Clinical trial results:
A phase III, open, single centre study to assess the safety, reactogenicity and immunogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate (10Pn-PD-DiT) vaccine (GSK 1024850A), when either given as a booster dose (at 15-21 months of age) in children previously primed with three doses of 10Pn-PD-DiT vaccine, or when given as a two-dose catch-up immunization (at 15-21 and 17-23 months of age) in unprimed children, all previously enrolled in the 10PN-PD-DIT-032 primary vaccination study in Nigeria.

Summary

EudraCT number	2012-000826-23
Trial protocol	Outside EU/EEA
Global end of trial date	16 February 2011

Results information

Result version number	v3 (current)
This version publication date	01 March 2023
First version publication date	25 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	113199

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01153893
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	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2011
Global end of trial reached?	Yes
Global end of trial date	16 February 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and reactogenicity of the 10Pn-PD-DiT vaccine in terms of occurrence of adverse events with grade 3 intensity after booster vaccination.

Protection of trial subjects:

The vaccine recipients were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2010
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	Nigeria: 107
Worldwide total number of subjects	107
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	107
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:

The duration of the study per subject can vary from 1 month (Synflorix/Infanrix primed Group) to 3 months (Synflorix/Infanrix unprimed Group), depending on the group allocation.
Out of the 107 subjects enrolled in the study, 3 did not start (2 due to the vaccine dose not being administered and 1 due to the non-allocation of a vaccine number).

Pre-assignment

Screening details:

Because of an issue with the informed consent of a child, the data of the child, who had a non-related to study medication serious adverse event, are not detailed in this analysis. Data were reanalyzed for the 104 subjects with data available.

Pre-assignment period milestones

Number of subjects started	107
Number of subjects completed	104

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Vaccine dose not administrated: 2
Reason: Number of subjects	Vaccine number not allocated: 1

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix/Infanrix primed Group

Arm description:

Subjects previously primed with the Synflorix vaccine in the primary study NCT00678301 received a booster dose of the Synflorix vaccine co-administered with a booster dose of the Infanrix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK1024850A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose, administered intramuscularly in the right thigh or deltoid muscle of the arm.

Investigational medicinal product name	Infanrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the left thigh or deltoid muscle of the arm.

Arm title	Synflorix/Infanrix unprimed Group

Arm description:

Unprimed subjects from the primary study NCT00678301, not previously vaccinated with any pneumococcal vaccine, received a 2-dose catch-up vaccination of Synflorix vaccine at 15-21 and 17-23 months of age and a booster dose of Infanrix vaccine co-administered with the first dose of Synflorix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK1024850A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses, administered intramuscularly in the right thigh or deltoid muscle of the arm.

Investigational medicinal product name	Infanrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the left thigh or deltoid muscle of the arm.

Number of subjects in period 1[1]	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group
Started	68	36
Completed	67	36
Not completed	1	0
Adverse event, serious fatal	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 107 subjects enrolled in the study, 3 did not start (2 due to the vaccine dose not being administered and 1 due to the non-allocation of a vaccine number).

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix/Infanrix primed Group
Reporting group description:	
Subjects previously primed with the Synflorix vaccine in the primary study NCT00678301 received a booster dose of the Synflorix vaccine co-administered with a booster dose of the Infanrix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.	
Reporting group title	Synflorix/Infanrix unprimed Group
Reporting group description:	
Unprimed subjects from the primary study NCT00678301, not previously vaccinated with any pneumococcal vaccine, received a 2-dose catch-up vaccination of Synflorix vaccine at 15-21 and 17-23 months of age and a booster dose of Infanrix vaccine co-administered with the first dose of Synflorix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.	

Reporting group values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group	Total
Number of subjects	68	36	104
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)	68	36	104
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: months			
arithmetic mean	16.7	16.4	
standard deviation	± 1	± 0.91	-
Gender categorical Units: Subjects			
Female	29	17	46
Male	39	19	58

End points

End points reporting groups

Reporting group title	Synflorix/Infanrix primed Group

Reporting group description:

Subjects previously primed with the Synflorix vaccine in the primary study NCT00678301 received a booster dose of the Synflorix vaccine co-administered with a booster dose of the Infanrix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Reporting group title	Synflorix/Infanrix unprimed Group

Reporting group description:

Unprimed subjects from the primary study NCT00678301, not previously vaccinated with any pneumococcal vaccine, received a 2-dose catch-up vaccination of Synflorix vaccine at 15-21 and 17-23 months of age and a booster dose of Infanrix vaccine co-administered with the first dose of Synflorix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Primary: Number of subjects reporting Grade 3 symptoms (solicited and unsolicited)

End point title	Number of subjects reporting Grade 3 symptoms (solicited and unsolicited)[1][2]

End point description:

Grade 3 symptom = severe symptom that prevented normal activity. Solicited local symptoms assessed were pain, redness and swelling. Solicited general symptoms assessed were drowsiness, fever, irritability and loss of appetite. Unsolicited AEs = Any AE reported in addition to those solicited during the clinical study. Also any "solicited" symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.
The Total Vaccinated cohort included all vaccinated subjects.

End point type	Primary

End point timeframe:

Within 31 days (Day 0 to Day 30) after administration of a booster dose of Synflorix vaccine in the Synflorix/Infanrix primed Group

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: These results were only assessed in the Synflorix/Infanrix primed Group.

End point values	Synflorix/Infanrix primed Group			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: Subjects				
Any symptom	3			
General symptoms	1			
Local symptoms	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes

End point description:

Vaccine pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Concentrations were expressed as geometric mean concentrations (GMCs) in microgram per milliliter (µg/mL). Pneumococcal serotype specific total imunoglobuline G (IgG) antibodies were measured by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA). The cut-off of the assay was 0.05 µg/mL. The According-To-Protocol cohort for immunogenicity included all evaluable subjects for whom immunogenicity data were available. This included subjects for whom assay results were available for antibodies against at least one pneumococcal vaccine serotype or protein D for the blood sample taken one month after vaccination.

End point type	Secondary

End point timeframe:

Prior to and one month after the booster immunisation for the Synflorix/Infanrix primed Group and prior to the first dose and one month after Dose 2 in the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	35		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [pre-booster;pre-vacc] (N=68,35)	0.29 (0.22 to 0.4)	0.03 (0.03 to 0.04)		
Anti-1 [post-booster;post-dose 2] (N=67,35)	8.72 (6.37 to 11.93)	3.17 (2.58 to 3.89)		
Anti-4 [pre-booster;pre-vacc] (N=68,35)	0.4 (0.31 to 0.5)	0.06 (0.04 to 0.09)		
Anti-4 [post-booster;post-dose 2] (N=67,35)	11.03 (9.06 to 13.42)	8.22 (6.75 to 10.02)		
Anti-5 [pre-booster;pre-vacc] (N=68,35)	0.49 (0.4 to 0.61)	0.05 (0.04 to 0.07)		
Anti-5 [post-booster;post-dose 2] (N=67,35)	10.34 (8.32 to 12.85)	2.87 (2.22 to 3.71)		
Anti-6B [pre-booster;pre-vacc] (N=68,35)	0.63 (0.48 to 0.83)	0.05 (0.03 to 0.08)		
Anti-6B [post-booster;post-dose 2] (N=67,35)	4.31 (3.37 to 5.52)	0.85 (0.52 to 1.38)		
Anti-7F [pre-booster;pre-vacc] (N=68,35)	0.73 (0.57 to 0.92)	0.05 (0.04 to 0.08)		
Anti-7F [post-booster;post-dose 2] (N=67,35)	10.3 (8.57 to 12.38)	6.07 (4.89 to 7.52)		
Anti-9V [pre-booster;pre-vacc] (N=67,35)	1.04 (0.78 to 1.39)	0.06 (0.04 to 0.1)		
Anti-9V [post-booster;post-dose 2] (N=67,35)	11.49 (9.02 to 14.65)	2.7 (2.05 to 3.55)		
Anti-14 [pre-booster;pre-vacc] (N=68,35)	1.13 (0.87 to 1.46)	0.14 (0.08 to 0.23)		
Anti-14 [post-booster;post-dose 2] (N=67,35)	14.14 (11.74 to 17.04)	10.59 (8.7 to 12.89)		

Anti-18C [pre-booster;pre-vacc] (N=68,35)	1.62 (1.3 to 2.04)	0.05 (0.03 to 0.09)		
Anti-18C [post-booster;post-dose 2] (N=67,35)	35.33 (27.73 to 45.02)	25.61 (19.7 to 33.3)		
Anti-19F [pre-booster;pre-vacc] (N=67,35)	1.2 (0.85 to 1.71)	0.14 (0.08 to 0.24)		
Anti-19F [post-booster;post-dose 2] (N=67,35)	9.26 (7.2 to 11.91)	7.16 (4.27 to 12.02)		
Anti-23F [pre-booster;pre-vacc] (N=68,35)	0.46 (0.32 to 0.68)	0.03 (0.02 to 0.04)		
Anti-23F [post-booster;post-dose 2] (N=67,35)	6.99 (5.21 to 9.39)	1.06 (0.66 to 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes

End point description:

Cross-reactive pneumococcal serotypes assessed were serotypes 6A and 19A. Concentrations were expressed as geometric mean concentrations (GMCs) in microgram per millilitre (µg/mL). The antibody concentrations against the cross-reactive pneumococcal serotypes 6A and 19A were determined by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA). The cut-off of the assay was 0.05 µg/mL.
The According-To-Protocol cohort for immunogenicity included all evaluable subjects for whom immunogenicity data were available. This included subjects for whom assay results were available for antibodies against at least one pneumococcal vaccine serotype or protein D for the blood sample taken one month after vaccination.

End point type	Secondary

End point timeframe:

Prior to and one month after the booster immunisation for the Synflorix/Infanrix primed Group and prior to the first dose and one month after Dose 2 in the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	35		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A [pre-booster;pre-vacc] (N=68,35)	0.19 (0.13 to 0.27)	0.05 (0.03 to 0.07)		
Anti-6A [post-booster;post-dose 2] (N=67,35)	0.81 (0.56 to 1.18)	0.24 (0.15 to 0.4)		
Anti-19A [pre-booster;pre-vacc] (N=68,35)	0.24 (0.17 to 0.36)	0.09 (0.05 to 0.17)		
Anti-19A [post-booster;post-dose 2] (N=67,35)	1.33 (0.88 to 2)	1.94 (1.13 to 3.33)		

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:

Vaccine pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Streptococcus pneumoniae opsonophagocytic activity was measured by a killing-assay using a HL 60 cell line. The results were presented as the dilution of serum (opsonic titre) able to sustain 50% killing of live pneumococci under the assay conditions. The cut-off of the assay is an opsonic titre of 8.
The According-To-Protocol cohort for immunogenicity included all evaluable subjects for whom immunogenicity data were available. This included subjects for whom assay results were available for antibodies against at least one pneumococcal vaccine serotype or protein D for the blood sample taken one month after vaccination.

End point type	Secondary

End point timeframe:

One month after the booster immunisation for the Synflorix/Infanrix primed Group and one month after Dose 2 in the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	35		
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-1 [post-booster;post-dose 2] (N=66,35)	1667.8 (1210.9 to 2297)	103.4 (67.7 to 157.9)		
Opsono-4 [post-booster;post-dose 2] (N=65,35)	3869.1 (3122.8 to 4793.9)	1482.9 (1211 to 1815.8)		
Opsono-5 [post-booster;post-dose 2] (N=67,35)	679.9 (515.9 to 895.9)	58.7 (38.6 to 89.4)		
Opsono-6B [post-booster;post-dose 2] (N=66,31)	1687.6 (1138.7 to 2501)	325.7 (118.1 to 898.6)		
Opsono-7F [post-booster;post-dose 2] (N=67,35)	11045.3 (8456.8 to 14426.3)	7980.2 (6287.8 to 10128.1)		
Opsono-9V [post-booster;post-dose 2] (N=66,35)	5300.1 (4329.3 to 6488.5)	6375.3 (4779.4 to 8504.1)		
Opsono-14 [post-booster;post-dose 2] (N=66,35)	2472 (1767.3 to 3457.8)	1797.8 (1241.4 to 2603.6)		

Opsono-18C [post-booster;post-dose 2] (N=67,35)	2323 (1403.1 to 3846.1)	4104.2 (2954.5 to 5701.2)		
Opsono-19F [post-booster;post-dose 2] (N=65,34)	683.5 (440 to 1062)	443.5 (203 to 968.8)		
Opsono-23F [post-booster;post-dose 2] (N=67,35)	5144.5 (3657.4 to 7236.3)	3081.7 (1389.3 to 6836.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity against cross-reactive pneumococcal serotypes

End point title	Opsonophagocytic activity against cross-reactive pneumococcal serotypes

End point description:

Cross-reactive pneumococcal serotypes assessed were serotypes 6A and 19A. Streptococcus pneumoniae opsonophagocytic activity was measured by a killing-assay using a HL 60 cell line. The results were presented as the dilution of serum (opsonic titre) able to sustain 50% killing of live pneumococci under the assay conditions. The cut-off of the assay is an opsonic titre of 8.
The According-To-Protocol cohort for immunogenicity included all evaluable subjects for whom immunogenicity data were available. This included subjects for whom assay results were available for antibodies against at least one pneumococcal vaccine serotype or protein D for the blood sample taken one month after vaccination.

End point type	Secondary

End point timeframe:

One month after the booster immunisation for the Synflorix/Infanrix primed Group and one month after Dose 2 in the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	35		
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-6A [post-booster;post-dose 2] (N=61,34)	213 (121.7 to 372.9)	313.9 (147.6 to 667.4)		
Opsono-19A [post-booster;post-dose 2] (N=66,35)	112.7 (66.7 to 190.5)	341.2 (159 to 732.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against protein D (PD)

End point title	Concentration of antibodies against protein D (PD)

End point description:

Anti-PD antibodies were determined using an ELISA assay. Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA units per milliliter (EL.U/mL). Concentration of specific PD antibodies was determined, using a standard reference serum. The cut-off of the assay is 100 ELISA units per milliliter (EL.U/mL).
The According-To-Protocol cohort for immunogenicity included all evaluable subjects for whom immunogenicity data were available. This included subjects for whom assay results were available for antibodies against at least one pneumococcal vaccine serotype or protein D for the blood sample taken one month after vaccination.

End point type	Secondary

End point timeframe:

Prior to and one month after the booster immunization for the Synflorix/Infanrix primed Group and prior to the first dose and one month after Dose 2 in the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	35		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [pre-booster;pre-vacc] (N=66,35)	270.4 (211.7 to 345.3)	61.5 (52 to 72.7)		
Anti-PD [post-booster;post-dose 2] (N=67,35)	2955.3 (2342 to 3729.2)	501.1 (345 to 727.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local Adverse Events (AEs)

End point title	Number of subjects reporting any and grade 3 solicited local Adverse Events (AEs)

End point description:

Solicited AEs = AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events was actively solicited from the subject or an observer during a specified post-vaccination follow-up period. Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling greather than (>) 30 millimeter (mm).
The Total Vaccinated cohort included all vaccinated subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) after vaccination

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	36		
Units: Subjects				
Any pain	27	13		
Grade 3 pain	0	0		
Any redness	1	1		
Redness > 30 mm	0	1		
Any swelling	4	2		
Swelling > 30 mm	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever (= axillary temperature greater than or equal to [≥] 37.5 °C). Any= occurrence of any general symptom regardless of intensity grade or relationship to vaccination Grade 3 drowsiness = drowsiness which prevented normal activity. Grade 3 irritability = crying that could not be comforted/ prevented normal activity. Grade 3 loss of appetite = not eating at all. Grade 3 fever = temperature >39.5°C. Related = solicited symptom assessed by the investigator as causally related to study vaccination.
The Total Vaccinated cohort included all vaccinated subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) after vaccination

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	36		
Units: Subjects				
Any drowsiness	2	0		
Grade 3 drowsiness	0	0		
Related drowsiness	2	0		
Fever > 39.5°C	0	1		
Related fever	8	3		
Any irritability	2	0		
Grade 3 irritability	0	0		
Related irritability	2	0		
Any loss of appetite	1	1		
Grade 3 loss of appetite	0	0		
Related loss of appetite	1	1		

Fever ≥ 37.5°C	8	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited AEs

End point title	Number of subjects reporting unsolicited AEs

End point description:

Unsolicited AEs = Any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study. Also any "solicited" symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.
The Total Vaccinated cohort included all vaccinated subjects.

End point type	Secondary

End point timeframe:

Within 31 days (Days 0-30) after vaccination

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	36		
Units: Subjects				
Any AE(s)	31	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.
The Total Vaccinated cohort included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the entire study period, from the vaccination visit at Day 0 up to the end of the follow-up visit at Month 1 for the Synflorix/Infanrix primed Group and up to Month 3 for the Synflorix/Infanrix unprimed Group

End point values	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	36		
Units: Subjects				
Any SAE(s)	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: Within 4 days (Days 0-3) after vaccination. Unsolicited AEs: Within 31 days (Days 0-30) after vaccination. SAEs: From Day 0 up to Month 1 for the Synflorix/Infanrix primed Group and up to Month 3 for the Synflorix/Infanrix unprimed Group.

Adverse event reporting additional description:

Because of an issue discovered with the informed consent obtained for one child after the original statistical analysis. The data of the child, who also had an SAE that was not considered to be related to the study medication by the investigator, have been removed from the results tables.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Synflorix/Infanrix primed Group

Reporting group description:

Subjects previously primed with the Synflorix vaccine in the primary study NCT00678301 received a booster dose of the Synflorix vaccine co-administered with a booster dose of the Infanrix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Reporting group title	Synflorix/Infanrix unprimed Group

Reporting group description:

Unprimed subjects from the primary study NCT00678301, not previously vaccinated with any pneumococcal vaccine, received a 2-dose catch-up vaccination of Synflorix vaccine at 15-21 and 17-23 months of age and a booster dose of Infanrix vaccine co-administered with the first dose of Synflorix vaccine at 15-21 months of age. Synflorix vaccine was administered intramuscularly in the right thigh or deltoid muscle of the arm. Infanrix vaccine was administered intramuscularly in the left thigh or deltoid muscle of the arm.

Serious adverse events	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 68 (1.47%)	0 / 36 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Drowning			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 68 (1.47%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Synflorix/Infanrix primed Group	Synflorix/Infanrix unprimed Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 68 (67.65%)	25 / 36 (69.44%)	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	8 / 68 (11.76%)	3 / 36 (8.33%)	
occurrences (all)	8	3	
Pain			
subjects affected / exposed	27 / 68 (39.71%)	13 / 36 (36.11%)	
occurrences (all)	27	13	
Swelling			
subjects affected / exposed	4 / 68 (5.88%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Eye disorders			
Conjunctivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 68 (4.41%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Enteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 68 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Infections and infestations			
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	13 / 68 (19.12%)	7 / 36 (19.44%)	
occurrences (all)	13	7	
Malaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 68 (11.76%)	10 / 36 (27.78%)	
occurrences (all)	8	10	
Furuncle			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	4 / 68 (5.88%)	1 / 36 (2.78%)	
occurrences (all)	4	1	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 68 (4.41%)	2 / 36 (5.56%)	
occurrences (all)	3	2	

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