Clinical trial results:
Immunogenicity and safety of GSK Biologicals' DTPa-IPV/Hib (Infanrix™-IPV/Hib) combined diphtheria-tetanus-acellular pertussis-inactivated poliovirus and Haemophilus influenzae type b (DTPa-IPV/Hib) conjugate vaccine (Infanrix™-IPV/Hib) [213503 (DTPA-IPV)] vaccine in healthy Russian infants.

Summary

EudraCT number	2013-005577-43
Trial protocol	Outside EU/EEA
Global end of trial date	13 November 2018

Results information

Result version number	v2 (current)
This version publication date	18 May 2019
First version publication date	27 October 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	116194

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02858440
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
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	GSK Clinical Trials, GlaxoSmithKline, 044 8773793718, 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	22 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 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 study vaccine in terms of seroprotection status for diphtheria, tetanus, Hib and poliovirus types 1, 2 and 3 antigens, and in terms of seropositivity to the pertussis antigens, one month after the third dose of primary vaccination.

Protection of trial subjects:

The subjects will be observed closely for at least 30 minutes following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2016
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: 235
Worldwide total number of subjects	235
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)	235
Children (2-11 years)	0
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	Not applicable
Blinding used	Not blinded

Arms

Arm title	DTPa-IPV/Hib Group

Arm description:

All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

Arm type	Experimental
Investigational medicinal product name	Infanrix-IPV/Hib
Investigational medicinal product code	
Other name	DTPa-IPV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Patients received four doses of Infanrix-IPV/Hib vaccine, at day 0, month 1.5, month 3 and month 15.

Number of subjects in period 1	DTPa-IPV/Hib Group
Started	235
Completed	223
Not completed	12
Consent withdrawn by subject	3
Migrated/moved from study area	4
Lost to follow-up	3
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	DTPa-IPV/Hib Group

Reporting group description:

All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

Reporting group values	DTPa-IPV/Hib Group	Total	
Number of subjects	235	235	
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)	235	235	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Weeks			
arithmetic mean	14.1		
standard deviation	± 1.2	-	
Sex: Female, Male Units: Subjects			
Female	111	111	
Male	124	124	
Race/Ethnicity, Customized Units: Subjects			
White - Caucasian / European Heritage	235	235	

End points

End points reporting groups

Reporting group title	DTPa-IPV/Hib Group

Reporting group description:

All subjects received three doses of primary vaccination of the study vaccine, Infanrix-IPV/Hib (DTPa-IPV/Hib), at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

Primary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T), post primary vaccination

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T), post primary vaccination[1]

End point description:

A seroprotected subject is a subject whose anti-D and anti-T antibody concentration was greater than or equal to (≥) 0.1 International Units per milliliter (IU/mL).

End point type	Primary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary 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: No formal statistical hypothesis testing was planned, results were summarized as descriptive statistics only.

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: Participants				
Anti-D antibody ≥ 0.1 IU/mL	176			
Anti-T antibody ≥ 0.1 IU/mL	176			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post primary vaccination

End point title	Number of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post primary vaccination[2]

End point description:

A seroprotected subject is a subject whose anti-poliovirus types 1, 2 and 3 antibody titer was ≥ 8 ED50.

End point type	Primary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary 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: No formal statistical hypothesis testing was planned, results were summarized as descriptive statistics only.

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	151			
Units: Participants				
Anti-Polio 1 antibody ≥ 8 ED50	151			
Anti-Polio 2 antibody ≥ 8 ED50	151			
Anti-Polio 3 antibody ≥ 8 ED50	150			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polyribosyl ribitol phosphate (anti-PRP), post primary vaccination

End point title	Number of seroprotected subjects for anti-polyribosyl ribitol phosphate (anti-PRP), post primary vaccination[3]

End point description:

A seroprotected subject is a subject whose anti-PRP antibody concentration was ≥ 0.15 micrograms per milliliters (µg/mL).

End point type	Primary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

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: No formal statistical hypothesis testing was planned, results were summarized as descriptive statistics only.

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: Participants				
Anti-PRP	179			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of seropositive subjects for anti-pertussis (anti- PT),

	anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN), post primary vaccination[4]

End point description:

A seropositive subject is a subject whose antibody concentration was ≥ 2.046 IU/mL for anti-FHA, ≥ 2.187 IU/mL for anti-PRN and ≥ 2.693 IU/mL for anti-PT.

End point type	Primary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

Notes:

[4] - 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: No formal statistical hypothesis testing was planned, results were summarized as descriptive statistics only.

