Clinical trial results:
A phase III, open-label, single-group, multi-centre study to assess the immunogenicity, safety and reactogenicity of GSK Biologicals' combined reduced antigen content diphtheria, tetanus and acellular pertussis (dTpa) vaccine, Boostrix, administered as a booster dose in healthy Russian subjects aged four years and older.

Summary

EudraCT number	2015-003405-42
Trial protocol	Outside EU/EEA
Global end of trial date	31 August 2018

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	201532

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03311659
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)	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 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2018
Global end of trial reached?	Yes
Global end of trial date	31 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to the dTpa vaccine in terms of seroprotection status for antibodies against diphtheria and tetanus antigens and in terms of seropositivity status for antibodies against the pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN)], one month after vaccination.

Protection of trial subjects:

Appropriate medical treatment was 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	26 January 2018
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	Russian Federation: 447
Worldwide total number of subjects	447
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)	130
Adolescents (12-17 years)	92
Adults (18-64 years)	113
From 65 to 84 years	101
85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 448 enrolled subjects, only 447 were vaccinated. One subject was withdrawn prior to vaccination.

Period 1

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

Arms

Arm title	dTpa group

Arm description:

Healthy female and male subjects with age 4 years and above and who received a single dose of Boostrix vaccine at Day 1.

Arm type	Other
Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	SB263855
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose at Day 1

Number of subjects in period 1	dTpa group
Started	447
Completed	446
Not completed	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	dTpa group
Reporting group description:	
Healthy female and male subjects with age 4 years and above and who received a single dose of Boostrix vaccine at Day 1.	

Reporting group values	dTpa group	Total	
Number of subjects	447	447	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	130	130	
Adolescents (12-17 years)	92	92	
Adults (18-64 years)	113	113	
From 65 to 84 years	101	101	
85 years and over	11	11	
Age continuous Units: years			
arithmetic mean	32.7		
standard deviation	± 27.29	-	
Sex: Female, Male Units: Subjects			
Female	241	241	
Male	206	206	
Race/Ethnicity, Customized Units: Subjects			
White-Caucasian/ European heritage	447	447	

End points

End points reporting groups

Reporting group title	dTpa group

Reporting group description:

Healthy female and male subjects with age 4 years and above and who received a single dose of Boostrix vaccine at Day 1.

Primary: Number of seroprotected subjects for anti-diphtheria (anti-D)

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D)[1]

End point description:

A seroprotected subject was a subject whose anti-D concentrations are greater than or equal to (≥) 0.1 International units per milliliter (IU/ml). Seroprotection was assessed by enzyme-linked immunosorbent assay (ELISA) method. In addition, sera with ELISA concentrations <0.1 IU/ml were tested for neutralising antibodies using a Vero-cell neutralisation assay. Both the ELISA test (antibody concentrations ≥ 0.1 IU/ml) and Vero-cell test (antibody concentration ≥ 0.01 IU/ml) defined the seroprotection status for the primary endpoint.

End point type	Primary

End point timeframe:

At Day 31

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: This endpoint was descriptive, hence no statistical analyses were available.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	441			
Units: Participants				
Anti-D antibody ≥ 0.1 IU/ml [N=438]	437			
Anti-D antibody ≥ 0.01 IU/ml [N=438]	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-tetanus (anti-T)

End point title	Number of seroprotected subjects for anti-tetanus (anti-T)[2]

End point description:

A seroprotected subject was a subject whose anti-T concentrations are greater than or equal to (≥) 0.1 International units per milliliter (IU/ml). Seroprotection was assessed by enzyme-linked immunosorbent assay (ELISA) method.

End point type	Primary

End point timeframe:

At Day 31

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: This endpoint was descriptive, hence no statistical analyses were available.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	441			
Units: Participants				
Anti-T antibody	439			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[3]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to the assay cut-off value. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN respectively.

End point type	Primary

End point timeframe:

At Day 31

Notes:

[3] - 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: This endpoint was descriptive, hence no statistical analyses were available.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	442			
Units: Participants				
Anti-PT antibody [N=440]	430			
Anti-FHA antibody [N=442]	442			
Anti-PRN antibody [N=436]	431			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to diphtheria and tetanus antigens, one month after vaccination

End point title	Number of subjects with a booster response to diphtheria and tetanus antigens, one month after vaccination

End point description:

Booster response to diphtheria (D) and tetanus (T) antigens was defined as: for subjects with pre-vaccination antibody concentration <0.1 IU/ml (i.e. below the seroprotection cut-off), antibody concentrations at least ≥0.4 IU/ml, one month after vaccination, and for subjects with pre-vaccination antibody concentration ≥0.1 IU/ml (i.e. equal or above the seroprotection cut-off), an increase in antibody concentrations of at least four times the pre-vaccination concentration, one month after vaccination. Seronegative (S-) subjects are those who have antibody concentration less than (<) 0.1 IU/mL and seropositive (S+) subjects are those who have antibody concentration ≥ 0.1 IU/mL prior to vaccination.

End point type	Secondary

End point timeframe:

At Day 31

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	441			
Units: Participants				
Anti-D antibody, S- [N=33]	26			
Anti-D antibody, S+ [N=398]	282			
Anti-D antibody, Overall [N=431]	308			
Anti-T antibody, S- [N=43]	38			
Anti-T antibody, S+ [N=398]	338			
Anti-T antibody, Overall [N=441]	376			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to the PT, FHA and PRN antigens, one month after vaccination

End point title	Number of subjects with a booster response to the PT, FHA and PRN antigens, one month after vaccination

End point description:

Booster response to PT, FHA and PRN antigens was defined as: for subjects with pre-vaccination antibody concentration below (<) the assay cut-off, post-vaccination antibody concentration ≥ 4 times the assay cut-off; for subjects with pre-vaccination antibody concentration between the assay cut-off and <4 times the assay cut-off, post-vaccination antibody concentration ≥ 4 times the pre-vaccination antibody concentration; and for subjects with pre-vaccination antibody concentration ≥ 4 times the assay cut-off, post-vaccination antibody concentration ≥ 2 times the pre-vaccination antibody concentration. Seronegative (S-) subjects are those who have antibody concentration less than (<) assay cut-off and seropositive (S+) subjects are those who have antibody concentration ≥ assay cut-off prior to vaccination. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN respectively.

End point type	Secondary

End point timeframe:

At Day 31

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	442			
Units: Participants				
Anti-PT antibody, S- {N=158]	138			
Anti-PT antibody, S+ (< 4*assay cut-off) [N=159]	140			
Anti-PT antibody, S+ (≥ 4*assay cut-off) [N=121]	97			
Anti-PT antibody, Overall [N=438]	375			
Anti-FHA antibody, S- [N=8]	8			
Anti-FHA antibody, S+ (< 4*assay cut-off) [N=57]	57			
Anti-FHA antibody, S+ (≥ 4*assay cut-off) [N=377]	345			
Anti-FHA antibody, Overall [N=442]	410			
Anti-PRN antibody, S- [N=68]	57			
Anti-PRN antibody, S+ (< 4*assay cut-off) [N=121]	114			
Anti-PRN antibody, S+ (≥ 4*assay cut-off) [N=245]	225			
Anti-PRN, Overall [N=434]	396			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D, anti-T, anti-PT, anti-FHA and anti-PRN antibody concentrations, one month after vaccination

End point title	Anti-D, anti-T, anti-PT, anti-FHA and anti-PRN antibody concentrations, one month after vaccination

End point description:

Antibody concentrations are presented as Geometric Mean Concentrations (GMCs) and expressed in International Units per milliliter (IU/mL). The cut-off for the assays were: 0.057 IU/mL for anti-D, 0.043 IU/mL for anti-T, 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN, respectively.

End point type	Secondary

End point timeframe:

At Day 31

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	442			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D antibody	6.287 (5.643 to 7.004)			

Anti-T antibody	13.507 (12.138 to 15.031)			
Anti-PT antibody	59.279 (52.907 to 66.418)			
Anti-FHA antibody	396.938 (362.876 to 434.197)			
Anti-PRN antibody	249.638 (213.233 to 292.258)			

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, swelling. Any = Occurrence of any local symptom regardless of its intensity grade. Any redness and swelling were defined as greater than (>) 0 millimeters (mm) diameter for all subjects.

End point type	Secondary

End point timeframe:

During the 4-day (Day 1–4) follow-up period after vaccination.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	447			
Units: Participants				
Pain	284			
Redness	207			
Swelling	174			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects aged below 6 years with solicited general symptoms

End point title	Number of subjects aged below 6 years with solicited general symptoms

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness, Loss of appetite and Fever. Any = Occurrence of any general symptom regardless of its intensity grade and relationship to the study vaccination. Fever was defined as temperature ≥38.0 degrees Celsius (°C). The location for measuring temperature was the axilla.

End point type	Secondary

End point timeframe:

During the 4-day (Day 1–4) follow-up period after vaccination.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Participants				
Drowsiness	1			
Irritability/Fussiness	5			
Loss of appetite	3			
Fever (≥ 38°C)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects aged above and equal to 6 years with solicited general symptoms

End point title	Number of subjects aged above and equal to 6 years with solicited general symptoms

End point description:

Assessed solicited general symptoms were Fatigue, Gastrointestinal symptoms (included nausea, vomiting, diarrhoea and/or abdominal pain), Headache and Fever. Any = Occurence of any general symptom regardless of its intensity grade and relationship to the study vaccination. Fever was defined as axilla temperature ≥ 38 degrees Celsius (°C).

End point type	Secondary

End point timeframe:

During the 4-day (Day 1–4) follow-up period after vaccination.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	429			
Units: Participants				
Fatigue	126			
Gastrointestinal symptoms	34			
Headache	107			
Fever (≥ 38°C), Overall	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with large swelling reactions

End point title	Number of subjects with large swelling reactions

End point description:

Large injection site reaction for subjects <6 years of age defined as a swelling with a diameter of >50 mm and for subjects >=6 years of age swelling with a diameter of >100 mm, noticeable diffuse swelling or noticeable increase in limb circumference. Any = Occurence of any large swelling regardless of its intensity grade and relationship to the study vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Day 1–4) follow-up period after vaccination.

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	447			
Units: Participants	1			

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:

Any unsolicited AE was defined as any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

During the 31-day (Day 1–31) follow-up period after vaccination

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	447			
Units: Participants	52			

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:

A SAE is any untoward medical occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Day 1 to Day 31

End point values	dTpa group			
Subject group type	Reporting group			
Number of subjects analysed	447			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse events (AEs) during the 31-day follow-up period after vaccination. Serious adverse events were reported during the whole study period (from Day 1 up to study conclusion at Day 31).

Adverse event reporting additional description:

Solicited adverse events were not reported in this section. They were defined for both age strata (subjects less than 6 years and subjects equal or greater than 6 years), and then, analyzed per age stratum. Please refer to the outcomes section for the results.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	dTpa group

Reporting group description:

Healthy female and male subjects with age 4 years and above and who received a single dose of Boostrix vaccine at Day 1.

Serious adverse events	dTpa group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 447 (0.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	dTpa group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 447 (11.63%)		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		

Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	2		
Body temperature increased			
subjects affected / exposed	2 / 447 (0.45%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 447 (1.34%)		
occurrences (all)	6		
Nasal congestion			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	6 / 447 (1.34%)		
occurrences (all)	6		
Rhinorrhoea			
subjects affected / exposed	2 / 447 (0.45%)		
occurrences (all)	2		
Sneezing			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 447 (2.68%)		
occurrences (all)	12		
Somnolence			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 447 (0.22%)		

occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Induration			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Injection site lymphadenopathy			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Injection site oedema			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Injection site pruritus			
subjects affected / exposed	2 / 447 (0.45%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	3 / 447 (0.67%)		
occurrences (all)	3		
Vaccination site erythema			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Vaccination site haematoma			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		

Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	3 / 447 (0.67%) 3 1 / 447 (0.22%) 1		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	1 / 447 (0.22%) 1 1 / 447 (0.22%) 1		
Musculoskeletal and connective tissue disorders Arthritis reactive subjects affected / exposed occurrences (all) Arthropathy subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 447 (0.22%) 1 1 / 447 (0.22%) 1 1 / 447 (0.22%) 1 1 / 447 (0.22%) 1 1 / 447 (0.22%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all)	1 / 447 (0.22%) 1 1 / 447 (0.22%) 1		

Ear infection			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	3 / 447 (0.67%)		
occurrences (all)	3		
Pneumonia bacterial			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	2 / 447 (0.45%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	7 / 447 (1.57%)		
occurrences (all)	7		
Respiratory tract infection viral			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	1 / 447 (0.22%)		
occurrences (all)	1		
Tracheitis			
subjects affected / exposed	3 / 447 (0.67%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2017	The protocol has been amended to implement the following changes: • The age at inclusion to study has been changed from 3 to 4 years of age in order to be in compliant with Boostrix's approved EU label wherein it is indicated for booster vaccination in individuals aged four years and older. • Wording "parents/Legally Acceptable Representative(s) (LAR[s])" is replaced by the wording "parents/adoptive parents". As per Russian legislation, only parents or adoptive parents can give consent for the enrolment of their child in a clinical trial. No other person is allowed to give consent on behalf of a minor to participate in a clinical trial. • The age groups are amended according to the approved Boostrix EU label and physiological particularities i.e, from 3-9 to 4-9 years (children), 10-19 to 10-17 years (adolescents), 20-64 to 18-64 years (adults) and ≥ 65 years (elderly population). • To reflect the upgrade to new version for protocol (15.0), ICF (8.0), eCRF, SPM and overall changes in the functions. • The inclusion criteria has been amended in order to clarify the following, - Children from four to seven years of age who have received diphtheria, tetanus and pertussis vaccination prior to study enrolment as per local recommendations will be enrolled - Subjects eight years of age and older who have received diphtheria, tetanus and pertussis vaccination to the best of their/subjects' parent(s)/subjects' adoptive parent(s) knowledge and did not receive an additional diphtheria, tetanus or pertussis vaccination within 5 years prior to enrolment in the study will be enrolled.
07 August 2017	This protocol amendment was developed after the comments from the Russian regulatory authorities [Ministry of Health (MoH)]. Adjustments to the text were made in certain sections for better readability and to clarify the inclusion and exclusion criteria for enrolment of subjects and the conduct of the study. In addition, adjustments for the reporting period and assessment of adverse events in the safety sections were made for consistency. Typos and errors were corrected throughout the document. The newly re-developed and re-validated GSK's DTPa ELISA cut-offs were updated as per the most recent CBER recommendation (2017).
31 October 2017	This protocol amendment was developed in order to accommodate older adults (approximately 58 years old and older) who were born before national recommendations in Russia for infant DTP vaccination, as well as those born when DTP vaccination coverage was low. The protocol amendment would also clarify inconsistencies present in the Protocol Amendment 2, between the English version and the Russian version. Following which, adjustments to the text were made in the inclusion criteria to clarify the enrolment of subjects for age group eight years and above. The wording parent(s)/adoptive parent(s) were aligned according to the local regulations. References for laboratory assays were updated and certain sections were modified to align with the rest of the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported