Clinical trial results:
An open, randomized, phase IIIa study to evaluate the safety and immunogenicity of GlaxoSmithKline Biologicals' 10-valent pneumococcal conjugate vaccine, when administered intramuscularly according to a 2-4-11 months vaccination schedule.

Summary

EudraCT number	2005-003437-41
Trial protocol	SE DK SK
Global end of trial date	25 January 2007

Results information

Result version number	v3 (current)
This version publication date	13 April 2023
First version publication date	14 March 2015
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	105539

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00307034
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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 June 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 January 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the post-dose 2 immune response elicited by GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered according to a 2-4-11 months vaccination schedule with co-administration of DTPa combined vaccine.

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/products 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	05 January 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 75
Country: Number of subjects enrolled	Sweden: 61
Country: Number of subjects enrolled	Denmark: 130
Country: Number of subjects enrolled	Norway: 85
Worldwide total number of subjects	351
EEA total number of subjects	351

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)	351
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: -

Pre-assignment period milestones

Number of subjects started	351
Number of subjects completed	351

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix I Group

Arm description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib), according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' 10-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 primary doses of 10Pn-PD-DiT vaccine were administered at 2 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 3rd dose of 10Pn-PD-DiT (i.e. booster dose) was administered at 11 months of age.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib, DTPa combined vaccine
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of DTPa combined vaccine were administered at 2 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine was administered at 11 months of age.

Investigational medicinal product name	Infanrix-IPV/Hib
Investigational medicinal product code	
Other name	DTPa-IPV/Hib, DTPa combined vaccine
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of DTPa combined vaccine were administered at 2 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine was administered at 11 months of age.

Arm title	Synflorix II Group

Arm description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib) at 2 and 4 months of age, followed by a booster dose of the Synflorix vaccine at 11 months of age, co-administered with one dose of the Infanrix combined vaccine, according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Arm type	Comparator
Investigational medicinal product name	GSK Biologicals' 10-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 primary doses of 10Pn-PD-DiT vaccine and 3 doses of DTPa combined vaccine were co-administered at 2, 3 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 4th dose of 10Pn-PD-DiT (i.e. booster dose) was co-administered with a 3rd dose of DTPa combined vaccine at 11 months of age.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib, DTPa combined vaccine
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of DTPa combined vaccine were administered at 2 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine was administered at 11 months of age.

Investigational medicinal product name	Infanrix-IPV/Hib
Investigational medicinal product code	
Other name	DTPa-IPV/Hib, DTPa combined vaccine
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of DTPa combined vaccine were administered at 2 and 4 months of age, with first vaccine dose administered at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine was administered at 11 months of age.

Number of subjects in period 1	Synflorix I Group	Synflorix II Group
Started	175	176
Completed	173	169
Not completed	2	7
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	2

Lost to follow-up	-	3

Baseline characteristics

Reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib), according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib) at 2 and 4 months of age, followed by a booster dose of the Synflorix vaccine at 11 months of age, co-administered with one dose of the Infanrix combined vaccine, according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Reporting group values	Synflorix I Group	Synflorix II Group	Total
Number of subjects	175	176	351
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: weeks			
arithmetic mean	12	12.1	
standard deviation	± 1.94	± 1.9	-
Gender categorical Units: Subjects			
Female	86	82	168
Male	89	94	183

End points

End points reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib), according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib) at 2 and 4 months of age, followed by a booster dose of the Synflorix vaccine at 11 months of age, co-administered with one dose of the Infanrix combined vaccine, according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Primary: Number of Seroprotected Subjects Against Pneumococcal Serotypes

End point title	Number of Seroprotected Subjects Against Pneumococcal Serotypes[1]

End point description:

A seroprotected subject was defined as a subject who had anti-pneumococcal serotypes antibody concentrations greater than or equal to (≥) the threshold value of 0.20 micrograms per milliliter (µg/mL). The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs). The results presented for the Group 1 correspond to the primary outcome.

End point type	Primary

End point timeframe:

One month post-dose 2 (Month 3) administration of Synflorix vaccine

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	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	153		
Units: Subjects				
Anti-1 (N= 153, 151)	149	149		
Anti-4 (N=153, 153)	150	152		
Anti-5 (N=152, 149)	146	149		
Anti-6B (N=149, 149)	83	94		
Anti-7F (N=153, 152)	148	151		
Anti-9V (N=152, 153)	142	152		
Anti-14 (N=152, 152)	146	152		
Anti-18C (N=152, 153)	146	152		

Anti-19F (N=152, 152)	141	146		
Anti-23F (N=153, 152)	106	118		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Seroprotected Subjects Against Pneumococcal Serotypes

End point title	Number of Seroprotected Subjects Against Pneumococcal Serotypes

End point description:

A seroprotected subject was defined as a subject who had anti-pneumococcal serotypes antibody concentrations greater than or equal to (≥) the threshold value of 0.20 micrograms per milliliter (µg/mL). The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs).

End point type	Secondary

End point timeframe:

One month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	149		
Units: Subjects				
Anti-1 at Month 9 (N= 149, 147)	77	101		
Anti-1 at Month 10 (N=156, 147)	155	147		
Anti-4 at Month 9 (N= 152, 149)	120	137		
Anti-4 at Month 10 (N=155, 147)	155	147		
Anti-5 at Month 9 (N= 148, 149)	121	133		
Anti-5 at Month 10 (N=155, 147)	155	147		
Anti-6B at Month 9 (N= 154, 148)	101	111		
Anti-6B at Month 10 (N=156, 147)	138	142		
Anti-7F at Month 9 (N= 151, 149)	135	146		
Anti-7F at Month 10 (N=156, 147)	156	147		
Anti-9V at Month 9 (N= 153, 149)	133	142		
Anti-9V at Month 10 (N=156, 147)	155	147		
Anti-14 at Month 9 (N= 151, 149)	140	147		
Anti-14 at Month 10 (N=156, 147)	155	145		
Anti-18C at Month 9 (N= 154, 149)	133	144		
Anti-18C at Month 10 (N=156, 147)	156	146		
Anti-19F at Month 9 (N= 153, 149)	140	143		
Anti-19F at Month 10 (N=156, 147)	150	144		
Anti-23F at Month 9 (N= 151, 148)	108	116		
Anti-23F at Month 10 (N=154, 147)	148	141		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Pneumococcal Serotypes

End point title	Antibody Concentrations Against Pneumococcal Serotypes

End point description:

The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 or post-dose 3 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	153		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 at Month 3 (N= 153, 151)	1.03 (0.9 to 1.18)	1.23 (1.07 to 1.42)		
Anti-1 at Month 9 (N= 149, 147)	0.21 (0.19 to 0.24)	0.3 (0.26 to 0.34)		
Anti-1 at Month 10 (N=156, 147)	1.85 (1.59 to 2.15)	1.88 (1.62 to 2.17)		
Anti-4 at Month 3 (N= 153, 153)	1.37 (1.21 to 1.55)	1.71 (1.47 to 1.99)		
Anti-4 at Month 9 (N= 152, 149)	0.4 (0.35 to 0.46)	0.64 (0.56 to 0.73)		
Anti-4 at Month 10 (N=155, 147)	3.06 (2.68 to 3.49)	3.47 (3.03 to 3.98)		
Anti-5 at Month 3 (N= 152, 149)	1.32 (1.14 to 1.52)	1.85 (1.63 to 2.1)		
Anti-5 at Month 9 (N= 148, 149)	0.43 (0.37 to 0.5)	0.59 (0.51 to 0.68)		
Anti-5 at Month 10 (N=155, 147)	2.65 (2.31 to 3.03)	3.21 (2.81 to 3.67)		
Anti-6B at Month 3 (N= 149, 149)	0.19 (0.15 to 0.24)	0.31 (0.25 to 0.38)		
Anti-6B at Month 9 (N= 154, 148)	0.28 (0.23 to 0.35)	0.44 (0.36 to 0.54)		
Anti-6B at Month 10 (N=156, 147)	1.12 (0.88 to 1.41)	1.85 (1.54 to 2.22)		

Anti-7F at Month 3 (N= 153, 152)	1.28 (1.13 to 1.46)	2.14 (1.9 to 2.4)		
Anti-7F at Month 9 (N= 151, 149)	0.55 (0.49 to 0.63)	0.92 (0.81 to 1.05)		
Anti-7F at Month 10 (N=156, 147)	2.81 (2.51 to 3.15)	3.88 (3.45 to 4.37)		
Anti-9V at Month 3 (N= 152, 153)	0.92 (0.81 to 1.05)	1.47 (1.29 to 1.68)		
Anti-9V at Month 9 (N= 153, 149)	0.52 (0.46 to 0.6)	0.87 (0.77 to 0.99)		
Anti-9V at Month 10 (N=156, 147)	2.95 (2.59 to 3.37)	3.97 (3.49 to 4.5)		
Anti-14 at Month 3 (N= 152, 152)	1.72 (1.45 to 2.05)	2.57 (2.22 to 2.97)		
Anti-14 at Month 9 (N= 151, 149)	0.77 (0.64 to 0.93)	1.53 (1.27 to 1.85)		
Anti-14 at Month 10 (N=156, 147)	4.19 (3.62 to 4.85)	5.47 (4.68 to 6.4)		
Anti-18C at Month 3 (N= 152, 153)	1.26 (1.06 to 1.51)	3.42 (2.87 to 4.07)		
Anti-18C at Month 9 (N= 154, 149)	0.59 (0.5 to 0.69)	1.14 (0.96 to 1.35)		
Anti-18C at Month 10 (N=156, 147)	6.24 (5.43 to 7.18)	7.2 (6.08 to 8.52)		
Anti-19F at Month 3 (N= 152, 152)	2.43 (1.97 to 2.98)	4.43 (3.6 to 5.45)		
Anti-19F at Month 9 (N= 153, 149)	1.04 (0.87 to 1.25)	1.7 (1.41 to 2.04)		
Anti-19F at Month 10 (N=156, 147)	5.58 (4.65 to 6.69)	6.95 (5.92 to 8.17)		
Anti-23F at Month 3 (N= 153, 152)	0.38 (0.3 to 0.47)	0.52 (0.42 to 0.63)		
Anti-23F at Month 9 (N= 151, 148)	0.32 (0.26 to 0.4)	0.44 (0.36 to 0.54)		
Anti-23F at Month 10 (N=154, 147)	2.41 (1.98 to 2.94)	2.78 (2.31 to 3.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Activity Against Vaccine Pneumococcal Serotypes

End point title	Opsonophagocytic Activity Against Vaccine Pneumococcal Serotypes

End point description:

Seropositivity status was defined as the opsonophacocytic activity against pneumococcal serotypes greater than or equal to (≥) the value of 8. The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 or post-dose 3 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	135		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1 at Month 3 (N= 130, 132)	21.9 (16.4 to 29.1)	26.5 (19.8 to 35.4)		
Opsono-1 at Month 9 (N= 136, 134)	5.1 (4.5 to 5.8)	6.7 (5.4 to 8.3)		
Opsono-1 at Month 10 (N=131, 126)	109.9 (76.1 to 158.7)	100.6 (68.9 to 146.9)		
Opsono-4 at Month 3 (N= 134, 132)	462.6 (410.4 to 521.4)	758.9 (647.8 to 888.9)		
Opsono-4 at Month 9 (N= 104, 114)	13.8 (9.7 to 19.6)	18.6 (12.7 to 27.2)		
Opsono-4 at Month 10 (N=125, 101)	634.6 (496.3 to 811.3)	1204 (990.7 to 1463.2)		
Opsono-5 at Month 3 (N= 132, 130)	48.3 (37.7 to 61.8)	68.4 (54 to 86.5)		
Opsono-5 at Month 9 (N= 133, 135)	9.9 (8.1 to 12)	10.7 (8.6 to 13.4)		
Opsono-5 at Month 10 (N=133, 121)	102.1 (75.8 to 137.6)	157.2 (123.1 to 200.7)		
Opsono-6B at Month 3 (N= 125, 126)	157.8 (104.7 to 237.8)	379.6 (272.4 to 529.1)		
Opsono-6B at Month 9 (N= 121, 124)	56.1 (34.9 to 90.4)	62.9 (40.2 to 98.5)		
Opsono-6B at Month 10 (N=132, 103)	220.3 (146.9 to 330.3)	468.5 (311.6 to 704.3)		
Opsono-7F at Month 3 (N= 127, 131)	844.8 (591.4 to 1206.7)	2176.5 (1759.2 to 2692.7)		
Opsono-7F at Month 9 (N= 113, 126)	148.5 (89.5 to 246.4)	380.6 (253 to 572.6)		
Opsono-7F at Month 10 (N=128, 109)	1843.4 (1494.2 to 2274.1)	3290.6 (2709.1 to 3996.8)		
Opsono-9V at Month 3 (N= 134, 132)	875.1 (732 to 1046.1)	1343.4 (1130.8 to 1596)		
Opsono-9V at Month 9 (N= 120, 134)	266.8 (205.1 to 347.1)	322.2 (256.4 to 405.1)		
Opsono-9V at Month 10 (N=129, 109)	1068.1 (874.7 to 1304.2)	1706.9 (1438.5 to 2025.3)		
Opsono-14 at Month 3 (N= 132, 131)	692.6 (559.1 to 858)	1125.3 (946.2 to 1338.3)		
Opsono-14 at Month 9 (N= 102, 123)	52.1 (32.4 to 84)	157.3 (108.5 to 228.1)		
Opsono-14 at Month 10 (N=107, 101)	835.5 (672.1 to 1038.5)	1280.7 (1054.5 to 1555.5)		
Opsono-18C at Month 3 (N= 134, 131)	56.2 (42.9 to 73.7)	218.6 (176.1 to 271.4)		
Opsono-18C at Month 9 (N= 122, 126)	8.3 (6.5 to 10.7)	16.9 (12.5 to 22.8)		
Opsono-18C at Month 10 (N=136, 130)	330 (259.1 to 420.3)	490.8 (395.3 to 609.4)		
Opsono-19F at Month 3 (N= 131, 128)	101 (74.9 to 136)	356.7 (263.2 to 483.4)		

Opsono-19F at Month 9 (N= 130, 134)	16.5 (12.9 to 21.1)	31.6 (24.5 to 40.8)		
Opsono-19F at Month 10 (N=131, 129)	251.3 (193.4 to 326.6)	734.7 (568.3 to 949.8)		
Opsono-23F at Month 3 (N= 131, 129)	489.7 (342.6 to 700)	1233.7 (991.7 to 1534.7)		
Opsono-23F at Month 9 (N= 112, 133)	190.7 (115.2 to 315.6)	150.7 (95.9 to 236.8)		
Opsono-23F at Month 10 (N=134, 121)	1047.3 (748.1 to 1466.3)	1528.9 (1171.2 to 1996)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Protein D (Anti-PD)

End point title	Antibody Concentrations Against Protein D (Anti-PD)

End point description:

Anti-protein D concentrations are expressed as geometric mean concentrations (GMCs), in enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). Seropositivity status was defined as Anti-PD antibody concentrations greater than or equal to (≥) the value of 100 EL.U/mL. This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 or post-dose 3 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	148		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD at Month 3 (N=149, 148)	861.8 (740.4 to 1003.1)	1223.3 (1066.5 to 1403.2)		
Anti-PD at Month 9 (N= 151, 148)	349.7 (294.2 to 415.7)	499.8 (425.3 to 587.2)		
Anti-PD at Month 10 (N= 154, 146)	1629.8 (1346.4 to 1972.8)	2113 (1808.9 to 2468.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Diphteria (Anti-D) and Tetanus (Anti-

T) Toxoids

End point title	Antibody Concentrations Against Diphteria (Anti-D) and Tetanus (Anti-T) Toxoids

End point description:

Concentrations of antibodies are presented as geometric mean concentrations, expressed as international units per milliliter (IU/mL). Seroprotection status was defined as anti-diphteria and anti-tetanus toxoid antibody concentrations greater than or equal to (≥) the value of 0.1 IU/mL. This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	151		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D at Month 3 (N=154, 151)	1.791 (1.503 to 2.133)	3.123 (2.621 to 3.723)		
Anti-D at Month 9 (N= 154, 148)	0.326 (0.275 to 0.386)	0.725 (0.622 to 0.846)		
Anti-D at Month 10 (N= 156, 148)	5.423 (4.815 to 6.108)	8.262 (7.339 to 9.301)		
Anti-T at Month 3 (N=154, 151)	2.504 (2.17 to 2.89)	4.602 (4.062 to 5.213)		
Anti-T at Month 9 (N= 153, 149)	0.565 (0.487 to 0.656)	1.191 (1.055 to 1.344)		
Anti-T at Month 10 (N= 156, 148)	7.678 (6.997 to 8.425)	9.597 (8.749 to 10.526)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Polyribosyl Ribitol Phosphate (Anti-PRP)

End point title	Antibody Concentrations Against Polyribosyl Ribitol Phosphate (Anti-PRP)

End point description:

Concentrations of antibodies are presented as geometric mean concentrations, expressed as micrograms per milliliter (µg/mL). Seroprotection status was defined as anti-polyribosyl ribitol phosphate (Anti-PRP) antibody concentrations greater than or equal to (≥) the cut-off values of 0.15 µg/mL and ≥ 1.0 µg/mL. This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 (Month 3) administration, one month before (Month 9) and one month after (Month 10) booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	148		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP at Month 3 (N=146, 147)	1.179 (0.893 to 1.556)	2.186 (1.648 to 2.9)		
Anti-PRP at Month 9 (N= 150, 148)	0.431 (0.349 to 0.532)	0.777 (0.613 to 0.984)		
Anti-PRP at Month 10 (N= 155, 147)	16.943 (13.485 to 21.287)	21.654 (17.263 to 27.161)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Pertussis Toxoid (Anti-PT), Filamentous Haemagglutinin (Anti-FHA) and Pertactin (Anti-PRN)

End point title	Antibody Concentrations Against Pertussis Toxoid (Anti-PT), Filamentous Haemagglutinin (Anti-FHA) and Pertactin (Anti-PRN)

End point description:

Concentrations of antibodies are presented as geometric mean concentrations, expressed as enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). Seropositivity status was defined as anti-pertussis toxoid (Anti-PT), anti-filamentous haemagglutinin (Anti-FHA) and anti-pertactin (Anti-PRN) antibody concentrations greater than or equal to (≥) the cut-off value of 5 EL.U/mL. This outcome concerns results for the Primary and Booster Phases of the study.

End point type	Secondary

End point timeframe:

One month post-dose 2 (Month 3) administration, one month before (Month 9) and after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	147		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT at Month 3 (N=145, 144)	36.1 (32.9 to 39.6)	33.8 (30.2 to 37.9)		
Anti-PT at Month 9 (N= 144, 145)	9.8 (8.7 to 11.1)	10.2 (8.9 to 11.7)		
Anti-PT at Month 10 (N= 149, 145)	78.2 (70.5 to 86.8)	65.5 (58.7 to 73.1)		

Anti-FHA at Month 3 (N=145, 144)	166.7 (150.1 to 185.2)	142.2 (125.6 to 161.1)		
Anti-FHA at Month 9 (N= 144, 145)	46.6 (41.3 to 52.6)	46.9 (41.1 to 53.6)		
Anti-FHA at Month 10 (N= 149, 144)	360.3 (323.7 to 401)	276.6 (249.4 to 306.7)		
Anti-PRN at Month 3 (N=145, 144)	83.9 (69.6 to 101.1)	89 (74.1 to 106.8)		
Anti-PRN at Month 9 (N= 144, 145)	13.7 (11.2 to 16.6)	18 (14.8 to 21.8)		
Anti-PRN at Month 10 (N= 150, 147)	275.5 (235.9 to 321.7)	209.3 (181.8 to 241)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against Hepatitis B Surface Antigen (Anti-HBs)

End point title	Antibody Concentrations Against Hepatitis B Surface Antigen (Anti-HBs)

End point description:

Concentrations of antibodies are presented as geometric mean concentrations, expressed as milli international units per milliliter (mIU/mL). Seroprotection status was defined as anti-hepatitis B surface antigen (anti-HBs) antibody concentrations greater than or equal to (≥) the cut-off value of 10 mIU/mL. This outcome concerns results for the Primary and Booster Phases of the study and included only the subset of subjects who received Infanrix Hexa as the co-administered vaccine.

End point type	Secondary

End point timeframe:

One month post-dose 2 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	46		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs at Month 3 (N=37, 38)	293.7 (195.9 to 440.5)	478.6 (294.8 to 776.9)		
Anti-HBs at Month 9 (N= 40, 46)	84.3 (55.4 to 128.2)	156.6 (106.4 to 230.4)		
Anti-HBs at Month 10 (N= 27, 28)	1892.3 (1012.2 to 3537.6)	2922.4 (2010.4 to 4248.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Titers Against Polio Type 1, 2 and 3 (Anti-polio 1, 2 and 3)

End point title	Antibody Titers Against Polio Type 1, 2 and 3 (Anti-polio 1, 2 and 3)

End point description:

Titers of antibodies are presented as geometric mean titers. Seroprotection status was defined as anti-polio types 1, 2 and 3 (Anti-polio 1, 2 and 3) antibody titers greater than or equal to (≥) the value of 8. This outcome concerns results for the Primary and Booster Phases of the study and included only the subset of subjects who received Infanrix Hexa as the co-administered vaccine.

End point type	Secondary

End point timeframe:

One month post-dose 2 (Month 3) administration, one month before (Month 9) and one month after (Month 10) the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	59		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-Polio 1 at Month 3 (N=47, 57)	88.5 (56.3 to 139.1)	99.1 (63.4 to 154.8)		
Anti-Polio 1 at Month 9 (N=45,39)	24.6 (15.6 to 38.8)	14.4 (8.9 to 23.1)		
Anti-Polio 1 at Month 10 (N=20,15)	1006.4 (541.8 to 1869.4)	645 (399.4 to 1041.7)		
Anti-Polio 2 at Month 3 (N=47,59)	57.7 (36.8 to 90.6)	40.5 (25 to 65.6)		
Anti-Polio 2 at Month 9 (N=44,40)	14.9 (10.7 to 20.9)	10.9 (7.2 to 16.4)		
Anti-Polio 2 at Month 10 (N=17,14)	522.4 (235.7 to 1157.7)	512.2 (186.4 to 1407.7)		
Anti-Polio 3 at Month 3 (N=50,57)	165.6 (109.3 to 250.8)	161 (98.7 to 262.8)		
Anti-Polio 3 at Month 9 (N=44,38)	15.1 (9.8 to 23.2)	14.7 (9 to 24.1)		
Anti-Polio 3 at Month 10 (N=5,11)	1910.8 (257.4 to 14185.3)	961.4 (388.3 to 2380.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster vaccine response to Anti-PT, Anti-FHA and Anti-PRN antibody

End point title	Number of subjects with booster vaccine response to Anti-PT, Anti-FHA and Anti-PRN antibody

End point description:

Booster vaccine response to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN), defined as the appearance of antibodies in subjects who were seronegative (Pre-booster status S-) (i.e., with antibody concentrations < 5 EL.U/mL) just before booster dose, and at least two-fold increase of pre-vaccination antibody concentrations in those who were seropositive (Pre-booster status S+) (i.e., with antibody concentrations ≥ 5 EL.U/mL) just before booster dose.

End point type	Secondary

End point timeframe:

One month after (Month 9) the administration of the booster dose of Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	142		
Units: Subjects				
Anti-PT-Pre-booster status S-(N=20,23)	20	23		
Anti-PT-Pre-booster status S+(N=117,117)	115	114		
Anti-PT-Pre-booster status Total(N=137,140)	135	137		
Anti-FHA-Pre-booster status S-(N=0,1)	0	1		
Anti-FHA-Pre-booster status S+(N=137,138)	132	129		
Anti-FHA-Pre-booster status Total(N=137,139)	132	130		
Anti-PRN-Pre-booster status S-(N=35,21)	35	21		
Anti-PRN-Pre-booster status S+(N=102,121)	101	119		
Anti-PRN-Pre-booster status Total(N=137,142)	136	140		

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

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm).
Across doses= across the 2 doses of the Synflorix vaccine in the Synflorix I Group and across the 3 doses of the Synflorix vaccine in the Synflorix II Group.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) period following the primary vaccination (across doses) and during the 4-day (Days 0-3) period following the booster vaccination (post Bst) with the Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	176		
Units: Subjects				
Any Pain, across doses (N=175;176)	92	110		
Grade 3 Pain, across doses (N=175;176)	14	12		
Any Redness, across doses (N=175;176)	137	135		
Grade 3 Redness, across doses (N=175;176)	4	6		
Any Swelling, across doses (N=175;176)	111	105		
Grade 3 Swelling, across doses (N=175;176)	20	16		
Any Pain, post Bst (N=174,169)	103	93		
Grade 3 Pain, post Bst (N=174,169)	7	5		
Any Redness, post Bst (N=174,169)	118	115		
Grade 3 Redness, post Bst (N=174,169)	20	20		
Any Swelling, post Bst (N=174,169)	97	99		
Grade 3 Swelling, post Bst (N=174,169)	19	15		

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 (Irr./Fuss.), loss of appetite (Loss Appet.) and fever (rectal temperature higher than [≥] 38.0 degrees Celsius [°C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity or relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Rectal temperature higher than (>) 40.0°C. Across doses= across the 2 doses of the Synflorix vaccine in the Synflorix I group and across the 3 doses of the Synflorix vaccine in the Synflorix II group.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) period following the primary vaccination (across doses) and during the 4-day (Days 0-3) period following the booster vaccination (post Bst) with the Synflorix vaccine

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	176		
Units: Subjects				
Any Drowsiness, across doses (N=175;176)	130	130		

Grade 3 Drowsiness, across doses (N=175,176)	9	4		
Related Drowsiness, across doses (N=175,176)	123	124		
Any Fever, across doses (N=175,176)	108	116		
Grade 3 Fever, across doses (N=175,176)	0	0		
Related Fever, across doses (N=175,176)	106	108		
Any Irr./Fuss., across doses (N=175,176)	149	158		
Grade 3 Irr./Fuss., across doses (N=175,176)	18	28		
Related Irr./Fuss., across doses (N=175,176)	142	147		
Any Loss Appet., across doses (N=175,176)	81	88		
Grade 3 Loss Appet., across doses (N=175,176)	5	1		
Related Loss Appet., across doses (N=175,176)	75	81		
Any Drowsiness, post Bst (N=174,169)	97	79		
Grade 3 Drowsiness, post Bst (N=174,169)	6	2		
Related Drowsiness, post Bst (N=174,169)	83	71		
Any Fever, post Bst (N=174,169)	96	78		
Grade 3 Fever, post Bst (N=174,169)	1	0		
Related Fever, post Bst (N=174,169)	84	67		
Any Irr./Fuss., post Bst (N=174,169)	113	104		
Grade 3 Irr./Fuss., post Bst (N=174,169)	6	2		
Related Irr./Fuss., post Bst (N=174,169)	99	89		
Any Loss Appet., post Bst (N=174,169)	61	56		
Grade 3 Loss Appet., post Bst (N=174,169)	3	0		
Related Loss Appet., post Bst (N=174,169)	53	43		

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 was defined as 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For the marketed products administered in the study, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse of the product. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) post-primary vaccination period, across doses

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	176		
Units: Subjects				
Any AE	78	114		

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 was defined as 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For the marketed products administered in the study, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse of the product. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) post booster vaccination period

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	171		
Units: Subjects				
Any AE	63	72		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events

End point title	Number of Subjects With Serious Adverse Events

End point description:

A SAE was defined as any medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject. AE(s)

considered as SAE(s) also included invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation, as per the medical or scientific judgement of the physician. Any = Occurrence of a SAE, regardless of relationship to vaccination.

End point type	Secondary

End point timeframe:

During the primary vaccination period

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	176		
Units: Subjects				
Any SAE	5	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events

End point title	Number of Subjects With Serious Adverse Events

End point description:

A SAE was defined as any medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject. AE(s) considered as SAE(s) also included invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation, as per the medical or scientific judgement of the physician. Any = Occurrence of a SAE, regardless of relationship to vaccination.

End point type	Secondary

End point timeframe:

During the booster vaccination period

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	171		
Units: Subjects				
Any SAE	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4 days post-primary vaccination (across doses) and post-booster dose. Unsolicited AEs: during 31 days post-primary vaccination (across doses) and post-booster dose. SAEs: during both primary and booster vaccination periods.

Adverse event reporting additional description:

Analysis of AEs and SAEs was done on subjects with at least 1 primary vaccination dose. Analysis of solicited symptoms was done on subjects with at least 1 primary dose and with results available. Occurrences (all and "related to the treatment") were not calculated during the analysis and are filled in with "subjects affected" similar information.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix Hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib), according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix (10Pn-PD-DiT) vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix Hexa (DTPa-HBV-IPV/Hib) or Infanrix-IPV/Hib (DTPa-IPV/Hib) at 2 and 4 months of age, followed by a booster dose of the Synflorix vaccine at 11 months of age, co-administered with one dose of the Infanrix combined vaccine, according to national recommendations. Synflorix vaccine was administered intramuscularly into the right anterolateral thigh and Infanrix combined vaccine was administered intramuscularly into the left anterolateral thigh.

Serious adverse events	Synflorix I Group	Synflorix II Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 175 (2.86%)	7 / 176 (3.98%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile convulsion	Additional description: Reported during Booster phase		
subjects affected / exposed[1]	1 / 174 (0.57%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Dyspepsia	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic	Additional description: Reported during Primary phase		
subjects affected / exposed	1 / 175 (0.57%)	0 / 176 (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			
Respiratory syncytial virus infection	Additional description: Reported during Primary phase		
subjects affected / exposed	1 / 175 (0.57%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral	Additional description: Reported during Primary phase		
subjects affected / exposed	1 / 175 (0.57%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection	Additional description: Reported during Primary phase		

subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis	Additional description: Reported during Primary phase		
subjects affected / exposed	1 / 175 (0.57%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection (Primary phase)	Additional description: Reported during Primary phase		
subjects affected / exposed	0 / 175 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection	Additional description: Reported during Primary phase		
subjects affected / exposed	1 / 175 (0.57%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media	Additional description: Reported during Booster phase		
subjects affected / exposed[2]	0 / 174 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: Reported during Booster phase		
subjects affected / exposed[3]	1 / 174 (0.57%)	0 / 171 (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 (Booster phase)	Additional description: Reported during Booster phase		
subjects affected / exposed[4]	1 / 174 (0.57%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

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

Non-serious adverse events	Synflorix I Group	Synflorix II Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 175 (98.86%)	175 / 176 (99.43%)	
General disorders and administration site conditions			
Pain (Primary phase)			
subjects affected / exposed	92 / 175 (52.57%)	110 / 176 (62.50%)	
occurrences (all)	92	110	
Redness (Primary phase)			
subjects affected / exposed	137 / 175 (78.29%)	135 / 176 (76.70%)	
occurrences (all)	137	135	
Swelling (Primary phase)			
subjects affected / exposed	111 / 175 (63.43%)	105 / 176 (59.66%)	
occurrences (all)	111	105	
Pain (Booster phase)			
subjects affected / exposed[5]	103 / 174 (59.20%)	93 / 169 (55.03%)	
occurrences (all)	103	93	
Redness (Booster phase)			
subjects affected / exposed[6]	118 / 174 (67.82%)	115 / 169 (68.05%)	
occurrences (all)	118	115	
Swelling (Booster phase)			
subjects affected / exposed[7]	97 / 174 (55.75%)	99 / 169 (58.58%)	
occurrences (all)	97	99	
Drowsiness (Primary phase)			
subjects affected / exposed	130 / 175 (74.29%)	130 / 176 (73.86%)	
occurrences (all)	130	130	
Fever - rectal (Primary phase)			

subjects affected / exposed	108 / 175 (61.71%)	116 / 176 (65.91%)	
occurrences (all)	108	116	
Irritability (Primary phase)			
subjects affected / exposed	149 / 175 (85.14%)	158 / 176 (89.77%)	
occurrences (all)	149	158	
Loss of appetite (Primary phase)			
subjects affected / exposed	81 / 175 (46.29%)	88 / 176 (50.00%)	
occurrences (all)	81	88	
Drowsiness (Booster phase)			
subjects affected / exposed[8]	97 / 174 (55.75%)	79 / 169 (46.75%)	
occurrences (all)	97	79	
Fever - rectal (Booster phase)			
subjects affected / exposed[9]	96 / 174 (55.17%)	78 / 169 (46.15%)	
occurrences (all)	96	78	
Irritability (Booster phase)			
subjects affected / exposed[10]	113 / 174 (64.94%)	104 / 169 (61.54%)	
occurrences (all)	113	104	
Loss of appetite (Booster phase)			
subjects affected / exposed[11]	61 / 174 (35.06%)	56 / 169 (33.14%)	
occurrences (all)	61	56	
Pyrexia (Primary phase)			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 175 (6.86%)	12 / 176 (6.82%)	
occurrences (all)	12	12	
Pyrexia (Booster phase)			
alternative assessment type: Non-systematic			
subjects affected / exposed[12]	8 / 174 (4.60%)	10 / 171 (5.85%)	
occurrences (all)	8	10	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 175 (6.29%)	8 / 176 (4.55%)	
occurrences (all)	11	8	
Vomiting			
subjects affected / exposed	4 / 175 (2.29%)	10 / 176 (5.68%)	
occurrences (all)	4	10	
Respiratory, thoracic and mediastinal			

disorders			
Cough (Primary phase)			
subjects affected / exposed	9 / 175 (5.14%)	9 / 176 (5.11%)	
occurrences (all)	9	9	
Cough (Booster phase)			
subjects affected / exposed[13]	6 / 174 (3.45%)	11 / 171 (6.43%)	
occurrences (all)	6	11	
Infections and infestations			
Nasopharyngitis (Primary phase)			
subjects affected / exposed	26 / 175 (14.86%)	46 / 176 (26.14%)	
occurrences (all)	26	46	
Nasopharyngitis (Booster phase)			
subjects affected / exposed[14]	16 / 174 (9.20%)	20 / 171 (11.70%)	
occurrences (all)	16	20	
Otitis media (Booster phase)			
subjects affected / exposed[15]	9 / 174 (5.17%)	7 / 171 (4.09%)	
occurrences (all)	9	7	

Notes:

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

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