Clinical trial results:
A phase IIIb open study to assess the safety and immunogenicity of GlaxoSmithKline (GSK) Biologicals´ 10-valent pneumococcal conjugate vaccine when co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa) vaccine in preterm infants as a 3-dose primary immunisation course during the first 6 months of life

Summary

EudraCT number	2006-002898-47
Trial protocol	GR ES
Global end of trial date	02 May 2008

Results information

Result version number	v2 (current)
This version publication date	10 March 2023
First version publication date	07 June 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	107737

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00390910
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	11 July 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 May 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and reactogenicity of GSK Biologicals´ 10-valent pneumococcal conjugate vaccine when administered as a 3-dose primary vaccination course and co-administered with DTPa-HBV-IPV/Hib vaccine in preterm infants.

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 from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	27 October 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 175
Country: Number of subjects enrolled	Greece: 111
Worldwide total number of subjects	286
EEA total number of subjects	286

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)	286
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:

For each subject the study duration was approximately 5 months for the active phase (Month 0 till one month after last vaccination) and 10 months when including the 5 months extended safety follow-up.

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	Overal 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	Synflorix + Infanrix hexa Group I

Arm description:

Very pre-tem infants born after a gestation period of 27-30 weeks (189-216 days).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT; 10 Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the right thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the left thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Arm title	Synflorix + Infanrix hexa Group II

Arm description:

Mild pre-tem infants born after a gestation period of 31-36 weeks (217-258 days).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT; 10 Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the right thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the left thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Arm title	Synflorix + Infanrix hexa Group III

Arm description:

Infants born after a full-term gestation period of more than 36 weeks (more than 258 days).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT; 10 Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the right thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular administration in the left thigh, 3 doses according to a 2-4-6 month of age schedule (Months 0, 2 and 4).

Number of subjects in period 1	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III
Started	50	87	149
Completed	48	83	139
Not completed	2	4	10
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	1	3	2
Migrated/moved from study area	-	-	3
Lost to follow-up	-	1	5

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix + Infanrix hexa Group I
Reporting group description:	
Very pre-tem infants born after a gestation period of 27-30 weeks (189-216 days).	
Reporting group title	Synflorix + Infanrix hexa Group II
Reporting group description:	
Mild pre-tem infants born after a gestation period of 31-36 weeks (217-258 days).	
Reporting group title	Synflorix + Infanrix hexa Group III
Reporting group description:	
Infants born after a full-term gestation period of more than 36 weeks (more than 258 days).	

Reporting group values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III
Number of subjects	50	87	149
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)	50	87	149
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 Units: weeks			
arithmetic mean	11	9.5	9.3
standard deviation	± 3.2	± 1.45	± 1.45
Gender categorical Units: Subjects			
Female	19	40	62
Male	31	47	87

Reporting group values	Total		
Number of subjects	286		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	286		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Units: weeks			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	121		
Male	165		

Subject analysis sets

Subject analysis set title	Pooled Group I + II
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pooled group consists of very preterm infants and mild preterm infants (Synflorix + Infanrix hexa Group I and Synflorix + Infanrix hexa Group II).

Reporting group values	Pooled Group I + II		
Number of subjects	137		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	137		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: weeks			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Synflorix + Infanrix hexa Group I
Reporting group description:	
Very pre-tem infants born after a gestation period of 27-30 weeks (189-216 days).	
Reporting group title	Synflorix + Infanrix hexa Group II
Reporting group description:	
Mild pre-tem infants born after a gestation period of 31-36 weeks (217-258 days).	
Reporting group title	Synflorix + Infanrix hexa Group III
Reporting group description:	
Infants born after a full-term gestation period of more than 36 weeks (more than 258 days).	
Subject analysis set title	Pooled Group I + II
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pooled group consists of very preterm infants and mild preterm infants (Synflorix + Infanrix hexa Group I and Synflorix + Infanrix hexa Group II).	

Primary: Number of subjects with core fever (rectal temperature) greater than (>) the cut-off

End point title	Number of subjects with core fever (rectal temperature) greater than (>) the cut-off[1][2]
End point description:	
Fever was measured as rectal temperature. Assessment of occurrences of fever > 39.0 °C was performed post doses 1, 2 and 3 of Synflorix or Infanrix hexa vaccine.	
End point type	Primary
End point timeframe:	
Within 4 days (Days 0-3) after each vaccine dose, administered according to a 3-dose schedule at 2-4-6 months of age (Month 0-2-4)	

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.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	146	135		
Units: Subjects				
Fever > 39.0°C, post Dose 1 [N=146;135]	5	2		
Fever > 39.0°C, post Dose 2 [N=141;133]	1	1		
Fever > 39.0°C, post Dose 3 [N=138;131]	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms[3]

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness greater than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

End point type	Secondary

End point timeframe:

Within 4 day (Days 0-3) after each vaccine dose, administered according to a 3-dose schedule at 2-4-6 months of age (Month 0-2-4)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	146	135		
Units: Subjects				
Any pain, Post Dose 1 [N=146,135]	58	40		
Grade 3 pain, Post Dose 1 [N=146,135]	6	6		
Any redness, Post Dose 1 [N=146,135]	67	39		
Grade 3 redness, Post Dose 1 [N=146,135]	0	1		
Any swelling, Post Dose 1 [N=146,135]	67	30		
Grade 3 swelling, Post Dose 1 [N=146,135]	2	1		
Any pain, Post Dose 2 [N=141;133]	39	39		
Grade 3 pain, Post Dose 2 [N=141;133]	1	9		
Any redness, Post Dose 2 [N=141;133]	72	41		
Grade 3 redness, Post Dose 2 [N=141;133]	7	0		
Any swelling, Post Dose 2 [N=141;133]	60	30		
Grade 3 swelling, Post Dose 2 [N=141;133]	4	0		
Any pain, Post Dose 3 [N=138;131]	42	30		
Grade 3 pain, Post Dose 3 [N=138;131]	6	3		
Any redness, Post Dose 3 [N=138;131]	66	33		
Grade 3 redness, Post Dose 3 [N=138;131]	9	3		
Any swelling, Post Dose 3 [N=138;131]	58	24		
Grade 3 swelling, Post Dose 3 [N=138;131]	6	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms

End point title	Number of subjects with any and Grade 3 solicited general symptoms[4]

End point description:

Solicited general symptoms assessed include drowsiness, fever [defined as rectal temperature greater than or equal to (≥) 38.0°C], irritability, and loss of appetite. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) greater than (>) 40.0 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) after each vaccine dose, administered according to a 3-dose schedule at 2-4-6 months of age (Month 0-2-4)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	146	135		
Units: Subjects				
Any drowsiness, Post Dose 1 [N=146,135]	53	44		
Grade 3 drowsiness, Post Dose 1 [N=146,135]	2	1		
Any fever(rectally), Post Dose 1 [N=146,135]	38	41		
Grade 3 fever(rectally), Post Dose 1 [N=146,135]	1	0		
Any irritability, Post Dose 1 [N=146,135]	73	53		
Grade 3 irritability, Post Dose 1 [N=146,135]	9	6		
Any loss of appetite, Post Dose 1 [N=146,135]	36	33		
Grade 3 loss of appetite, Post Dose 1 [N=146,135]	0	0		
Any drowsiness, Post Dose 2 [N=141;133]	34	32		
Grade 3 drowsiness, Post Dose 2 [N=141;133]	0	1		
Any fever(rectally), Post Dose 2 [N=141;133]	34	40		
Grade 3 fever(rectally), Post Dose 2 [N=141;133]	0	0		
Any irritability, Post Dose 2 [N=141;133]	53	51		
Grade 3 irritability, Post Dose 2 [N=141;133]	2	4		
Any loss of appetite, Post Dose 2 [N=141;133]	23	35		

Grade 3 loss of appetite, Post Dose 2 [N=141;133]	0	2		
Any drowsiness, Post Dose 3 [N=138;131]	22	18		
Grade 3 drowsiness, Post Dose 3 [N=138;131]	1	4		
Any fever(rectally), Post Dose 3 [N=138;131]	25	16		
Grade 3 fever(rectally), Post Dose 3 [N=138;131]	1	0		
Any irritability, Post Dose 3 [N=138;131]	44	40		
Grade 3 irritability, Post Dose 3 [N=138;131]	1	3		
Any loss of appetite, Post Dose 3 [N=138;131]	22	26		
Grade 3 loss of appetite, Post Dose 3 [N=138;131]	0	1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events

End point description:

An AE is 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. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) after each vaccine dose, administered according to a 3-dose schedule at 2-4-6 months of age (Month 0-2-4)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	149	137		
Units: Subjects				
Any AEs	58	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs)

End point title	Number of subjects with any serious adverse events (SAEs)[6]

End point description:

Serious adverse events (SAEs) assessed included medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/ incapacity.

End point type	Secondary

End point timeframe:

Throughout the active phase of the study (from the first vaccine administration (Month 0) up to 1 month after the third vaccine administration (Month 5)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	149	137		
Units: Subjects				
Any SAEs	13	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs)

End point title	Number of subjects with any serious adverse events (SAEs)[7]

End point description:

Serious adverse events (SAEs) assessed included medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/ incapacity.

End point type	Secondary

End point timeframe:

Throughout the entire study period starting from the first vaccine dose administration (Month 0) up to the end of the 6-month safety follow-up (ESFU- Month 10)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint presents statistics for the Synflorix + Infanrix hexa Group III and the Pooled Group I + II.

End point values	Synflorix + Infanrix hexa Group III	Pooled Group I + II		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	149	137		
Units: Subjects				
Any SAEs	19	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F greater than or equal to the cut-off

End point title	Number of subjects with concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F greater than or equal to the cut-off

End point description:

The cut-off for the assay was ≥ 0.20 microgram per mililiter (µg/ mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	82	131	
Units: Subjects				
Anti-1 [N=42;82;130]	41	82	129	
Anti-4 [N=41;82;130]	40	81	130	
Anti-5 [N=42;82;129]	42	82	129	
Anti-6B [N=41;82;131]	38	78	123	
Anti-7F [N=41;82;131]	41	82	131	
Anti-9V [N=41;82;132]	40	82	132	
Anti-14 [N=41;82;132]	41	82	132	
Anti-18C [N=41;81;132]	41	81	130	
Anti-19F [N=42;82;132]	42	82	132	
Anti-23F [N=41;82;131]	39	79	125	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F greater than or equal to the cut-off

End point title	Number of subjects with concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F greater than or equal to the cut-off

End point description:

The cut-off for the assay was ≥ 0.05 microgram per mililiter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	82	132	
Units: Subjects				
Anti-1 [N=42;82;130]	42	82	130	
Anti-4 [N=41;82;130]	41	82	130	
Anti-5 [N=42;82;129]	42	82	129	
Anti-6B [N=41;82;131]	40	81	131	
Anti-7F [N=41;82;131]	41	82	131	
Anti-9V [N=41;82;132]	41	82	132	
Anti-14 [N=41;82;132]	41	82	132	
Anti-18C [N=41;81;132]	41	81	131	
Anti-19F [N=42;82;132]	42	82	132	
Anti-23F [N=41;82;131]	39	81	129	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point description:

Seropositivity status, defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	82	132	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [N=42;82;130]	0.97 (0.75 to 1.26)	1.1 (0.93 to 1.3)	1.35 (1.18 to 1.55)	
Anti-4 [N=41;82;130]	1.53 (1.19 to 1.98)	1.88 (1.61 to 2.2)	2.42 (2.13 to 2.74)	
Anti-5 [N=42;82;129]	1.45 (1.13 to 1.86)	1.93 (1.65 to 2.25)	2.31 (2 to 2.66)	

Anti-6B [N=41;82;131]	0.85 (0.61 to 1.19)	1.11 (0.89 to 1.37)	1.18 (1 to 1.39)	
Anti-7F [N=41;82;131]	1.87 (1.47 to 2.39)	2.37 (2.07 to 2.73)	2.69 (2.39 to 3.03)	
Anti-9V [N=41;82;132]	1.43 (1.17 to 1.74)	1.69 (1.44 to 1.99)	2.41 (2.13 to 2.73)	
Anti-14 [N=41;82;132]	3.52 (2.81 to 4.42)	3.28 (2.77 to 3.89)	3.71 (3.21 to 4.3)	
Anti-18C [N=41;81;132]	3.28 (2.51 to 4.29)	4.86 (3.92 to 6.02)	5.22 (4.27 to 6.38)	
Anti-19F [N=42;82;132]	3.6 (2.83 to 4.57)	4.8 (4.15 to 5.55)	4.56 (3.95 to 5.26)	
Anti-23F [N=41;82;131]	1.05 (0.74 to 1.49)	1.33 (1.07 to 1.65)	1.54 (1.28 to 1.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F ≥ the cut-off value

End point title	Number of subjects with opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F ≥ the cut-off value

End point description:

The cut-off for the assay was ≥ 8.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	74	113	
Units: Subjects				
Opsono-1 [N=34;72;110]	20	49	80	
Opsono-4 [N=36;73;111]	36	72	110	
Opsono-5 [N=34;74;109]	29	69	104	
Opsono-6B [N=35;69;104]	30	59	85	
Opsono-7F [N=36;74;113]	36	74	113	
Opsono-9V [N=36;72;103]	36	72	103	
Opsono-14 [N=36;73;112]	36	73	110	
Opsono-18C [N=34;68;102]	34	65	99	
Opsono-19F [N=35;74;110]	31	71	105	
Opsono-23F [N=36;72;109]	35	70	109	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point title	Opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point description:

Seropositivity status, defined as Opsonophagocytic activity against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F ≥ 8.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	74	113	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1 [N=34;72;110]	23 (13 to 40.6)	30.3 (20.5 to 44.8)	46.3 (33.4 to 64.1)	
Opsono-4 [N=36;73;111]	644.1 (474.6 to 874)	500.9 (384.5 to 652.5)	543.5 (450.6 to 655.5)	
Opsono-5 [N=34;74;109]	45.2 (27.7 to 73.8)	70.8 (52.3 to 95.7)	94.8 (75.7 to 118.7)	
Opsono-6B [N=35;69;104]	278.3 (125.5 to 617.3)	305.1 (180.1 to 516.9)	268.2 (167.5 to 429.4)	
Opsono-7F [N=36;74;113]	4086.3 (2834.3 to 5891.3)	3047.3 (2422.2 to 3833.7)	2395.2 (1973.2 to 2907.5)	
Opsono-9V [N=36;72;103]	930.5 (603.1 to 1435.6)	837.9 (642.7 to 1092.3)	1144.8 (922.3 to 1421)	
Opsono-14 [N=36;73;112]	775.4 (539 to 1115.5)	901.6 (699.8 to 1161.6)	644.6 (514.9 to 807)	
Opsono-18C [N=34;68;102]	262.5 (159.4 to 432.4)	321.5 (220.9 to 467.7)	251 (189 to 333.4)	
Opsono-19F [N=35;74;110]	104.2 (61.5 to 176.5)	201.1 (149.7 to 270.1)	182.7 (139.2 to 239.7)	
Opsono-23F [N=36;72;109]	1659.4 (975.1 to 2824)	1147.2 (843 to 1561.2)	1558.8 (1302.6 to 1865.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A ≥ the cut-off value

End point title	Number of subjects with concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A ≥ the cut-off value

End point description:

The cut-off for the assay was ≥ 0.05 microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	81	131	
Units: Subjects				
Anti-6A [N=42;81;129]	32	68	114	
Anti-19A [N=42;81;131]	26	72	120	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A

End point description:

Seropositivity status was defined as anti-pneumococcal cross-reactive serotypes 6A and 19A antibody concentrations ≥ 0.05 microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	81	131	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A [N=42;81;129]	0.14 (0.09 to 0.2)	0.21 (0.15 to 0.28)	0.2 (0.16 to 0.25)	
Anti-19A [N=42;81;131]	0.08 (0.06 to 0.11)	0.21 (0.16 to 0.28)	0.26 (0.21 to 0.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A ≥ the cut-off

End point title	Number of subjects with opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 8.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	69	105	
Units: Subjects				
Opsono-6A [N=33;66;96]	25	54	58	
Opsono-19A [N=31;69;105]	2	10	17	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A

End point title	Opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A

End point description:

Seropositivity status, defined as Opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A ≥ 8.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd dose of the primary vaccination course with 10Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine.

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	69	105	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [N=33;66;96]	114.5 (52.8 to 248.5)	157.3 (95.8 to 258.4)	49.5 (31.8 to 76.9)	
Opsono-19A [N=31;69;105]	4.5 (3.8 to 5.4)	7.1 (4.9 to 10.1)	7 (5.4 to 9.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with concentrations of antibodies against protein D (Anti-PD) ≥ the cut-off

End point title	Number of subjects with concentrations of antibodies against protein D (Anti-PD) ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 100 enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	82	130	
Units: Subjects				
Anti-PD	42	82	130	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (Anti-PD)

End point title	Concentrations of antibodies against protein D (Anti-PD)

End point description:

Seropositivity status was defined as anti-PD antibody concentrations ≥ 100 ELISA units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	82	130	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	1688.6 (1320.1 to 2159.8)	1415.4 (1167.1 to 1716.5)	1496.8 (1283.4 to 1745.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (Anti DT) and anti-tetanus toxoids (Anti TT) antibody concentrations ≥ the cut-off

End point title	Number of subjects with anti-diphtheria (Anti DT) and anti-tetanus toxoids (Anti TT) antibody concentrations ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 0.1 international units per milliliter (IU/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	61	
Units: Subjects				
Anti-diphtheria	18	41	61	
Anti-tetanus	18	41	61	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-diphtheria and tetanus toxoids ≥ the cut-off

End point title	Antibody concentrations for anti-diphtheria and tetanus toxoids ≥ the cut-off

End point description:

Seroprotection status was defined as anti-diphtheria toxoid or anti-tetanus toxoid antibody concentrations ≥ 0.1 IU/mL.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	61	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria	2.495 (1.664 to 3.741)	3.23 (2.628 to 3.969)	3.077 (2.481 to 3.817)	
Anti-tetanus	7.745 (6.284 to 9.545)	8.617 (7.216 to 10.29)	7.695 (6.838 to 8.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration ≥ the cut-off

End point title	Number of subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 0.15 microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	63	
Units: Subjects				
Anti-PRP	18	41	63	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration ≥ the cut-off

End point title	Number of subjects with anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentration ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 1.0 microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	63	
Units: Subjects				
Anti-PRP	16	38	60	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol-phosphate (Anti-PRP) antibody concentrations ≥ the cut-off

End point title	Anti-polyribosyl-ribitol-phosphate (Anti-PRP) antibody concentrations ≥ the cut-off

End point description:

Seroprotection status was defined as anti-PRP antibody concentrations ≥ 0.15 µg/mL and ≥ 1.0 µg/mL.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	63	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	4.031 (2.261 to 7.184)	5.804 (4.12 to 8.178)	7.952 (5.839 to 10.831)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ the cut-off

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 5 ELISA unit per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	61	
Units: Subjects				
Anti-PT [N=18;41;61]	18	41	61	
Anti-FHA [N=18;41;61]	18	41	61	
Anti-PRN [N=17;40;60]	17	40	60	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentration for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Antibody concentration for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point description:

Seropositivity status was defined as anti-PT, anti-FHA, anti-PRN antibody concentrations ≥ 5 EL.U/mL.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	41	61	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=18;41;61]	41.9 (27.6 to 63.7)	37.9 (30.7 to 46.7)	47.3 (40.2 to 55.7)	
Anti-FHA [N=18;41;61]	188.6 (133.4 to 266.6)	169 (139.6 to 204.7)	163.1 (138.3 to 192.3)	
Anti-PRN [N=17;40;60]	127.6 (81.5 to 199.6)	109.1 (85.7 to 139)	119.1 (101.1 to 140.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-Hepatitis B surface antigen (HBs) antibody concentrations ≥ the cut-off

End point title	Number of subjects with anti-Hepatitis B surface antigen (HBs) antibody concentrations ≥ the cut-off

End point description:

The cut-off for the assay was ≥ 10 milli-international units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	26	12	
Units: Subjects				
Anti-HBs	8	26	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (HBs) antibody concentrations

End point title	Anti-hepatitis B surface antigen (HBs) antibody concentrations

End point description:

Seroprotection status was defined as Anti-HBs antibody concentrations ≥ 10 mIU/mL.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	26	12	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	431.9 (240.7 to 775.2)	356 (221.1 to 573.4)	462.9 (221.1 to 969.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polio type 1, 2 and 3 antibody titres

End point title	Number of subjects with anti-polio type 1, 2 and 3 antibody titres

End point description:

The cut-off for the assay was ≥ 8.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	22	29	
Units: Subjects				
Anti-Polio 1 [N= 12;22;29]	12	22	29	
Anti-Polio 2 [N= 12;22;29]	12	22	29	
Anti-Polio 3 [N= 11;21;29]	10	21	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for polio type 1, 2 and 3 ≥ the cut-off

End point title	Antibody titers for polio type 1, 2 and 3 ≥ the cut-off

End point description:

Seroprotection status, defined as Anti-polio type 1, Anti-polio type 2 and Anti-polio type 3 antibody titers ≥ 8.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	22	29	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 [N= 12;22;29]	271.3 (132.9 to 554)	189.5 (109.9 to 326.8)	230.1 (166 to 319)	
Anti-Polio 2 [N= 12;22;29]	341.7 (214 to 545.6)	319 (172.5 to 589.8)	194.4 (121.7 to 310.7)	
Anti-Polio 3 [N= 11;21;29]	248.4 (67.9 to 908.7)	344.7 (192.2 to 618.3)	384.8 (245.3 to 603.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response to anti-pertussis toxoid, anti-filamentous haemagglutinin and anti-pertactin

End point title	Number of subjects with vaccine response to anti-pertussis toxoid, anti-filamentous haemagglutinin and anti-pertactin

End point description:

Vaccine response to PT, FHA and PRN was defined as appearance of antibodies in subjects who were initially seronegative (S-), or at least maintenance of pre-vaccination antibody concentrations in those who were initially seropositive (S+). For the Synflorix + Infanrix hexa Group I, no subjects presented initial seropositivity for PT and PRN antigens.

End point type	Secondary

End point timeframe:

One month after the 3rd vaccine dose (Month 5)

End point values	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II	Synflorix + Infanrix hexa Group III	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	27	45	
Units: Subjects				
Anti-PT, S- [N=18;27;45]	18	27	45	
Anti-PT, S+ [N=0;10;13]	0	8	12	
Anti-FHA, S- [N=15;22;18]	15	22	18	
Anti-FHA, S+ [N=3;17;41]	3	17	41	
Anti-PRN, S- [N= 17;34;45]	17	34	45	
Anti-PRN, S+ [N=0;4;12]	0	4	12	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Solicited local and general symptoms: during the 4-day post vaccination; Unsolicited AEs: during the 31-day post vaccination; SAEs:during the whole study period (Month 0 - Month 10, including the 5 months extended safety follow-up).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	Synflorix + Infanrix hexa Group III
Reporting group description: Infants born after a full-term gestation period of more than 36 weeks (more than 258 days)	
Reporting group title	Synflorix + Infanrix hexa Group I
Reporting group description: Very preterm infants born after a gestation period of 27-30 weeks (189-216 days)	
Reporting group title	Synflorix + Infanrix hexa Group II
Reporting group description: Mild preterm infants born after a gestation period of 31-36 weeks (217-258 days)	

Serious adverse events	Synflorix + Infanrix hexa Group III	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 149 (12.75%)	17 / 50 (34.00%)	11 / 87 (12.64%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Skull fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural hygroma			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 149 (1.34%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocythaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tympanic membrane perforation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia, obstructive			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachypnoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Breath holding			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Vesicoureteric reflux			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	3 / 149 (2.01%)	4 / 50 (8.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 149 (2.01%)	3 / 50 (6.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 149 (1.34%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 149 (0.67%)	2 / 50 (4.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	2 / 149 (1.34%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 149 (1.34%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 149 (0.00%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 149 (0.00%)	0 / 50 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	1 / 50 (2.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 149 (0.67%)	0 / 50 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Synflorix + Infanrix hexa Group III	Synflorix + Infanrix hexa Group I	Synflorix + Infanrix hexa Group II
Total subjects affected by non-serious adverse events			
subjects affected / exposed	136 / 149 (91.28%)	42 / 50 (84.00%)	76 / 87 (87.36%)
General disorders and administration site conditions			
Injection site nodule			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 149 (6.71%)	0 / 50 (0.00%)	4 / 87 (4.60%)
occurrences (all)	14	0	4
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	71 / 149 (47.65%)	22 / 50 (44.00%)	45 / 87 (51.72%)
occurrences (all)	106	29	70
Pain			
subjects affected / exposed	84 / 149 (56.38%)	24 / 50 (48.00%)	41 / 87 (47.13%)
occurrences (all)	139	34	75
Erythema			

subjects affected / exposed	102 / 149 (68.46%)	24 / 50 (48.00%)	49 / 87 (56.32%)
occurrences (all)	205	32	81
Swelling			
alternative assessment type: Non-systematic			
subjects affected / exposed	98 / 149 (65.77%)	20 / 50 (40.00%)	35 / 87 (40.23%)
occurrences (all)	185	27	57
Somnolence			
subjects affected / exposed	65 / 149 (43.62%)	20 / 50 (40.00%)	44 / 87 (50.57%)
occurrences (all)	109	30	64
Irritability			
subjects affected / exposed	100 / 149 (67.11%)	22 / 50 (44.00%)	53 / 87 (60.92%)
occurrences (all)	171	38	106
Decreased appetite			
subjects affected / exposed	51 / 149 (34.23%)	19 / 50 (38.00%)	46 / 87 (52.87%)
occurrences (all)	81	30	64
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 149 (6.71%)	1 / 50 (2.00%)	9 / 87 (10.34%)
occurrences (all)	12	1	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported