Clinical trial results:
A phase IV, single-blind, randomized, multicenter study to assess the immunogenicity and safety of GSK Biologicals' dTpa vaccine (Boostrix™) using a new syringe presentation in healthy adolescents aged 10–15 years.

Summary

EudraCT number	2013-003768-30
Trial protocol	Outside EU/EEA
Global end of trial date	03 September 2012

Results information

Result version number	v2
This version publication date	24 July 2016
First version publication date	13 May 2015
Version creation reason	• Correction of full data set Data (typos and numbers) were corrected.

Trial information

Trial identification

Sponsor protocol code	114778

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01362322
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.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	10 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2012
Global end of trial reached?	Yes
Global end of trial date	03 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that Boostrix™ administered using the new syringe presentation is non-inferior to Boostrix™ administered using the previous syringe presentation, in terms of immune response to all vaccine antigens, one month after booster vaccination.

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	05 July 2011
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	Mexico: 376
Country: Number of subjects enrolled	Chile: 295
Worldwide total number of subjects	671
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)	671
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	Single blind
Roles blinded	Subject

Arms

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

Arm description: -

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

Dosage and administration details:

One dose of vaccine, in a new syringe presentation, was administered in the deltoid of the non-dominant arm, at Day 0.

Arm title	Boostrix-Prev Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Boostrix™
Investigational medicinal product code	
Other name	dTpa
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of vaccine, in a previous syringe presentation, was administered in the deltoid of the non-dominant arm, at Day 0.

Number of subjects in period 1	Boostrix-New Group	Boostrix-Prev Group
Started	335	336
Completed	330	329
Not completed	5	7
Consent withdrawn by subject	3	1
Lost to follow-up	2	6

Baseline characteristics

Reporting groups	
Reporting group title	Boostrix-New Group
Reporting group description: -	
Reporting group title	Boostrix-Prev Group
Reporting group description: -	

Reporting group values	Boostrix-New Group	Boostrix-Prev Group	Total
Number of subjects	335	336	671
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	11.9	11.9	
standard deviation	± 1.59	± 1.61	-
Gender categorical			
Units: Subjects			
Female	179	178	357
Male	156	158	314

End points

End points reporting groups

Reporting group title	Boostrix-New Group
Reporting group description: -	
Reporting group title	Boostrix-Prev Group
Reporting group description: -	

Primary: Anti-D and Anti-T antibody concentrations

End point title	Anti-D and Anti-T antibody concentrations
End point description:	
End point type	Primary
End point timeframe:	
Before (PRE) and one month after (POST) booster vaccination	

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D PRE	0.472 (0.403 to 0.553)	0.456 (0.392 to 0.53)		
Anti-D POST	6.784 (6.178 to 7.45)			

Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	ANCOVA
Parameter estimate	Adjusted Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.09

Notes:

[1] - The upper limit (UL) of the 95% confidence interval (CI) on the geometric mean concentration (GMC) ratios [Boostrix-Prev Group over Boostrix-New Group] for anti-diphtheria (anti-D)antibodies was ≤ 1.5 (clinical limit for non-inferiority).

Statistical analysis title	Adjusted ratios of GMCs for anti-T

Statistical analysis description:

To demonstrate that the Boostrix™ vaccine administered using the new-syringe presentation was non-inferior to Boostrix™ vaccine administered using the previous-syringe, in terms of immune response to all vaccine antigens, one month after booster vaccination.

Comparison groups	Boostrix-New Group v Boostrix-Prev Group
Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	ANCOVA
Parameter estimate	Adjusted Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.1

Notes:

[2] - The upper limit (UL) of the 95% confidence interval (CI) on the geometric mean concentration (GMC) ratios [Boostrix-Prev Group over Boostrix-New Group] for anti-tetanus (anti-T) antibodies was ≤ 1.5 (clinical limit for non-inferiority).

Primary: Anti-PT, Anti-FHA, Anti-PRN antibody concentrations

End point title	Anti-PT, Anti-FHA, Anti-PRN antibody concentrations

End point description:

End point type	Primary

End point timeframe:

Before (PRE) and one month after (POST) booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT PRE [N=320;319]	7.5 (6.6 to 8.7)	7.2 (6.3 to 8.2)		
Anti-PT POST [N=318;318]	140.2 (126 to 156.1)	125.9 (112.7 to 140.7)		
Anti-FHA PRE [N=316;315]	48.9 (43.3 to 55.2)	49.4 (43.6 to 56)		
Anti-FHA POST [N=319;319]	1080.2 (995.2 to 1172.5)	1013.7 (940 to 1093.2)		
Anti-PRN PRE [N=321;319]	14 (12.3 to 15.9)	13.4 (11.9 to 15)		
Anti-PRN POST [N=321;318]	652.4 (572.1 to 743.9)	619.2 (546 to 702.2)		

Statistical analyses

Statistical analysis title	Adjusted ratios of GMCs for anti-PT

Statistical analysis description:

To demonstrate that the Boostrix™ vaccine administered using the new-syringe presentation was non-inferior to Boostrix™ vaccine administered using the previous-syringe, in terms of immune response to all vaccine antigens, one month after booster vaccination.

Comparison groups	Boostrix-New Group v Boostrix-Prev Group
Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	ANCOVA
Parameter estimate	Adjusted Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.04

Notes:

[3] - The upper limit (UL) of the 95% confidence interval (CI) on the geometric mean concentration (GMC) ratios [Boostrix-Prev Group over Boostrix-New Group] for anti-pertussis toxoid (anti-PT) antibodies was ≤ 1.5 (clinical limit for non-inferiority).

Statistical analysis title	Adjusted ratios of GMCs for anti-FHA

Statistical analysis description:

To demonstrate that the Boostrix™ vaccine administered using the new-syringe presentation was non-inferior to Boostrix™ vaccine administered using the previous-syringe, in terms of immune response to all vaccine antigens, one month after booster vaccination.

Comparison groups	Boostrix-New Group v Boostrix-Prev Group

Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	ANCOVA
Parameter estimate	Adjusted Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.03

Notes:

[4] - The upper limit (UL) of the 95% confidence interval (CI) on the geometric mean concentration (GMC) ratios [Boostrix-Prev Group over Boostrix-New Group] for anti-filamentous haemagglutinin (anti-FHA) antibodies was ≤ 1.5 (clinical limit for non-inferiority).

Statistical analysis title	Adjusted ratios of GMCs for anti-PRN

Statistical analysis description:

To demonstrate that the Boostrix™ vaccine administered using the new-syringe presentation was non-inferior to Boostrix™ vaccine administered using the previous-syringe, in terms of immune response to all vaccine antigens, one month after booster vaccination.

Comparison groups	Boostrix-New Group v Boostrix-Prev Group
Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	ANCOVA
Parameter estimate	Adjusted Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.13

Notes:

[5] - The upper limit (UL) of the 95% confidence interval (CI) on the geometric mean concentration (GMC) ratios [Boostrix-Prev Group over Boostrix-New Group] for anti-pertactin (anti-PRN) antibodies was ≤ 1.5 (clinical limit for non-inferiority).

Secondary: Number of seropositive subjects against Diphtheria and Tetanus with antibody concentrations (anti-D, anti-T) above or equal to (≥)0.1 IU/mL

End point title	Number of seropositive subjects against Diphtheria and Tetanus with antibody concentrations (anti-D, anti-T) above or equal to (≥)0.1 IU/mL

End point description:

A seroprotected subject was defined as a subject whose antibody concentration was greater than or equal to (≥) 0.1. international units per milliliter (IU/mL), as assessed by the Enzyme Linked Immunosorbent Assay (ELISA). The POST results are the primary outcome variables.

End point type	Secondary

End point timeframe:

Before (PRE) and one month after (POST) booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: subjects				
Anti-D PRE	284	286		
Anti-D POST	320	319		
Anti-T PRE	311	314		
Anti-T POST	321	319		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against Diphtheria and Tetanus with antibody concentrations (anti-D, anti-T) above ≥1 IU/mL

End point title	Number of seroprotected subjects against Diphtheria and Tetanus with antibody concentrations (anti-D, anti-T) above ≥1 IU/mL

End point description:

End point type	Secondary

End point timeframe:

Before (PRE) and one month after (POST) booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: subjects				
Anti-D PRE	83	89		
Anti-D POST	315	310		
Anti-T PRE	151	143		
Anti-T POST	321	319		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutin (anti-FHA) and anti pertactin (anti-PRN) antibody concentrations ≥5 ELISA units per milliliter (EU/mL)

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutin (anti-FHA) and anti pertactin (anti-PRN) antibody concentrations ≥5 ELISA units per milliliter (EU/mL)

End point description:

End point type	Secondary

End point timeframe:

Before (PRE) and one month after (POST) booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: subjects				
Anti-PT PRE [N=320;319]	175	175		
Anti-PT POST [N=318;318]	316	315		
Anti-FHA PRE [N=316;315]	310	310		
Anti-FHA POST [N=319;319]	319	319		
Anti-PRN PRE [N=321;319]	269	272		
Anti-PRN POST [N=321;318]	321	318		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster response to diphtheria and tetanus antibodies

End point title	Number of subjects with booster response to diphtheria and tetanus antibodies

End point description:

End point type	Secondary

End point timeframe:

One month after booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	319		
Units: subjects				
Anti-D	257	252		
Anti-T	266	270		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to PT, FHA and PRN antibodies.

End point title	Number of subjects with a booster response to PT, FHA and PRN antibodies.

End point description:

End point type	Secondary

End point timeframe:

One month after booster vaccination

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	318		
Units: subjects				
Anti-PT [N=317;318]	298	295		
Anti-FHA [N=314;315]	305	304		
Anti-PRN [N=321;318]	315	317		

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:

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) post vaccination period

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	329		
Units: subjects				
Any Pain	237	248		
Any Redness	113	94		
Any Swelling	98	90		

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:

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) post vaccination period

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	329		
Units: subjects				
Any Fatigue	83	86		
Any Gastrointestinal symptoms	32	42		
Any Headache	88	108		
Any Temperature	9	6		

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)

End point description:

End point type	Secondary

End point timeframe:

Within 31 days (Days 0-30) post vaccination period

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	336		
Units: subjects				
Any unsolicited AEs	44	45		

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:

End point type	Secondary

End point timeframe:

During the entire study period

End point values	Boostrix-New Group	Boostrix-Prev Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	336		
Units: subjects				
Any SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period, Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Boostrix-New Group
Reporting group description: -	
Reporting group title	Boostrix-Prev Group

Reporting group description: -

Serious adverse events	Boostrix-New Group	Boostrix-Prev Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 335 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Boostrix-New Group	Boostrix-Prev Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	237 / 335 (70.75%)	248 / 336 (73.81%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	237 / 330 (71.82%)	248 / 329 (75.38%)	
occurrences (all)	237	248	
Redness			

subjects affected / exposed[2]	113 / 330 (34.24%)	98 / 329 (29.79%)	
occurrences (all)	94	90	
Swelling			
subjects affected / exposed[3]	98 / 330 (29.70%)	90 / 329 (27.36%)	
occurrences (all)	98	90	
Fatigue			
subjects affected / exposed[4]	83 / 330 (25.15%)	86 / 329 (26.14%)	
occurrences (all)	83	86	
Gastrointestinal symptoms			
subjects affected / exposed[5]	32 / 330 (9.70%)	42 / 329 (12.77%)	
occurrences (all)	32	42	
Headache			
subjects affected / exposed[6]	88 / 330 (26.67%)	108 / 329 (32.83%)	
occurrences (all)	88	108	

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: Solicited local and general symptoms were reported only for subjects with a symptom sheet 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: Solicited local and general symptoms were reported only for subjects with a symptom sheet 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: Solicited local and general symptoms were reported only for subjects with a symptom sheet 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: Solicited local and general symptoms were reported only for subjects with a symptom sheet completed.

[5] - 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: Solicited local and general symptoms were reported only for subjects with a symptom sheet completed.

[6] - 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: Solicited local and general symptoms were reported only for subjects with a symptom sheet completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2012	At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code. The Emergency unblinding is not applicable for open and single blind studies anymore. Therefore the section has been deleted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported