Clinical trial results:
A phase IV, open-label, non-randomised, multi-centre study to assess the immunogenicity and safety of Infanrix hexa? administered as primary vaccination in healthy infants born to mothers given Boostrix? during pregnancy or post-delivery in 116945 [DTPA (BOOSTRIX)-047].

Summary

EudraCT number	2014-001117-41
Trial protocol	ES CZ Outside EU/EEA FI IT
Global end of trial date	07 March 2018

Results information

Result version number	v1 (current)
This version publication date	06 April 2019
First version publication date	06 April 2019

Trial information

Trial identification

Sponsor protocol code	201330

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02422264
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 Response Center, GlaxoSmithKline, 044 8664357343, 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	26 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunological response to Infanrix hexa in terms of seroprotection status for diphtheria, tetanus, hepatitis B, poliovirus and Hib antigens, and in terms of vaccine response for the pertussis antigens, one month after the last dose of the primary vaccination in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination 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. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 38
Country: Number of subjects enrolled	Canada: 144
Country: Number of subjects enrolled	Czech Republic: 71
Country: Number of subjects enrolled	Finland: 52
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Spain: 282
Worldwide total number of subjects	601
EEA total number of subjects	419

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	601

months)	
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:

Out of 601 subjects enrolled in the study, only 592 were vaccinated.

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

Are arms mutually exclusive?	Yes
Arm title	dTpa Group

Arm description:

Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Arm type	Experimental
Investigational medicinal product name	Infanrix hexa Prevnar 13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects received Infanrix hexa co-administered with Prevnar 13 at 2, 4 and 6 months or 2, 3 and 4 months, depending on the immunization schedule of the country. In some countries/regions, Prevnar 13 was given as a 2-dose schedule at 2 and 4 months of age.

Arm title	Control Group

Arm description:

Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa Prevnar 13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects received Infanrix hexa co-administered with Prevnar 13 at 2, 4 and 6 months or 2, 3 and 4 months, depending on the immunization schedule of the country. In some countries/regions, Prevnar 13 was given as a 2-dose schedule at 2 and 4 months of age.

Number of subjects in period 1	dTpa Group	Control Group
Started	296	305
Completed	291	301
Not completed	5	4
Consent withdrawn by subject	1	2
Migrated/moved from study area	3	1
Subject vaccinated outside of the study	-	1
Serious Adverse Event	1	-

Baseline characteristics

Reporting groups	
Reporting group title	dTpa Group
Reporting group description:	
Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.	
Reporting group title	Control Group
Reporting group description:	
Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.	

Reporting group values	dTpa Group	Control Group	Total
Number of subjects	296	305	601
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	296	305	601
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Age at Dose 1			
Units: Weeks			
arithmetic mean	8.7	8.9	
standard deviation	± 1.6	± 1.8	-
Sex: Female, Male Units: Subjects			
Female	141	144	285
Male	155	161	316
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	4	9	13
Asian - East Asian Heritage	2	0	2
Asian - South East Asian Heritage	3	0	3
White - Arabic / North African Heritage	1	3	4
White - Caucasian / European Heritage	268	285	553
Mixed origin	18	8	26

End points

End points reporting groups

Reporting group title	dTpa Group

Reporting group description:

Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Reporting group title	Control Group

Reporting group description:

Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Primary: Number of subjects with vaccine response against Pertussis Toxoid (PT), Filamentous Haemagglutinin (FHA) and Pertactin (PRN) antigens

End point title	Number of subjects with vaccine response against Pertussis Toxoid (PT), Filamentous Haemagglutinin (FHA) and Pertactin (PRN) antigens[1]

End point description:

Vaccine response to the PT, FHA and PRN antigens, is defined as the appearance of antibodies in subjects who were initially seronegative (i.e., with concentrations lower than (<) the cut-off value of the assay), or at least maintenance of pre-vaccination antibody concentrations in subjects who were initially seropositive (i.e., with concentrations greater than or equal to (≥) the cut-off value of the assay). Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA, 2.187 IU/mL for anti-PRN.

End point type	Primary

End point timeframe:

1 month after the last dose of the 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	251		
Units: Participants				
anti-PT antibody	185	249		
anti-FHA antibody	95	238		
anti-PRN antibody	90	225		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentration above or equal to the assay cut-off

End point title	Number of seroprotected subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentration above or equal to the assay cut-off[2]

End point description:

A seroprotected subject is a subject whose antibody concentration/titre was ≥ the level defining clinical protection, of 0.1 International Units per milliliter (IU/mL).

End point type	Primary

End point timeframe:

1 month after the last dose of the 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: Participants				
anti-D antibody	264	271		
anti-T antibody	266	271		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects with anti Hepatitis B (anti-HBs) antibody concentration above or equal to the assay cut-off

End point title	Number of seroprotected subjects with anti Hepatitis B (anti-HBs) antibody concentration above or equal to the assay cut-off[3]

End point description:

A seroprotected subject is a subject whose antibody concentration/titre was ≥ to the level defining clinical protection, of 10 micro International Units per milliliter (mIU/mL).

End point type	Primary

End point timeframe:

1 month after the last dose of the 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	263		
Units: Participants	251	259		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects with anti-poliovirus type 1, 2 and 3 antibody concentration above or equal to 8

End point title	Number of seroprotected subjects with anti-poliovirus type 1, 2 and 3 antibody concentration above or equal to 8[4]

End point description:

A seroprotected subject is a subject whose antibody titre was ≥ the level defining clinical protection, of 8 ED50.

End point type	Primary

End point timeframe:

1 month after the last dose of the 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	245		
Units: Participants				
anti-Polio 1 antibody	233	242		
anti-Polio 2 antibody	239	235		
anti-Polio 3 antibody	228	236		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration above or equal to the assay cut-off

End point title	Number of seroprotected subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration above or equal to the assay cut-off[5]

End point description:

A seroprotected subject is a subject whose antibody concentration/titre was ≥ the level defining clinical protection, of 0.15 micrograms per milliliter (µg/mL).

End point type	Primary

End point timeframe:

1 month after the last dose of the primary vaccination

Notes:

[5] - 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	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: Participants	255	256		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations.

End point title	Anti-D and anti-T antibody concentrations.

End point description:

Antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in IU/mL.

End point type	Secondary

End point timeframe:

Before the first dose of Infanrix hexa

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	253		
Units: IU/mL				
geometric mean (confidence interval 95%)				
anti-D antibody, before dose 1	0.423 (0.354 to 0.506)	0.089 (0.076 to 0.103)		
anti-T antibody, before dose 1	2.152 (1.925 to 2.406)	0.378 (0.330 to 0.434)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations.

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations.

End point description:

Anti-PT, anti-FHA and anti-PRN antibody concentrations were expressed as GMCs and measured in IU/mL.

End point type	Secondary

End point timeframe:

Before the first dose of Infanrix hexa

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	253		
Units: IU/ml				
geometric mean (confidence interval 95%)				
anti-PT antibody	11.9 (10.3 to 13.6)	2.2 (2.0 to 2.5)		
anti-FHA antibody	88.3 (77.7 to 100.4)	6.6 (5.7 to 7.7)		
anti-PRN antibody	70.5 (56.1 to 88.5)	4.5 (3.7 to 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations

End point description:

Antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in IU/mL.

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: IU/ml				
geometric mean (confidence interval 95%)				
anti-Diphtheria antibody	1.747 (1.598 to 1.910)	2.746 (2.502 to 3.015)		
anti-Tetanus antibody	2.347 (2.135 to 2.582)	2.278 (2.069 to 2.508)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-Polio type 1, 2 and 3 antibody titers

End point description:

Anti-Polio type 1, 2 and 3 antibody titers were expressed as geometric mean titers (GMT).

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	245		
Units: Titers				
geometric mean (confidence interval 95%)				
anti-Polio 1 antibody	432.1 (351.8 to 530.9)	489.9 (402.6 to 596.0)		
anti-Polio 2 antibody	424.6 (342.7 to 526.2)	388.4 (306.3 to 492.6)		
anti-Polio 3 antibody	730.6 (596.5 to 894.9)	775.6 (645.9 to 931.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

Anti-PRP antibody concentrations were expressed as GMCs and measured in µg/mL.

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: µg/mL				
geometric mean (confidence interval 95%)	1.862 (1.554 to 2.231)	1.717 (1.428 to 2.064)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA, anti-PRN antibody concentrations

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

End point description:

Anti-PT, anti-FHA, anti-PRN antibody concentrations were expressed as GMCs and measured in IU/mL.

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: IU/mL				
geometric mean (confidence interval 95%)				
anti-PT antibody	32.7 (30.2 to 35.3)	54.7 (51.0 to 58.6)		
anti-FHA antibody	68.5 (63.5 to 73.9)	103.5 (95.6 to 112.1)		
anti-PRN antibody	60.5 (54.2 to 67.6)	92.0 (81.6 to 103.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pneumococcal antibody concentrations

End point title	Anti-pneumococcal antibody concentrations

End point description:

Assessed anti-pneumococcal serotypes were (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F), expressed as GMCs and measured in µg/mL.

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	237		
Units: µg/mL				
geometric mean (confidence interval 95%)				
anti-PnPS 1 antibody	1.61 (1.43 to 1.80)	1.92 (1.73 to 2.14)		
anti-PnPS 3 antibody	0.54 (0.49 to 0.60)	0.60 (0.55 to 0.67)		
anti-PnPS 4 antibody	1.20 (1.07 to 1.35)	1.56 (1.40 to 1.75)		
anti-PnPS 5 antibody	1.09 (0.96 to 1.24)	1.27 (1.13 to 1.43)		

anti-PnPS 6A antibody	2.16 (1.89 to 2.47)	2.59 (2.27 to 2.95)		
anti-PnPS 6B antibody	1.37 (1.12 to 1.68)	1.44 (1.20 to 1.73)		
anti-PnPS 7F antibody	2.39 (2.15 to 2.65)	2.67 (2.43 to 2.93)		
anti-PnPS 9V antibody	1.33 (1.19 to 1.50)	1.64 (1.47 to 1.83)		
anti-PnPS 14 antibody	5.70 (4.99 to 6.52)	6.57 (5.71 to 7.56)		
anti-PnPS 18C antibody	1.61 (1.42 to 1.82)	1.79 (1.59 to 2.01)		
anti-PnPS 19A antibody	1.61 (1.43 to 1.82)	2.01 (1.78 to 2.27)		
anti-PnPS 19F antibody	2.57 (2.35 to 2.82)	3.24 (2.92 to 3.60)		
anti-PnPS 23F antibody	0.86 (0.74 to 0.99)	1.02 (0.88 to 1.17)		

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. Solicited local symptoms were assessed by each and across dose.

End point type	Secondary

End point timeframe:

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

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	303		
Units: Participants				
Any Pain, Dose 1	120	120		
Any Redness, Dose 1	128	116		
Any Swelling, Dose 1	81	87		
Any Pain, Dose 2	109	101		
Any Redness, Dose 2	139	139		
Any Swelling, Dose 2	98	95		
Any Pain, Dose 3	85	94		
Any Redness, Dose 3	122	134		
Any Swelling, Dose 3	77	109		
Any Pain, Across Doses	175	184		
Any Redness, Across Doses	205	203		
Any Swelling, Across Doses	157	168		

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

End point description:

Assessed solicited general symptoms were drowsiness, irritability/fussiness, loss of appetite and fever [defined as axillary route temperature ≥ 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Solicited general symptoms were assessed by each and across dose.

End point type	Secondary

End point timeframe:

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

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	303		
Units: Participants				
Any Drowsiness, Dose 1	166	174		
Any Irritability / Fussiness, Dose 1	187	191		
Any Loss of Appetite, Dose 1	85	94		
Any Temperature/(Axillary) (≥37.5°C), Dose 1	64	69		
Any Drowsiness, Dose 2	142	149		
Any Irritability / Fussiness, Dose 2	182	194		
Any Loss of Appetite, Dose 2	69	94		
Any Temperature/(Axillary) (≥37.5°C), Dose 2	62	76		
Any Drowsiness, Dose 3	99	104		
Any Irritability / Fussiness, Dose 3	142	161		
Any Loss of Appetite, Dose 3	64	63		
Any Temperature/(Axillary) (≥37.5°C), Dose 3	52	47		
Any Drowsiness, Across Doses	216	232		
Any Irritability/Fussiness, Across Doses	255	257		
Any Loss of appetite, Across Doses	142	157		
Any Temperature/(Axillary) (≥37.5°C), Across Doses	125	126		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events

End point title	Number of subjects with unsolicited adverse events

End point description:

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

End point type	Secondary

End point timeframe:

During the 31-day (days 0-30) follow-up period after each vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	305		
Units: Participants	161	173		

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 assessed included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.

End point type	Secondary

End point timeframe:

From Day 0, prior to vaccination until the study end, at Month 3 or 5 (depending on vaccination schedule of the country)

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	305		
Units: Participants	7	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against diphtheria (anti-D) and tetanus (anti-T) antibody concentration above or equal to the assay cut-off.

End point title	Number of seroprotected subjects against diphtheria (anti-D) and tetanus (anti-T) antibody concentration above or equal to the assay cut-off.

End point description:

A seroprotected subject is a subject whose antibody concentration was ≥ the level defining clinical protection, of 0.1 IU/mL.

End point type	Secondary

End point timeframe:

Before the first dose of Infanrix hexa

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	253		
Units: Participants				
anti-D antibody	200	110		
anti-T antibody	240	225		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentration above or equal to the assay cut-off.

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentration above or equal to the assay cut-off.

End point description:

A seropositive subject is a subject whose antibody concentration is ≥ the assay cut-off defined. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA,2.187 IU/mL for anti-PRN

End point type	Secondary

End point timeframe:

Before the first dose of Infanrix hexa

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	253		
Units: Participants				
anti-PT antibody	218	88		
anti-FHA antibody	242	210		
anti-PRN antibody	231	151		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

Anti-HBs antibody concentrations were expressed as geometric mean concentrations (GMCs) and measured in mIU/mL.

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	263		
Units: mIU/ml				
geometric mean (confidence interval 95%)	1322.8 (1116.7 to 1567.0)	1339.2 (1132.8 to 1583.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA, anti-PRN antibody concentration above or equal to the assay cut-off.

End point title	Number of subjects with anti-PT, anti-FHA, anti-PRN antibody concentration above or equal to the assay cut-off.

End point description:

A seropositive subject is a subject whose antibody concentration is ≥ the assay cut-off defined. Assay cut-off was 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA,2.187 IU/mL for anti-PRN

End point type	Secondary

End point timeframe:

1 month after the last dose of the primary vaccination

End point values	dTpa Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	271		
Units: Participants				
anti-PT antibody	266	271		
anti-FHA antibody	266	271		
anti-PRN antibody	266	269		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 4-day (Day 0-Day 3) and unsolicited AEs were collected during the 31-day (days 0-30) follow-up period after each vaccination. SAEs were collected from Day 0 until the study end (Month 3 or 5).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Control Group

Reporting group description:

Infants born to mothers belonging to the Control group in study NCT02377349 [DTPA (BOOSTRIX)-047], i.e. who received a single dose of placebo during pregnancy and a dose of Boostrix immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Reporting group title	dTpa Group

Reporting group description:

Infants born to mothers belonging to the Boostrix Group in study NCT02377349 [DTPA (BOOSTRIX)-047] i.e. who received a single dose of Boostrix during pregnancy and a dose of placebo immediately post-delivery. All infants in this group received Infanrix hexa co-administered with Prevenar 13 according to the routine national immunisation schedule.

Serious adverse events	Control Group	dTpa Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 305 (5.57%)	7 / 296 (2.36%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haemorrhage			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cytomegalovirus infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniosynostosis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptorchism			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dandy-walker syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear malformation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcephaly			

subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Milk allergy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	4 / 305 (1.31%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection bacterial			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (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: 0 %

Non-serious adverse events	Control Group	dTpa Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	294 / 305 (96.39%)	292 / 296 (98.65%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Infantile haemangioma			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Peripheral coldness			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 305 (0.00%)	3 / 296 (1.01%)	
occurrences (all)	0	3	
Injection site bruising			
subjects affected / exposed	2 / 305 (0.66%)	2 / 296 (0.68%)	
occurrences (all)	2	2	
Injection site mass			
subjects affected / exposed	1 / 305 (0.33%)	3 / 296 (1.01%)	
occurrences (all)	2	4	
Injection site induration			

subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Injection site swelling			
subjects affected / exposed	169 / 305 (55.41%)	157 / 296 (53.04%)	
occurrences (all)	292	256	
Injection site nodule			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	139 / 305 (45.57%)	133 / 296 (44.93%)	
occurrences (all)	208	203	
Thirst			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Vaccination site erythema			
subjects affected / exposed	2 / 305 (0.66%)	0 / 296 (0.00%)	
occurrences (all)	2	0	
Vaccination site pain			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Vaccination site swelling			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Vessel puncture site bruise			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Injection site erythema			
subjects affected / exposed	203 / 305 (66.56%)	205 / 296 (69.26%)	
occurrences (all)	389	389	
Injection site pain			
subjects affected / exposed	184 / 305 (60.33%)	175 / 296 (59.12%)	
occurrences (all)	315	314	
Irritability postvaccinal			
subjects affected / exposed	257 / 305 (84.26%)	255 / 296 (86.15%)	
occurrences (all)	546	511	
Immune system disorders			

Milk allergy			
subjects affected / exposed	2 / 305 (0.66%)	1 / 296 (0.34%)	
occurrences (all)	2	1	
Reproductive system and breast disorders			
Genital labial adhesions			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 305 (4.26%)	6 / 296 (2.03%)	
occurrences (all)	14	6	
Choking			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	6 / 305 (1.97%)	0 / 296 (0.00%)	
occurrences (all)	6	0	
Rhinorrhoea			
subjects affected / exposed	5 / 305 (1.64%)	3 / 296 (1.01%)	
occurrences (all)	5	3	
Psychiatric disorders			
Emotional distress			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Irritability			
subjects affected / exposed	3 / 305 (0.98%)	2 / 296 (0.68%)	
occurrences (all)	3	2	
Investigations			
Body temperature increased			
subjects affected / exposed	2 / 305 (0.66%)	2 / 296 (0.68%)	
occurrences (all)	2	2	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Bite			

subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Injury			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Road traffic accident			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	0 / 305 (0.00%)	2 / 296 (0.68%)	
occurrences (all)	0	2	
Congenital, familial and genetic disorders			
Congenital torticollis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Phimosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Nervous system disorders			
Aphonia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
External hydrocephalus			

subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	232 / 305 (76.07%)	216 / 296 (72.97%)	
occurrences (all)	427	407	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dacryostenosis acquired			
subjects affected / exposed	2 / 305 (0.66%)	1 / 296 (0.34%)	
occurrences (all)	2	1	
Eye discharge			
subjects affected / exposed	2 / 305 (0.66%)	0 / 296 (0.00%)	
occurrences (all)	2	0	
Eye irritation			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Eye swelling			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Pupils unequal			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Abnormal faeces			

subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Change of bowel habit			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	9 / 305 (2.95%)	8 / 296 (2.70%)	
occurrences (all)	10	9	
Diarrhoea			
subjects affected / exposed	2 / 305 (0.66%)	8 / 296 (2.70%)	
occurrences (all)	2	8	
Flatulence			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Enteritis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Gastric disorder			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 305 (1.97%)	8 / 296 (2.70%)	
occurrences (all)	6	8	
Gingival pain			
subjects affected / exposed	1 / 305 (0.33%)	4 / 296 (1.35%)	
occurrences (all)	1	5	
Haematochezia			
subjects affected / exposed	3 / 305 (0.98%)	0 / 296 (0.00%)	
occurrences (all)	3	0	
Infantile colic			
subjects affected / exposed	2 / 305 (0.66%)	2 / 296 (0.68%)	
occurrences (all)	2	2	
Infrequent bowel movements			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Odynophagia			

subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Mucous stools			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Oral mucosal erythema			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Regurgitation			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Sandifer’s syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Teething			
subjects affected / exposed	14 / 305 (4.59%)	14 / 296 (4.73%)	
occurrences (all)	16	21	
Toothache			
subjects affected / exposed	1 / 305 (0.33%)	2 / 296 (0.68%)	
occurrences (all)	1	2	
Umbilical hernia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	4 / 305 (1.31%)	6 / 296 (2.03%)	
occurrences (all)	4	6	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	8 / 305 (2.62%)	1 / 296 (0.34%)	
occurrences (all)	8	1	
Dermatitis atopic			
subjects affected / exposed	6 / 305 (1.97%)	4 / 296 (1.35%)	
occurrences (all)	7	4	

Dermatitis diaper			
subjects affected / exposed	4 / 305 (1.31%)	3 / 296 (1.01%)	
occurrences (all)	4	3	
Dry skin			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Dyshidrotic eczema			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	5 / 305 (1.64%)	5 / 296 (1.69%)	
occurrences (all)	5	5	
Erythema			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	9 / 305 (2.95%)	4 / 296 (1.35%)	
occurrences (all)	9	4	
Rash erythematous			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Rash macular			
subjects affected / exposed	2 / 305 (0.66%)	0 / 296 (0.00%)	
occurrences (all)	2	0	
Seborrhoeic dermatitis			
subjects affected / exposed	2 / 305 (0.66%)	2 / 296 (0.68%)	
occurrences (all)	2	2	
Urticaria			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Head deformity			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Pain in extremity			

subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Positional plagiocephaly			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Posture abnormal			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Torticollis			
subjects affected / exposed	0 / 305 (0.00%)	2 / 296 (0.68%)	
occurrences (all)	0	2	
Epiphysiolysis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Adenoiditis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Bronchiolitis			
subjects affected / exposed	11 / 305 (3.61%)	5 / 296 (1.69%)	
occurrences (all)	12	5	
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	5 / 305 (1.64%)	4 / 296 (1.35%)	
occurrences (all)	6	4	
Candida nappy rash			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Candida infection			
subjects affected / exposed	0 / 305 (0.00%)	2 / 296 (0.68%)	
occurrences (all)	0	2	
Conjunctivitis			
subjects affected / exposed	13 / 305 (4.26%)	6 / 296 (2.03%)	
occurrences (all)	14	6	

Croup infectious			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	10 / 305 (3.28%)	6 / 296 (2.03%)	
occurrences (all)	12	6	
Enterovirus infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Erythema infectiosum			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Exanthema subitum			
subjects affected / exposed	3 / 305 (0.98%)	1 / 296 (0.34%)	
occurrences (all)	3	1	
Eye infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	2	
Fungal skin infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Furuncle			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	8 / 305 (2.62%)	5 / 296 (1.69%)	
occurrences (all)	8	5	
Gastroenteritis viral			
subjects affected / exposed	1 / 305 (0.33%)	3 / 296 (1.01%)	
occurrences (all)	1	3	
Hand-foot-and-mouth disease			
subjects affected / exposed	2 / 305 (0.66%)	0 / 296 (0.00%)	
occurrences (all)	2	0	
Impetigo			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	

Influenza			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	3 / 305 (0.98%)	3 / 296 (1.01%)	
occurrences (all)	3	3	
Nail infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	15 / 305 (4.92%)	20 / 296 (6.76%)	
occurrences (all)	17	21	
Oral candidiasis			
subjects affected / exposed	2 / 305 (0.66%)	4 / 296 (1.35%)	
occurrences (all)	2	4	
Oral fungal infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	3 / 305 (0.98%)	0 / 296 (0.00%)	
occurrences (all)	3	0	
Pharyngitis			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Otitis media acute			
subjects affected / exposed	2 / 305 (0.66%)	3 / 296 (1.01%)	
occurrences (all)	3	3	
Pharyngotonsillitis			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Respiratory tract infection			
subjects affected / exposed	9 / 305 (2.95%)	4 / 296 (1.35%)	
occurrences (all)	12	5	
Respiratory tract infection viral			
subjects affected / exposed	8 / 305 (2.62%)	4 / 296 (1.35%)	
occurrences (all)	8	4	

Rhinitis			
subjects affected / exposed	8 / 305 (2.62%)	2 / 296 (0.68%)	
occurrences (all)	8	2	
Tonsillitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 296 (0.34%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	32 / 305 (10.49%)	36 / 296 (12.16%)	
occurrences (all)	38	41	
Urinary tract infection			
subjects affected / exposed	2 / 305 (0.66%)	3 / 296 (1.01%)	
occurrences (all)	2	3	
Varicella zoster virus infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	1 / 305 (0.33%)	1 / 296 (0.34%)	
occurrences (all)	1	1	
Viral rash			
subjects affected / exposed	2 / 305 (0.66%)	0 / 296 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 296 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	157 / 305 (51.48%)	142 / 296 (47.97%)	
occurrences (all)	252	219	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2016	Given the fact that only infants born from mothers vaccinated in the previous study (116945 [DTPA (BOOSTRIX)-047) can be enrolled in the current study, the enrolment in DTPA (BOOSTRIX)-047 study has an impact on this current study (e.g. cohorts to be investigated). Initially, the DTPA (BOOSTRIX)-047 study was opened only in countries using 3-dose primary vaccination series against diphtheria, tetanus and pertussis in infants. Nevertheless, the 2-dose primary vaccination schedule in infants is also meaningful for different regions in the world (e.g. Europe). It was therefore decided to open the DTPA (BOOSTRIX)-047, and therefore the current study to countries using 2-dose primary vaccination series in infants with the aim to increase the scientific value of the study and generate clinical data in diverse infant vaccination schedules. The notion of end of study was added and Section 11.5 describing the posting of information on public registry was revised accordingly. The names and functions of the contributing authors have been updated. The name of GSK Biologicals' Global Vaccines Clinical Laboratories (GVCL) department has been updated to Clinical Laboratory Sciences (CLS) and the name of outsourced laboratory (Quest Diagnostic laboratory is now called Q² Solutions) has also been updated. In addition, minor updates including typos, abbreviations, clarifications of wording were done throughout the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported