

**Clinical trial results:**

A phase IV, open, non-randomised, multicentre study to assess the reactogenicity and immunogenicity of a booster dose of GSK Biologicals' combined reduced-antigen-content diphtheria-tetanus, acellular pertussis and inactivated poliovirus vaccine dTpa-IPV (Boostrix-Polio) when administered in healthy subjects aged 9-13 years, 5 years after previous booster vaccination with dTpa-IPV in the study 711866/001 (dTpa-IPV-001).

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2007-003477-94
Trial protocol	DE
Global end of trial date	08 July 2008

Results information

Result version number	v2
This version publication date	20 November 2018
First version publication date	01 May 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Data correction due to a system error in EudraCT – Results

Trial information**Trial identification**

Sponsor protocol code	110947
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00635128
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	22 April 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2008
Global end of trial reached?	Yes
Global end of trial date	08 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the incidence of grade 3 local reactions occurring during the 4-day (Day 0–Day 3) follow-up period after administration of a booster dose of dTpa-IPV vaccine in healthy children and adolescents aged 9 to 13 years, 5 years after a previous booster dose of the same vaccine in the study 711866/001 (dTpa-IPV-001).

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 415
Worldwide total number of subjects	415
EEA total number of subjects	415

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)	415
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 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Boostrix-Polio Group

Arm description:

Subjects received a single dose of Boostrix™-Polio vaccine.

Arm type	Experimental
Investigational medicinal product name	Boostrix™-Polio
Investigational medicinal product code	
Other name	dTPa-IPV vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

Arm title	Boostrix + IPV Mérieux Group
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Arm description:

Subjects received a single dose of Boostrix™ and IPV Mérieux® vaccines, respectively.

Arm type	Experimental
Investigational medicinal product name	Boostrix™
Investigational medicinal product code	
Other name	dTPa vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

Investigational medicinal product name	IPV Mérieux®
Investigational medicinal product code	
Other name	IPV vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single booster dose of the vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

Number of subjects in period 1	Boostrix-Polio Group	Boostrix + IPV Mérieux Group
Started	351	64
Completed	351	64

Baseline characteristics

Reporting groups

Reporting group title	Boostrix-Polio Group
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Reporting group description:

Subjects received a single dose of Boostrix™-Polio vaccine.

Reporting group title	Boostrix + IPV Mérieux Group
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Reporting group description:

Subjects received a single dose of Boostrix™ and IPV Mérieux® vaccines, respectively.

Reporting group values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group	Total
Number of subjects	351	64	415
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			
arithmetic mean	11.4	11.3	
standard deviation	± 0.97	± 0.72	-
Gender categorical Units: Subjects			
Female	169	32	201
Male	182	32	214

End points

End points reporting groups

Reporting group title	Boostrix-Polio Group
Reporting group description:	Subjects received a single dose of Boostrix™-Polio vaccine.
Reporting group title	Boostrix + IPV Mérieux Group
Reporting group description:	Subjects received a single dose of Boostrix™ and IPV Mérieux® vaccines, respectively.
Subject analysis set title	All subjects
Subject analysis set type	Sub-group analysis
Subject analysis set description:	Boostrix-Polio Group and Boostrix + IPV Mérieux Group, subjects who received one dose of dTpa-IPV vaccine and one dose of dTpa + IPV vaccines.

Primary: Number of subjects with any Grade 3 local adverse events (AEs)

End point title	Number of subjects with any Grade 3 local adverse events (AEs) ^[1]
End point description:	Safety results are presented for all subjects. Grade 3 symptoms: symptoms that prevented normal activity.
End point type	Primary
End point timeframe:	During the 4-day follow-up period (Day 0-3) after booster 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	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	415			
Units: Subjects				
Local symptoms [N=415]	41			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with 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 follow-up period (Day 0-3) after booster vaccination

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	415			
Units: Subjects				
Any Pain	302			
Any Redness	195			
Any Swelling	163			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms
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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 and relationship to vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Day 0-3) follow-up period after booster vaccination

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	414			
Units: Subjects				
Any Fatigue	101			
Any Gastrointestinal	45			
Any Headache	88			
Any Temperature	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (\geq) 0.1 international units per milliliter (IU/mL) and \geq 1 IU/mL

End point title	Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (\geq) 0.1 international units per milliliter (IU/mL) and \geq 1
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IU/mL

End point description:

End point type Secondary

End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	62		
Units: Subjects				
Anti-diphtheria \geq 0.1 IU/mL Pre [N=334;62]	298	53		
Anti-diphtheria \geq 0.1 IU/mL Post [N=336;62]	336	62		
Anti-diphtheria \geq 1 IU/mL Pre [N=334;62]	91	13		
Anti-diphtheria \geq 1 IU/mL Post [N=336;62]	308	55		
Anti-tetanus \geq 0.1 IU/mL Pre [N=335;62]	330	61		
Anti-tetanus \geq 0.1 IU/mL Post [N=336;62]	336	62		
Anti-tetanus \geq 1 IU/mL Pre [N=335;62]	181	35		
Anti-tetanus \geq 1 IU/mL Post [N=336;62]	335	61		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point title Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point description:

End point type Secondary

End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	62		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria Pre [N=334;62]	0.51 (0.429 to 0.608)	0.446 (0.305 to 0.651)		
Anti-diphtheria Post [N=336;62]	4.784 (4.302 to 5.32)	4.153 (3.089 to 5.585)		
Anti-tetanus Pre [N=335;62]	1.197 (1.045 to 1.37)	1.067 (0.797 to 1.429)		
Anti-tetanus Post [N=336;62]	11.81 (11.011 to 12.667)	9.518 (7.879 to 11.498)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ 5 ELISA unit per milliliter (EL.U/ml)

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ 5 ELISA unit per milliliter (EL.U/ml)
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End point description:

End point type	Secondary
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End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	62		
Units: Subjects				
Anti-PT Pre [N=330;62]	134	21		
Anti-PT Post [N=335;62]	334	59		
Anti-FHA Pre [N=333;60]	332	60		
Anti-FHA Post [N=336;61]	336	61		
Anti-PRN Pre [N=335;62]	325	57		
Anti-PRN Post [N=336;62]	336	62		

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	62		
Units: EL.U/ml				
geometric mean (confidence interval 95%)				
Anti-PT Pre [N=330;62]	5.2 (4.7 to 5.9)	4.5 (3.6 to 5.6)		
Anti-PT Post [N=335;62]	41.6 (38.1 to 45.3)	32 (24.5 to 41.9)		
Anti-FHA Pre [N=333;60]	69.8 (62.1 to 78.4)	70.1 (52.5 to 93.5)		
Anti-FHA Post [N=336;61]	662.7 (613.2 to 716.1)	733.9 (610.4 to 882.5)		
Anti-PRN Pre [N=335;62]	46.8 (41.5 to 52.8)	41.1 (30 to 56.2)		
Anti-PRN Post [N=336;62]	570.8 (527.4 to 617.7)	460.4 (353.3 to 600)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polio type 1, 2 and 3 antibody titers \geq 8

End point title	Number of subjects with anti-polio type 1, 2 and 3 antibody titers \geq 8
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End point description:

End point type	Secondary
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End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	62		
Units: Subjects				
Anti-polio 1, Pre [N=333;62]	329	60		
Anti-polio 1, Post [N=335;62]	335	62		
Anti-polio 2, Pre [N=334;62]	333	62		
Anti-polio 2, Post [N=335;62]	335	62		
Anti-polio 3, Pre [N=334;62]	324	60		
Anti-polio 3, Post [N=333;62]	333	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers

End point title	Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers
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End point description:

End point type	Secondary
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End point timeframe:

Prior to and one month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	62		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1, Pre [N=333;62]	138.7 (123 to 156.4)	128.9 (96.1 to 172.7)		
Anti-polio 1, Post [N=335;62]	1359.6 (1213.4 to 1523.3)	1088.9 (866.5 to 1368.4)		
Anti-polio 2, Pre [N=334;62]	166.3 (149.5 to 185)	179.2 (142.9 to 224.7)		
Anti-polio 2, Post [N=335;62]	1629.4 (1475.2 to 1799.7)	1309.5 (1035.2 to 1656.3)		
Anti-polio 3, Pre [N=334;62]	117.2 (102.8 to 133.5)	118.4 (83.4 to 168)		
Anti-polio 3, Post [N=333;62]	1882.4 (1687.9 to 2099.3)	1712.5 (1329.2 to 2206.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of subjects with booster response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)
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End point description:

Booster vaccine response was defined as appearance of antibodies in subjects who were seronegative at the pre-vaccination time point (i.e. with concentrations < 5 EL.U/mL) or at least 2-fold increase of pre-vaccination antibody concentrations in subjects who were seropositive at the pre-vaccination time point (i.e. with concentrations < 5 EL.U/mL).

End point type	Secondary
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End point timeframe:

One month after booster vaccination

End point values	Boostrix-Polio Group	Boostrix + IPV Mérieux Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	62		
Units: Subjects				
Anti-PT [N=330;62]	308	56		
Anti-FHA [N=333;60]	311	56		
Anti-PRN [N=335;62]	319	61		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with unsolicited adverse events (AEs)
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End point description:

AEs results are presented for all subjects. 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
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End point timeframe:

During the 31-day (Day 0–30) follow-up period after booster vaccination

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	415			
Units: Subjects				
Any AEs	64			

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:	
SAEs results are presented for all subjects. Assessed SAEs 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:	
Following booster vaccination	

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	415			
Units: Subjects				
SAEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local/general during the 4-day period; AEs during the 31-Day period; SAEs following booster vaccination.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	All Subjects
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Reporting group description:

Boostrix-Polio Group and Boostrix + IPV Mériex Group, subjects who received one dose of Boostrix™ - Polio vaccine and one dose of Boostrix™ + IPV Mériex® vaccines.

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 415 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	302 / 415 (72.77%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	302 / 415 (72.77%)		
occurrences (all)	302		
Redness			
subjects affected / exposed	195 / 415 (46.99%)		
occurrences (all)	195		
Swelling			
subjects affected / exposed	163 / 415 (39.28%)		
occurrences (all)	163		

Fatigue			
subjects affected / exposed ^[1]	101 / 414 (24.40%)		
occurrences (all)	101		
Gastrointestinal			
subjects affected / exposed ^[2]	45 / 414 (10.87%)		
occurrences (all)	45		
Headache			
subjects affected / exposed ^[3]	88 / 414 (21.26%)		
occurrences (all)	88		
Temperature (Axillary)			
subjects affected / exposed ^[4]	14 / 414 (3.38%)		
occurrences (all)	14		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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