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: Participants				
Anti-FHA antibody ≥ 2.046 IU/mL	175			
Anti-PRN antibody ≥ 2.187 IU/mL	175			
Anti-PT antibody ≥ 2.693 IU/mL	174			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-D and anti-T, post booster vaccination

End point title	Number of seroprotected subjects for anti-D and anti-T, post booster vaccination

End point description:

A seroprotected subject is a subject whose anti-D and anti-T antibody concentration is ≥ 0.1 IU/mL.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: Participants				
anti-D antibody	188			
anti-T antibody	188			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post booster vaccination

End point title	Number of seroprotected subjects for anti-poliovirus types 1, 2 and 3, post booster vaccination

End point description:

A seroprotected subject is a subject whose anti-poliovirus types 1, 2 and 3 antibody titer is ≥ 8 ED50.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176[5]			
Units: Participants				
anti-Polio 1 antibody	176			
anti-Polio 2 antibody	169			
anti-Polio 3 antibody	167			

Notes:

[5] - The number of subjects analysed was different for the 3 serotypes (176, 169 and 167, respectively).

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-PRP, post booster vaccination

End point title	Number of seroprotected subjects for anti-PRP, post booster vaccination

End point description:

A seroprotected subject is a subject whose anti-PRP antibody concentration is ≥ 0.15 µg/mL.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: Participants				
Anti-PRP	188			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti- PT, anti-FHA and anti-PRN, post booster vaccination

End point title	Number of seropositive subjects for anti- PT, anti-FHA and anti-PRN, post booster vaccination

End point description:

A seropositive subject is a subject whose antibody concentration is ≥ 2.046 IU/mL for anti-FHA, ≥ 2.187 IU/mL for anti-PRN and ≥ 2.693 IU/mL for anti-PT.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188[6]			
Units: Participants				
anti-PT antibody	188			
anti-FHA antibody	188			
anti-PRN antibody	187			

Notes:

[6] - The number of subjects analysed was different for the 3 antibodies (188, 188 and 187, respectively).

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-D and anti-T, post primary vaccination

End point title	Antibody concentrations for anti-D and anti-T, post primary vaccination

End point description:

The antibody concentrations for anti-D and anti-T were presented as geometric mean concentrations (GMCs) and expressed as IU/mL.

End point type	Secondary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: IU/mL				
geometric mean (confidence interval 95%)				

Anti-D antibody	3.24 (2.84 to 3.68)			
Anti-T antibody	3.14 (2.81 to 3.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-D and anti-T, post booster vaccination

End point title	Antibody concentrations for anti-D and anti-T, post booster vaccination

End point description:

The antibody concentrations for anti-D and anti-T were presented as geometric mean concentrations (GMCs) and expressed as IU/mL.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: IU/mL				
geometric mean (confidence interval 95%)				
anti-D antibody	12.11 (10.82 to 13.56)			
anti-T antibody	8.18 (7.35 to 9.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for anti-polio types 1, 2 and 3, post primary vaccination

End point title	Antibody titers for anti-polio types 1, 2 and 3, post primary vaccination

End point description:

The antibody titers for anti-polio types 1, 2 and 3 were presented as geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	151			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 antibody	613.9 (505.5 to 745.5)			
Anti-Polio 2 antibody	591.6 (487.3 to 718.3)			
Anti-Polio 3 antibody	827.4 (674.7 to 1014.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for anti-polio types 1, 2 and 3, post booster vaccination

End point title	Antibody titers for anti-polio types 1, 2 and 3, post booster vaccination

End point description:

The antibody titers for anti-polio types 1, 2 and 3 were presented as geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176[7]			
Units: Titers				
geometric mean (confidence interval 95%)				
anti-Polio 1 antibody	2185.4 (1901.1 to 2512.3)			
anti-Polio 2 antibody	2944.1 (2601.3 to 3332.2)			
anti-Polio 3 antibody	3684.6 (3225.3 to 4209.3)			

Notes:

[7] - The number of subjects analysed was different for the 3 serotypes (176, 169 and 167, respectively).

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentration for anti-PRP, post primary vaccination

End point title	Antibody concentration for anti-PRP, post primary vaccination

End point description:

The antibody concentrations for anti-PRP were presented as geometric mean concentrations (GMCs) and expressed as µg/mL.

End point type	Secondary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	2.97 (2.48 to 3.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentration for anti-PRP, post booster vaccination

End point title	Antibody concentration for anti-PRP, post booster vaccination

End point description:

The antibody concentrations for anti-PRP were presented as geometric mean concentrations (GMCs) and expressed as µg/mL.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	28.72 (24.70 to 33.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post primary vaccination

End point title	Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post primary vaccination

End point description:

The antibody concentrations for anti-PT, anti-FHA and anti-PRN were presented as GMCs and expressed as IU/mL.

End point type	Secondary

End point timeframe:

At Month 4 (i.e. one month after 3rd dose of primary vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-FHA antibody	120.2 (107.0 to 135.1)			
Anti-PRN antibody	166.1 (146.8 to 187.8)			
Anti-PT antibody	65.0 (57.7 to 73.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post booster vaccination

End point title	Antibody concentrations for anti-PT, anti-FHA and anti-PRN, post booster vaccination

End point description:

The antibody concentrations for anti-PT, anti-FHA and anti-PRN were presented as GMCs and expressed as IU/mL.

End point type	Secondary

End point timeframe:

At Month 16 (i.e. one month after booster vaccination)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	188[8]			
Units: IU/mL				
geometric mean (confidence interval 95%)				
anti-FHA antibody	268.4 (242.4 to 297.2)			
anti-PRN antibody	563.4 (495.6 to 640.5)			
anti-PT antibody	107.9 (96.5 to 120.7)			

Notes:

[8] - The number of subjects analysed was different for the 3 antibodies (188, 188 and 187, respectively).

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local adverse events (AEs) following each dose of primary vaccination

End point title	Number of subjects with any solicited local adverse events (AEs) following each dose of primary vaccination

End point description:

The solicited local AEs assessed were pain, redness and swelling at the injection site. Any = Occurrence of the AE regardless of the intensity grade.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after each primary vaccination dose (i.e. at Day 0, at Month 1.5 and at Month 3)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	232[9]			
Units: Participants				
Any Pain, Dose 1	58			
Any Redness, Dose 1	83			
Any Swelling, Dose 1	45			
Any Pain, Dose 2	47			
Any Redness, Dose 2	89			
Any Swelling, Dose 2	58			
Any Pain, Dose 3	50			
Any Redness, Dose 3	96			
Any Swelling, Dose 3	63			

Notes:

[9] - The number of subjects analysed for dose 1, dose 2 and dose 3 was 232, 229 and 226, respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local AEs following booster vaccination

End point title	Number of subjects with any solicited local AEs following booster vaccination

End point description:

The solicited local AEs assessed were pain, redness, and swelling at the injection site. Any = Occurrence of the AE regardless of the intensity grade.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after booster vaccination dose (i.e. at Month 15)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	225			
Units: Participants				
Any Pain	71			
Any Redness	101			
Any Swelling	73			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general AEs following each dose of primary vaccination

End point title	Number of subjects with any solicited general AEs following each dose of primary vaccination

End point description:

The solicited general AEs assessed were drowsiness, irritability/fussiness, loss of appetite and fever. Any = Occurrence of the AE regardless of the intensity grade. Any fever = Fever (axillary) ≥ 37.5°C.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after each primary vaccination dose (i.e. at Day 0, at Month 1.5 and at Month 3)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	232[10]			
Units: Participants				
Any Drowsiness, Dose 1	82			
Any Irritability / Fussiness, Dose 1	100			
Any Loss Of Appetite, Dose 1	33			

Any Temperature/(Axillary) (°C), Dose 1	14			
Any Drowsiness, Dose 2	69			
Any Irritability / Fussiness, Dose 2	104			
Any Loss Of Appetite, Dose 2	34			
Any Temperature/(Axillary) (°C), Dose 2	32			
Any Drowsiness, Dose 3	65			
Any Irritability / Fussiness, Dose 3	106			
Any Loss Of Appetite, Dose 3	43			
Any Temperature/(Axillary) (°C), Dose 3	28			

Notes:

[10] - The number of subjects analysed for dose 1, dose 2 and dose 3 was 232, 229 and 226, respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general AEs following booster vaccination

End point title	Number of subjects with any solicited general AEs following booster vaccination

End point description:

The solicited general AEs assessed were drowsiness, irritability/fussiness, loss of appetite and fever. Any = Occurrence of the AE regardless of the intensity grade. Any fever = Fever (axillary) ≥ 37.5°C.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after booster vaccination dose (i.e. at Month 15)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	225			
Units: Participants				
Any Drowsiness	54			
Any Irritability / Fussiness	88			
Any Loss Of Appetite	40			
Any Temperature/(Axillary) (°C)	26			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited AEs following each dose of primary vaccination

End point title	Number of subjects with unsolicited AEs following each dose of primary vaccination

End point description:

An unsolicited AE was defined as any AE reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any =

Occurrence of the AE regardless of the intensity grade.

End point type	Secondary

End point timeframe:

During the 31-day (Days 0-30) follow-up period after each primary vaccination dose (i.e. at Day 0, at Month 1.5 and at Month 3)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	235			
Units: Participants				
Any AEs	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited AEs following booster vaccination

End point title	Number of subjects with unsolicited AEs following booster vaccination

End point description:

An unsolicited AE was defined as any AE reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of the AE regardless of the intensity grade.

End point type	Secondary

End point timeframe:

During the 31-day (Days 0-30) follow-up period after booster vaccination dose (i.e. at Month 15)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	225			
Units: Participants				
Any AEs	13			

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:

The SAEs assessed included any untoward medical occurrences that resulted in death, were life-

threatening, required hospitalisation or prolongation of existing hospitalisation or resulted in disability/incapacity. Any = Occurrence of the AE regardless of the intensity grade.

End point type	Secondary

End point timeframe:

During the entire study period (i.e. from Day 0 until Month 16)

End point values	DTPa-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	235			
Units: Participants				
Any SAEs	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local & general AEs: during the 4-day (Days 0-3) follow-up period after each primary & booster vaccination. Unsolicited AEs: during the 31-day (Days 0-30) follow-up period after each primary & booster vaccination. SAEs: from Day 0 until Month 16

Adverse event reporting additional description:

Solicited local and general AEs, unsolicited AEs, and SAEs were reported for the Primary Epoch and for the Booster Epoch.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	DTPa-IPV/Hib Group

Reporting group description:

All subjects received three doses of primary vaccination of the study vaccine, DTPa-IPV/Hib, at 3, 4.5 and 6 months of age and a single dose of booster vaccination at 18 months of age. The vaccine was administered intramuscularly into the upper side of the thigh on the right/left side.

Serious adverse events	DTPa-IPV/Hib Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 235 (1.28%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Patent ductus arteriosus			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proctitis			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastric infection			
subjects affected / exposed	1 / 235 (0.43%)		
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-IPV/Hib Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	201 / 235 (85.53%)		
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Dystonia			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Hydrocephalus			

subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
Idiopathic intracranial hypertension			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Motor dysfunction			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Poor quality sleep			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	131 / 235 (55.74%)		
occurrences (all)	270		
Tremor			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	140 / 235 (59.57%)		
occurrences (all)	369		
Injection site pain			
subjects affected / exposed	103 / 235 (43.83%)		
occurrences (all)	226		
Injection site swelling			
subjects affected / exposed	102 / 235 (43.40%)		
occurrences (all)	239		
Pyrexia			
subjects affected / exposed	67 / 235 (28.51%)		
occurrences (all)	104		
Irritability postvaccinal			

subjects affected / exposed occurrences (all)	157 / 235 (66.81%) 398		
Immune system disorders Food allergy subjects affected / exposed occurrences (all) Hypersensitivity subjects affected / exposed occurrences (all)	 1 / 235 (0.43%) 1 2 / 235 (0.85%) 2		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Infantile colic subjects affected / exposed occurrences (all) Regurgitation subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 235 (0.43%) 2 1 / 235 (0.43%) 1 1 / 235 (0.43%) 2 1 / 235 (0.43%) 1 2 / 235 (0.85%) 2 1 / 235 (0.43%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 2 / 235 (0.85%) 2 4 / 235 (1.70%) 4		
Skin and subcutaneous tissue disorders			

Dermatitis allergic			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Dermatitis atopic			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	5 / 235 (2.13%)		
occurrences (all)	5		
Rash papular			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Nightmare			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 235 (1.28%)		
occurrences (all)	3		
Ear infection			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	3 / 235 (1.28%)		
occurrences (all)	3		
Pharyngitis			

subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	5 / 235 (2.13%)		
occurrences (all)	6		
Rhinitis			
subjects affected / exposed	15 / 235 (6.38%)		
occurrences (all)	18		
Tracheitis			
subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
Tracheobronchitis			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	4 / 235 (1.70%)		
occurrences (all)	7		
Urinary tract infection			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	2 / 235 (0.85%)		
occurrences (all)	2		
Enteritis infectious			
subjects affected / exposed	1 / 235 (0.43%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	93 / 235 (39.57%)		
occurrences (all)	150		

Iron deficiency subjects affected / exposed occurrences (all)	1 / 235 (0.43%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2016	Amendment 1 was assessed to: as per Russian legislation, only parents or adoptive parents can give consent for the enrolment of their child in a clinical trial. No other persons are allowed to give consent on behalf of a minor to participate in a clinical trial. Therefore the wording "parents/Legally Acceptable Representative(s) (LAR[s])" should be replaced by the wording "parents/adoptive parents". This change was implemented by the local team in the Russian translation of the protocol and informed consent form after obtaining approval from competent authorities and ethics committees in order to meet Russian legislation requirements. The purpose of this amendment is to replace "parents/LAR(s)" by "parents/adoptive parents" in order to ensure consistency in wording between local protocol and central protocol; in addition, the list of study personnel and the function names have been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported