presented as geometric mean concentrations (GMCs) and expressed in mIU/mL.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti- measles	2743.9 (2411.4 to 3122.2)	2863 (2534.6 to 3233.9)		
Anti- varicella	856.7 (671.8 to 1092.4)	909.9 (721 to 1148.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses to anti-diphtheria and anti-tetanus.

End point title	Number of subjects with booster responses to anti-diphtheria and anti-tetanus.

End point description:

Booster responses to anti-D and anti-T were defined as: For initially seronegative subjects (pre-vaccination concentration < cut-off of 0.1 IU/mL), antibody concentrations at least four times the assay cut-off (post-vaccination concentration ≥ 0.4 IU/mL). For initially seropositive subjects (pre-vaccination concentration ≥ 0.1 IU/mL), an increase in antibody concentrations of at least four times the pre-vaccination concentration.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	143		
Units: Subjects				
Ant-D [N=136;143]	130	136		
Anti-T [N=137;143]	137	142		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses to anti-poliovirus types 1, 2 and 3.

End point title	Number of subjects with booster responses to anti-poliovirus types 1, 2 and 3.

End point description:

Booster response to the poliovirus antigens was defined as: For initially seronegative subjects (pre-vaccination antibody titre < cut-off of 8), antibody titre ≥ 32. For initially seropositive subjects (pre-vaccination antibody titres ≥ 8), an increase in antibody titres of at least four times the pre-vaccination titre.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-Polio 1 [N=139;144]	115	112		
Anti-Polio 2 [N=139;143]	113	122		
Anti-Polio 3 [N=138;144]	126	127		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses to anti-PT, anti-FHA and anti-PRN.

End point title	Number of subjects with booster responses to anti-PT, anti-FHA and anti-PRN.

End point description:

Booster response to the PT, FHA and PRN antigens was defined as: For initially seronegative subjects (pre-vaccination concentration < cut-off of 5 EL.U/mL), antibody concentrations at least four times the cut-off (post-vaccination concentration ≥ 20 EL.U/mL). For initially seropositive subjects with pre-vaccination concentration ≥ 5 EL.U/mL and < 20 EL.U/mL, an increase in antibody concentrations of at least four times the pre-vaccination concentration. For initially seropositive subjects with pre-vaccination concentration ≥ 20 EL.U/mL, an increase in antibody concentrations of at least two times the pre-vaccination concentration.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	143		
Units: Subjects				
Anti-PT [N=137;141]	123	130		
Anti-FHA [N=136;140]	129	134		
Anti-PRN [N=137;143]	129	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti-measles, anti-mumps, anti-

rubella and anti-varicella

End point title	Number of seroconverted subjects for anti-measles, anti-mumps, anti-rubella and anti-varicella

End point description:

Seroconversion for anti-measles, anti-mumps, anti-rubella and anti-varicella was defined as the appearance of antibodies after vaccination in subjects who were seronegative before vaccination. There were no seronegative subjects for anti-rubella antibodies, prior to vaccination.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Subjects				
Anti-measles [N=2;1]	2	1		
Anti-mumps [N=13;13]	13	12		
Anti-rubella [N=0;0]	0	0		
Anti-varicellas [N=36;34]	35	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms.

End point title	Number of subjects with any solicited local symptoms.

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Pain	96	96		
Redness	58	66		
Swelling	55	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms.

End point title	Number of subjects with any solicited general symptoms.

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal, headache and temperature [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Fatigue	40	36		
Gastrointestinal	23	15		
Headache	18	20		
Temperature	32	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs).

End point title	Number of subjects with any unsolicited adverse events (AEs).

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 31 days (Days 0-30) post-vaccination period

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Subjects with any AE(s)	23	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

End point title	Number of subjects with serious adverse events (SAEs).

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

During the whole study period

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Subjects with any SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-mumps antibody concentrations.

End point title	Anti-mumps antibody concentrations.

End point description:

Antibody concentrations were assessed by ELISA, presented as geometric mean concentrations (GMCs) and expressed in U/mL.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-mumps	4141.3 (3590.5 to 4776.5)	3837.6 (3275.1 to 4496.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rubella antibody concentrations.

End point title	Anti-rubella antibody concentrations.

End point description:

Antibody concentrations were assessed by ELISA, presented as geometric mean concentrations (GMCs) and expressed in IU/mL.

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-rubella	154.5 (141.3 to 168.9)	162.5 (145.8 to 181)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN antibodies

End point title	Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN antibodies

End point description:

A seropositive subject was defined as a subject with anti-PT, anti-FHA and anti-PRN concentrations ≥ 5.0 IU/mL. Antibody concentrations have been assessed by ELISA.

End point type	Secondary

End point timeframe:

At Month 1 post-vaccination

End point values	Boostrix Polio Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-PT	139	144		
Anti-FHA	139	144		
Anti-PRN	138	87		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 4-day follow-up period after vaccination (Day 0 - Day 3); Unsolicited AEs: 31-day follow-up period after vaccination (Day 0 - Day 30); SAEs: throughout the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

Reporting group title	Tetravac Group

Reporting group description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Tetravac vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Tetravac vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm.

Reporting group title	Boostrix Group

Reporting group description:

Healthy male or female children, between and including 5 to 6 years of age, who were primed with three doses of Infanrix vaccine according to the Italian 3-5-11 month vaccination schedule, additionally received a single booster dose of Boostrix Polio vaccine co-administered with a single dose of Priorix Tetra vaccine at Day 0. Boostrix Polio vaccine was administered intramuscularly in the deltoid region of the left upper arm, while the Priorix Tetra vaccine was administered subcutaneously in the deltoid region of the right upper arm.

Serious adverse events	Tetravac Group	Boostrix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 152 (0.00%)	0 / 151 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Tetravac Group	Boostrix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 152 (76.97%)	117 / 151 (77.48%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	96 / 152 (63.16%)	96 / 151 (63.58%)	
occurrences (all)	96	96	

Redness			
subjects affected / exposed	66 / 152 (43.42%)	58 / 151 (38.41%)	
occurrences (all)	66	58	
Swelling			
subjects affected / exposed	62 / 152 (40.79%)	55 / 151 (36.42%)	
occurrences (all)	62	55	
Fatigue			
subjects affected / exposed	36 / 152 (23.68%)	40 / 151 (26.49%)	
occurrences (all)	36	40	
Gastrointestinal			
subjects affected / exposed	15 / 152 (9.87%)	23 / 151 (15.23%)	
occurrences (all)	15	23	
Headache			
subjects affected / exposed	20 / 152 (13.16%)	18 / 151 (11.92%)	
occurrences (all)	20	18	
Temperature			
subjects affected / exposed	30 / 152 (19.74%)	32 / 151 (21.19%)	
occurrences (all)	30	32	

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

None reported