Clinical trial results:
A phase III long-term follow-up study to assess immunological memory induced following primary and booster vaccination with GSK Biologicals' 10-valent pneumococcal conjugate vaccine (10Pn-PD-DiT), through evaluation of early antibody responses after an additional dose of 10Pn-PD-DiT at 40-48 months of age, to evaluate in the fourth year of life, the immunogenicity and safety of a 2-dose catch-up immunization course with the 10Pn-PD-DiT vaccine and the impact of pneumococcal vaccination on nasopharyngeal carriage.

Summary

EudraCT number	2008-008104-41
Trial protocol	CZ
Global end of trial date	29 July 2011

Results information

Result version number	v3 (current)
This version publication date	20 May 2023
First version publication date	02 August 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	112801

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00950833
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000673-PIP01-09
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	19 August 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2010
Global end of trial reached?	Yes
Global end of trial date	29 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the immunological memory induced following primary vaccination in study 10PN-PD-DIT-010 (107017) and booster vaccination in study 10PN-PD-DIT-014 (107137) with the 10Pn-PD-DiT vaccine, through evaluation of early antibody responses after an additional dose of 10Pn-PD-DiT at 40-48 months of age, compared to the unprimed group.
Criteria for immune memory:
The immune memory will be demonstrated if the lower limit of the 95% CI around the GMC ratios (pooled primed groups over unprimed group) is higher than 1 for all 10 vaccine serotypes.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2009
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	Czech Republic: 466
Worldwide total number of subjects	466
EEA total number of subjects	466

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)	0
Children (2-11 years)	466
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of the 466 subjects enrolled in the study, 5 subjects were not included in the Total effective cohort as they did not meet eligibility criteria. Out of the 461 subjects enrolled in the Total effective cohort, 18 subjects were not included in the Total vaccinated cohort as these subjects withdrew before the first vaccination visit (Visit 2).

Pre-assignment period milestones

Number of subjects started	466
Number of subjects completed	443

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 18
Reason: Number of subjects	Vaccine not administered: 5

Period 1

Period 1 title	Overall Study (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 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects received prophylactic antipyretic (AP) treatment with paracetamol.

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly in the deltoid muscle at Month 9 (40-48 months of age).

Arm title	Synflorix II Group

Arm description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered

intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects did not receive any prophylactic antipyretic (AP) treatment.

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly in the deltoid region at Month 9 (40-48 months of age).

Arm title	Synflorix III Group

Arm description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were not previously primed with Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), but vaccinated with Nimenrix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study 2 doses of Synflorix vaccine at Month 9 (40-48 months of age) and at Month 11 (42-50 months of age), administered intramuscularly in the deltoid muscle.

Arm type	Active comparator
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses administered intramuscularly in the deltoid muscle at Month 9 (40-48 months of age) and Month 11 (42-50 months of age).

Number of subjects in period 1[1]	Synflorix I Group	Synflorix II Group	Synflorix III Group
Started	112	108	223
Completed	112	108	223

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 466 subjects enrolled in the study, 5 subjects were not included in the Total effective cohort
as they did not meet eligibility criteria. Out of the 461 subjects enrolled in the Total effective cohort, 18 subjects were not included in the Total vaccinated cohort as these subjects withdrew before the first vaccination visit (Visit 2).

Baseline characteristics

Reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects received prophylactic antipyretic (AP) treatment with paracetamol.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects did not receive any prophylactic antipyretic (AP) treatment.

Reporting group title	Synflorix III Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were not previously primed with Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), but vaccinated with Nimenrix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study 2 doses of Synflorix vaccine at Month 9 (40-48 months of age) and at Month 11 (42-50 months of age), administered intramuscularly in the deltoid muscle.

Reporting group values	Synflorix I Group	Synflorix II Group	Synflorix III Group
Number of subjects	112	108	223
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)	0	0	0
Children (2-11 years)	112	108	223
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	39.2	39.1	37.7
standard deviation	± 1.53	± 1.54	± 3.36
Gender categorical Units: Subjects			
Female	60	48	99
Male	52	60	124

Reporting group values	Total		
Number of subjects	443		
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)	443		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	207		
Male	236		

Subject analysis sets

Subject analysis set title	Pooled primed Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

For the purpose of the analysis, subjects from Synflorix I Group and Synflorix II Group have been pooled into a sub-group.

Reporting group values	Pooled primed Group		
Number of subjects	220		
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)	220		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months			
arithmetic mean	39.15		
standard deviation	± 1.53		

Gender categorical Units: Subjects			
Female	108		
Male	112		

End points

End points reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects received prophylactic antipyretic (AP) treatment with paracetamol.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects did not receive any prophylactic antipyretic (AP) treatment.

Reporting group title	Synflorix III Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were not previously primed with Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), but vaccinated with Nimenrix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study 2 doses of Synflorix vaccine at Month 9 (40-48 months of age) and at Month 11 (42-50 months of age), administered intramuscularly in the deltoid muscle.

Subject analysis set title	Pooled primed Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

For the purpose of the analysis, subjects from Synflorix I Group and Synflorix II Group have been pooled into a sub-group.

Primary: Antibody concentrations against vaccine pneumococcal serotypes

End point title	Antibody concentrations against vaccine pneumococcal serotypes[1]

End point description:

Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) have been assessed by 22F-inhibition enzyme linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.05 µg/mL.
The analysis was performed on the According-to-Protocol (ATP) cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Primary

End point timeframe:

At 7-10 days after the first vaccine dose

Notes:

[1] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	204	215		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=204;215)	1.24 (1.07 to 1.42)	7.63 (6.57 to 8.86)		
Anti-4 (N=204;215)	4.52 (3.96 to 5.17)	12.95 (11.37 to 14.75)		
Anti-5 (N=202;215)	0.72 (0.63 to 0.84)	9.76 (8.44 to 11.29)		
Anti-6B (N=203;215)	0.27 (0.22 to 0.33)	7.67 (6.7 to 8.78)		
Anti-7F (N=204;215)	1.37 (1.19 to 1.58)	6.51 (5.69 to 7.46)		
Anti-9V (N=202;213)	0.69 (0.58 to 0.83)	9.75 (8.46 to 11.24)		
Anti-14 (N=204;214)	1.01 (0.8 to 1.27)	23.07 (20.03 to 26.57)		
Anti-18C (N=204;214)	3.25 (2.71 to 3.9)	32.54 (28.15 to 37.61)		
Anti-19F (N=204;214)	4.31 (3.59 to 5.17)	39.84 (34.12 to 46.51)		
Anti-23F (N=204;215)	0.25 (0.2 to 0.32)	9.24 (7.86 to 10.86)		

Statistical analyses

Statistical analysis title	Immune response non-inferiority - Anti-1

Statistical analysis description:

To demonstrate the immunological memory induced for anti-pneumococcal serotype 1 following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMC ratio
Point estimate	6.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.03
upper limit	7.58

Notes:

[2] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 1.

Statistical analysis title	Immune response non-inferiority - Anti-4

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 4 induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMC ratio
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.38
upper limit	3.45

Notes:

[3] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled SynflorixI+II Group over Synflorix Group) was higher than 1 for pneumococcal serotype 4.

Statistical analysis title	Immune response non-inferiority - Anti-5

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 6B induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMC ratio
Point estimate	13.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.96
upper limit	16.55

Notes:

[4] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 5.

Statistical analysis title	Immune response non-inferiority - Anti-6B

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 6B induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group

Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMC ratio
Point estimate	28.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.54
upper limit	36.81

Notes:

[5] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 6B.

Statistical analysis title	Immune response non-inferiority - Anti-7F

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 7F induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	4.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	5.78

Notes:

[6] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 7F.

Statistical analysis title	Immune response non-inferiority - Anti-9V

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 9V induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	GMC ratio
Point estimate	14.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	11.21
upper limit	17.75

Notes:

[7] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 9V.

Statistical analysis title	Immune response non-inferiority - Anti-14

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 14 induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMC ratio
Point estimate	22.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.51
upper limit	30

Notes:

[8] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 14.

Statistical analysis title	Immune response non-inferiority - Anti-18C

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 18C induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	10.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.95
upper limit	12.61

Notes:

[9] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 18C.

Statistical analysis title	Immune response non-inferiority - Anti-19F

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 19F induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMC ratio
Point estimate	9.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.29
upper limit	11.74

Notes:

[10] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 19F.

Statistical analysis title	Immune response non-inferiority - Anti-23F

Statistical analysis description:

To demonstrate the immunological memory for anti-pneumococcal serotype 23F induced following primary vaccination in study 107017 (NCT00370318) and booster vaccination in study 107137 (NCT00496015) with the Synflorix vaccine, through evaluation of early antibody responses after an additional dose of Synflorix vaccine at 40-48 months of age, compared to the Synflorix III Group.

Comparison groups	Synflorix III Group v Pooled primed Group
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	GMC ratio
Point estimate	36.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.59
upper limit	48.34

Notes:

[11] - The immune memory would be demonstrated if the lower limit (LL) of the 95% confidence interval (CI) around the geometric mean concentration (GMC) ratios (Pooled Synflorix I+II Group over Synflorix III Group) was higher than 1 for pneumococcal serotype 23F.

Secondary: Antibody concentrations against vaccine pneumococcal serotypes

End point title	Antibody concentrations against vaccine pneumococcal serotypes[12]

End point description:

Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) have been assessed by 22F-inhibition ELISA, presented as GMCs and expressed in µg/mL. The seropositivity cut-off value of the assay was an antibody concentration ≥ 0.05 µg/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to the first study vaccine dose (At Day 0)

Notes:

[12] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	209	215		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=208;215)	0.09 (0.08 to 0.11)	0.27 (0.23 to 0.33)		
Anti-4 (N=206;213)	0.05 (0.04 to 0.06)	0.2 (0.17 to 0.23)		
Anti-5 (N=208;212)	0.1 (0.09 to 0.11)	0.41 (0.36 to 0.47)		
Anti-6B (N=202;212)	0.1 (0.08 to 0.12)	0.8 (0.61 to 1.05)		
Anti-7F (N=209;215)	0.06 (0.05 to 0.07)	0.48 (0.41 to 0.56)		
Anti-9V (N=203;211)	0.07 (0.06 to 0.09)	0.5 (0.41 to 0.61)		
Anti-14 (N=203;213)	0.28 (0.22 to 0.36)	1.21 (0.97 to 1.5)		
Anti-18C (N=205;215)	0.09 (0.07 to 0.11)	0.65 (0.54 to 0.79)		
Anti-19F (N=208;215)	0.44 (0.32 to 0.59)	2.35 (1.75 to 3.15)		
Anti-23F (N=207;215)	0.08 (0.07 to 0.1)	0.96 (0.72 to 1.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against vaccine pneumococcal serotypes

End point title	Opsonophagocytic activity (OPA) titers against vaccine pneumococcal serotypes[13]

End point description:

Seropositivity status was defined as the opsonophagocytic activity (OPA) against pneumococcal serotypes ≥ the value of 8, presented as geometric mean titers (GMTs). The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F).
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to (Day 0/PRE) and 7-10 days after (POST) the first vaccine dose

Notes:

[13] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	191	199		
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-1, PRE (N=191;199)	5.4 (4.7 to 6.2)	10.2 (8 to 12.9)		
Opsono-1, POST (N=182;194)	632 (524.4 to 761.7)	3106.5 (2670 to 3614.5)		
Opsono-4, PRE (N=174;189)	9.1 (6.8 to 12.1)	18.1 (13.1 to 24.9)		
Opsono-4, POST (N=187;195)	13109.9 (11080.6 to 15510.7)	27273.3 (22682.9 to 32792.6)		
Opsono-5, PRE (N=185;199)	4 (4 to 4.1)	8.9 (7.6 to 10.5)		
Opsono-5, POST (N=182;194)	145.8 (111.7 to 190.3)	1020 (874 to 1190.2)		
Opsono-6B, PRE (N=173;183)	46.7 (29.8 to 73.3)	163.5 (108.5 to 246.4)		
Opsono-6B, POST (N=184;192)	1472.2 (1053.2 to 2057.8)	5789.5 (4637.3 to 7227.9)		
Opsono-7F, PRE (N=167;187)	973.4 (798.5 to 1186.6)	1112.3 (951.4 to 1300.4)		
Opsono-7F, POST (N=186;191)	13647.4 (11801.9 to 15781.3)	19988.9 (16834.5 to 23734.2)		
Opsono-9V, PRE (N=156;171)	268.2 (192.2 to 374.3)	481.8 (394.6 to 588.1)		
Opsono-9V, POST (N=186;194)	14668.8 (12476.1 to 17247)	17952.5 (14699.2 to 21925.7)		
Opsono-14, PRE (N=166;184)	145.3 (97.5 to 216.6)	267.6 (196.9 to 363.8)		
Opsono-14, POST (N=187;195)	4454.3 (3921.1 to 5059.9)	16256.8 (13573 to 19471.4)		
Opsono-18C, PRE (N=169;186)	5.7 (4.7 to 7)	14.2 (10.6 to 19.2)		
Opsono-18C, POST (N=180;188)	9092.2 (7381.2 to 11199.9)	7413.8 (6072.3 to 9051.6)		
Opsono-19F, PRE (N=186;192)	12.9 (9.6 to 17.2)	79.5 (55.4 to 113.9)		
Opsono-19F, POST (N=190;192)	902.5 (659.2 to 1235.6)	6271.1 (4814.8 to 8168)		
Opsono-23F, PRE (N=166;189)	220.6 (132 to 368.7)	462.7 (292.9 to 730.9)		
Opsono-23F, POST (N=189;197)	5776.5 (4686.8 to 7119.5)	15613.5 (12386.9 to 19680.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine pneumococcal cross-reactive serotypes 6A and 19A

End point title	Antibody concentrations against vaccine pneumococcal cross-reactive serotypes 6A and 19A[14]

End point description:

The vaccine pneumococcal cross-reactive serotypes 6A and 19A have been assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in µg/mL. The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to (Day 0/PRe) and 7-10 days after (PI) the first vaccine dose

Notes:

[14] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	207	215		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A, PRE (N=207;214)	0.11 (0.09 to 0.13)	0.39 (0.3 to 0.5)		
Anti-6A, PI (N=203;215)	0.2 (0.17 to 0.25)	2.4 (2.01 to 2.85)		
Anti-19A, PRE (N=207;215)	0.22 (0.18 to 0.28)	0.52 (0.41 to 0.67)		
Anti-19A, PI (N=203;214)	0.65 (0.52 to 0.82)	6.75 (5.41 to 8.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal

	cross-reactive serotypes 6A and 19A[15]

End point description:

Seropositivity status was defined as the opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A (Opsono-16A and opsono-19A) ≥ the value of 8, presented as geometric mean titers (GMTs).
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to (Day 0/PRE) and 7-10 days after (PI) the first vaccine dose

Notes:

[15] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	183	191		
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-6A, PRE (N=167;178)	49 (32.4 to 74)	95.2 (65.3 to 138.7)		
Opsono-6A, PI (N=180;191)	863.3 (619.3 to 1203.4)	2408.4 (1815.7 to 3194.5)		
Opsono-19A, PRE (N=183;190)	10.3 (7.9 to 13.4)	15.9 (11.7 to 21.6)		
Opsono-19A, PI (N=175;191)	880.5 (622.7 to 1245)	2104.9 (1560.9 to 2838.7)		

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)[16]

End point description:

Anti-protein D (anti-PD) concentrations were presented as geometric mean concentrations (GMCs), expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off value of the assay was an antibody concentration ≥ 100 EL.U/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against protein D were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to (Day 0/PRE) and 7-10 days after (PI) the first vaccine dose

Notes:

[16] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	204	215		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE (N=198;210)	105.6 (93.8 to 119)	464.2 (401.6 to 536.5)		
Anti-PD, PI (N=204;215)	374.3 (315.1 to 444.6)	2673.7 (2359.1 to 3030.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Memory B-cell detection for vaccine polysaccharides (PS)

End point title	Memory B-cell detection for vaccine polysaccharides (PS)

End point description:

B-cell detection for the pneumococcal serotype specific polysaccharides (1, 5, 6B, 18C, 19F, 23F and C) was tabulated for a subset of subjects from each group. The results are expressed as the frequencies of antigen-specific memory B-cells within the total memory B-cell population.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

Prior to (Day 0/PRE) and 7-10 days after (POST) the first vaccine dose

End point values	Synflorix I Group	Synflorix II Group	Synflorix III Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	107	210	
Units: Memory B-cells				
arithmetic mean (standard deviation)				
1 PS, PRE (N=23;22;47)	288.6 (± 352.5)	269.5 (± 432.2)	254.8 (± 368.4)	
5 PS, PRE (N=26;27;42)	139.4 (± 214.7)	141.9 (± 232.4)	81.5 (± 109.2)	
6B PS, PRE (N=20;22;44)	372 (± 545.5)	327.2 (± 554.4)	639.9 (± 846.5)	
18C PS, PRE (N=26;26;42)	537.7 (± 641.8)	530.9 (± 693.8)	135.2 (± 200.6)	
19F PS, PRE (N=20;22;44)	169.7 (± 415.3)	149.1 (± 194.4)	164.5 (± 343.4)	

23F PS, PRE (N=23;22;45)	112.6 (± 176.1)	285 (± 484.3)	185.6 (± 270.1)	
C-PS, PRE (N=70;71;133)	475.9 (± 682.3)	462.5 (± 704.5)	469.9 (± 639.2)	
1 PS, POST (N=23;23;43)	1488.8 (± 1584.2)	1017.4 (± 1309.9)	755.9 (± 1017.4)	
5 PS, POST (N=28;23;37)	233.5 (± 235.7)	406.6 (± 447.8)	152.6 (± 231)	
6B PS, POST (N=16;24;42)	629.1 (± 773.2)	1265.8 (± 1738.6)	526 (± 648.6)	
18C PS, POST (N=28;23;36)	3839 (± 5960.5)	8308.4 (± 7166.9)	2053.8 (± 2122.2)	
19F PS, POST (N=16;23;42)	1056.7 (± 1334)	1092.4 (± 1724.3)	708.2 (± 1609.4)	
23F PS, POST (N=23;23;43)	579.8 (± 632.5)	1123.7 (± 2095.4)	327.9 (± 470.5)	
C-PS, POST (N=67;70;123)	679.2 (± 885.8)	915.5 (± 1191.3)	762.6 (± 1039.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine pneumococcal serotypes

End point title	Antibody concentrations against vaccine pneumococcal serotypes[17]

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-inhibition ELISA, presented as geometric mean concentrations (GMCs), expressed in µg/mL. The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

At Month 12, one month after the second vaccine dose

Notes:

[17] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	209			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=209)	2.33 (2.13 to 2.54)			
Anti-4 (N=209)	6.26 (5.73 to 6.84)			
Anti-5 (N=209)	2.69 (2.44 to 2.96)			

Anti-6B (N=209)	0.84 (0.73 to 0.97)			
Anti-7F (N=208)	3.63 (3.33 to 3.95)			
Anti-9V (N=209)	1.73 (1.56 to 1.93)			
Anti-14 (N=209)	5.21 (4.6 to 5.89)			
Anti-18C (N=209)	13.59 (11.91 to 15.51)			
Anti-19F (N=209)	11.83 (10.35 to 13.52)			
Anti-23F (N=209)	0.99 (0.86 to 1.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against vaccine pneumococcal serotypes

End point title	Opsonophagocytic activity (OPA) titers against vaccine pneumococcal serotypes[18]

End point description:

Seropositivity status was defined as the opsonophagocytic activity (OPA) against pneumococcal serotypes ≥ the value of 8, presented as geometric mean titers (GMTs). The vaccine pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F).
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

At Month 12, one month after the second vaccine dose

Notes:

[18] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	201			
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-1 (N=201)	125.6 (105 to 150.1)			
Opsono-4 (N=200)	2451.2 (2203.6 to 2726.8)			
Opsono-5 (N=198)	57.2 (47.3 to 69.1)			
Opsono-6B (N=196)	1345 (1066.8 to 1695.7)			

Opsono-7F (N=198)	6527.2 (5836.5 to 7299.6)			
Opsono-9V (N=197)	6091.6 (5328.7 to 6963.8)			
Opsono-14 (N=197)	4544.9 (4030.2 to 5125.4)			
Opsono-18C (N=196)	3827.5 (3367.5 to 4350.4)			
Opsono-19F (N=201)	1251 (1045.6 to 1496.8)			
Opsono-23F (N=198)	4629.1 (3890.6 to 5507.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine pneumococcal cross-reactive serotypes 6A and 19A

End point title	Antibody concentrations against vaccine pneumococcal cross-reactive serotypes 6A and 19A[19]

End point description:

The vaccine pneumococcal cross-reactive serotypes 6A and 19A have been assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in µg/mL. The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

At Month 12, one month after the second vaccine dose

Notes:

[19] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	209			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A	0.51 (0.43 to 0.6)			
Anti-19A	1.99 (1.68 to 2.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A[20]

End point description:

Seropositivity status was defined as the opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A (opsono-16A and opsono-19A) ≥ the value of 8, presented as geometric mean titers (GMTs).
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against at least one pneumococcal vaccine serotype were available after vaccination.

End point type	Secondary

End point timeframe:

At Month 12, one month after the second vaccine dose

Notes:

[20] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-6A (N=193)	918.6 (742.7 to 1136.1)			
Opsono-19A (N=196)	597.6 (467.2 to 764.4)			

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)[21]

End point description:

Anti-protein D (anti-PD) concentrations were presented as geometric mean concentrations (GMCs), expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off value of the assay was an antibody concentration ≥ 100 EL.U/mL.
The analysis was performed on the ATP cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures and assay results for antibodies against protein D were available after vaccination.

End point type	Secondary

End point timeframe:

At Month 12, one month after the second vaccine dose

Notes:

[21] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	209			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	785.9 (695.7 to 887.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rabbit complement-mediated serum bactericidal activity titers against Neisseria meningitidis serogroups (rSBA-Men)

End point title	Rabbit complement-mediated serum bactericidal activity titers against Neisseria meningitidis serogroups (rSBA-Men)[22]

End point description:

The Neisseria meningitidis serogroups assessed using rabbit complement were: A, C, W-135 and Y (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY), presented as geometric mean titers (GMTs). The seropositivity cut-off of the assay was an antibody titer ≥ 8.
The analysis was performed on the ATP cohort for antibody persistence, which included all subjects with the vaccine administration documented, for whom assay results were available for antibodies against each considered antigen for the blood sample taken before the administration of Synflorix vaccine.

End point type	Secondary

End point timeframe:

At 25-36 months post-vaccination in previous 107137 (NCT00496015) study

Notes:

[22] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	83			
Units: Titres				
geometric mean (confidence interval 95%)				
rSBA-MenA (N=66)	325.5 (243.9 to 434.5)			
rSBA-MenC (N=80)	63.6 (41.2 to 98)			
rSBA-MenY (N=83)	372.2 (270 to 513)			
rSBA-MenW-135 (N=83)	247.6 (190.7 to 321.5)			

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[23]

End point description:

Assessed solicited local symptoms 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 spreading beyond 30 millimeters (mm) of injection site. This outcome measure refers only to the primed groups.
The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

Notes:

[23] - 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 is only reporting values for the Synflorix I Group and the Synflorix II Group.

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	108		
Units: Subjects				
Any pain	75	67		
Grade 3 pain	7	5		
Any redness	58	60		
Grade 3 redness	13	12		
Any swelling	43	41		
Grade 3 swelling	11	11		

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[24]

End point description:

Assessed solicited local symptoms 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 spreading beyond 30 millimeters (mm) of injection site. This outcome measure refers only to the unprimed group.

The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses

Notes:

[24] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: Subjects				
Any pain, D1 (N=223)	150			
Grade 3 pain, D1 (N=223)	13			
Any redness, D1 (N=223)	102			
Grade 3 redness, D1 (N=223)	23			
Any swelling, D1 (N=223)	78			
Grade 3 swelling, D1 (N=223)	14			
Any pain, D2 (N=222)	121			
Grade 3 pain, D2 (N=222)	12			
Any redness, D2 (N=222)	93			
Grade 3 redness, D2 (N=222)	12			
Any swelling, D2 (N=222)	65			
Grade 3 swelling, D2 (N=222)	3			
Any pain, Across (N=223)	167			
Grade 3 pain, Across (N=223)	23			
Any redness, Across (N=223)	127			
Grade 3 redness, Across (N=223)	29			
Any swelling, Across (N=223)	101			
Grade 3 swelling, Across (N=223)	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

End point title	Number of subjects with any, grade 3 and related solicited general symptoms[25]

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination. Grade 3 drowsiness = drowsiness that 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 = fever > 39.5 °C. Related = symptom assessed by the investigator as causally related to study vaccination. This outcome measure refers only to the primed groups.
The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

Notes:

[25] - 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 is only reporting values for the Synflorix I Group and the Synflorix II Group.

End point values	Synflorix I Group	Synflorix II Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	108		
Units: Subjects				
Any drowsiness	41	34		
Related drowsiness	0	0		
Grade 3 drowsiness	26	26		
Any Irritability	33	26		
Related Irritability	1	0		
Grade 3 Irritability	21	16		
Any loss of appetite	23	15		
Related loss of appetite	1	1		
Grade 3 loss of appetite	13	10		
Any fever (Axillary/37.5°C)	12	8		
Grade 3 fever (Axillary/39.5°C)	0	1		
Related fever	10	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

End point title	Number of subjects with any, grade 3 and related solicited general symptoms[26]

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination. Grade 3 drowsiness = drowsiness that 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 = fever > 39.5 °C. Related = symptom assessed by the investigator as causally related to study vaccination. This outcome measure refers only to the unprimed group.
The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses

Notes:

[26] - 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 is only reporting values for the Synflorix III Group.

End point values	Synflorix III Group			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: Subjects				
Any drowsiness, D1 (N=223)	79			
Grade 3 drowsiness, D1 (N=223)	1			
Related drowsiness, D1 (N=223)	56			
Any Irritability, D1 (N=223)	69			
Grade 3 Irritability, D1 (N=223)	2			
Related irritability, D1 (N=223)	49			
Any loss of appetite, D1 (N=223)	47			
Grade 3 loss of appetite, D1 (N=223)	5			
Related loss of appetite, D1 (N=223)	32			
Any fever (Axillary/37.5°C), D1 (N=223)	23			
Grade 3 fever (Axillary/39.5°C), D1 (N=223)	1			
Related fever, D1 (N=223)	15			
Any drowsiness, D2 (N=222)	60			
Grade 3 drowsiness, D2 (N=222)	1			
Related drowsiness, D2 (N=222)	43			
Any Irritability, D2 (N=222)	59			
Grade 3 Irritability, D2 (N=222)	1			
Related irritability, D2 (N=222)	44			
Any loss of appetite, D2 (N=222)	26			
Grade 3 loss of appetite, D2 (N=222)	1			
Related loss of appetite, D2 (N=222)	16			
Any fever (Axillary/37.5°C), D2 (N=222)	9			
Grade 3 fever (Axillary/39.5°C), D2 (N=222)	1			
Related fever, D2 (N=222)	5			
Any drowsiness, Across (N=223)	102			
Grade 3 drowsiness, Across (N=223)	2			
Related drowsiness, Across (N=223)	73			
Any Irritability, Across (N=223)	98			
Grade 3 Irritability, Across (N=223)	3			
Related irritability, Across (N=223)	74			
Any loss of appetite, Across (N=223)	61			
Grade 3 loss of appetite, Across (N=223)	6			
Related loss of appetite, Across (N=223)	42			
Any fever (Axillary/37.5°C), Across (N=223)	30			
Grade 3 fever (Axillary/39.5°C), Across (N=223)	2			
Related fever, Across (N=223)	19			

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 (AEs)

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.
The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

Within 31 days (Days 0-30) after each vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix III Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	108	223	
Units: Subjects				
Any AE(s)	24	29	73	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.
The analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Month 10 or Month 12)

End point values	Synflorix I Group	Synflorix II Group	Synflorix III Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	108	223	
Units: Subjects				
Any SAE(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with Streptococcus pneumoniae (vaccine serotypes)

End point title	Number of nasopharyngeal swabs with Streptococcus pneumoniae (vaccine serotypes)[27]

End point description:

Positive cultures of S. pneumoniae Synflorix vaccine serotypes identified in the nasopharynx were recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[27] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Swabs				
31-44 months (N=210;216)	40	21		
40-48 months (N=208;212)	46	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with S.pneumoniae (cross-reactive serotypes)

End point title	Number of nasopharyngeal swabs with S.pneumoniae (cross-reactive serotypes)[28]

End point description:

Positive cultures of S. pneumoniae cross- reactive serotypes identified in the nasopharynx were recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[28] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Swabs				
31-44 months (N=210;216)	9	13		
40-48 months (N=208;212)	19	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with S.pneumoniae (non-vaccine and non-cross-reactive serotypes)

End point title	Number of nasopharyngeal swabs with S.pneumoniae (non-vaccine and non-cross-reactive serotypes)[29]

End point description:

Positive cultures of S. pneumoniae non- Synflorix vaccine, non-cross-reactive serotypes identified in the nasopharynx were recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[29] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Swabs				
31-44 months (N=210;216)	25	34		
40-48 months (N=208;212)	27	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with Haemophilus influenzae

End point title	Number of nasopharyngeal swabs with Haemophilus

End point description:

Positive cultures of H. influenzae identified in the nasopharynx were recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[30] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Swabs				
31-44 months (N=210;216)	43	54		
40-48 months (N=208;212)	89	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new acquisition of S. pneumoniae (vaccine serotypes) in nasopharyngeal swabs

End point title	Number of subjects with new acquisition of S. pneumoniae (vaccine serotypes) in nasopharyngeal swabs[31]

End point description:

The number of subjects with new acquisition of S. pneumoniae (Synflorix vaccine serotypes) detected in nasopharyngeal swabs was recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[31] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Subjects				
31-44 months (N=210;216)	39	20		
40-48 months (N=208;212)	41	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new acquisition of S. pneumoniae (cross-reactive serotypes) in nasopharyngeal swabs

End point title	Number of subjects with new acquisition of S. pneumoniae (cross-reactive serotypes) in nasopharyngeal swabs[32]

End point description:

The number of subjects with new acquisition of S. pneumoniae (cross-reactive serotypes) detected in nasopharyngeal swabs was recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[32] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Subjects				
31-44 months (N=210;216)	9	13		
40-48 months (N=208;212)	18	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new acquisition of S. pneumoniae (non-vaccine and non-cross-reactive serotypes) in nasopharyngeal swabs

End point title	Number of subjects with new acquisition of S. pneumoniae (non-vaccine and non-cross-reactive serotypes) in nasopharyngeal swabs[33]

End point description:

The number of subjects with new acquisition of S. pneumoniae (non-vaccine and non-cross-reactive serotypes) detected in nasopharyngeal swabs was recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[33] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Subjects				
31-44 months (N=210;216)	24	32		
40-48 months (N=208;212)	25	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new acquisition of H. influenzae in nasopharyngeal swabs

End point title	Number of subjects with new acquisition of H. influenzae in nasopharyngeal swabs[34]

End point description:

The number of subjects with new acquisition of H. influenzae detected in nasopharyngeal swabs was recorded.
The analysis was performed on the ATP cohort for carriage, which included all evaluable subjects for whom carriage outcome measures were available after the swab time point.

End point type	Secondary

End point timeframe:

At 31-44 months of age and prior to the first vaccine dose, at 40-48 months of age

Notes:

[34] - 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 is only reporting values for the Synflorix III Group and the Pooled primed Group.

End point values	Synflorix III Group	Pooled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	216		
Units: Subjects				
31-44 months (N=210;216)	35	49		
40-48 months (N=208;212)	70	50		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4-day (Days 0-3) follow-up periods after vaccination. Unsolicited AEs: within the 31-day (Days 0-30) follow-up periods after vaccination. SAEs: during the entire study period (from Day 0 up to Month 10/12).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Synflorix I Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects received prophylactic antipyretic (AP) treatment with paracetamol.

Reporting group title	Synflorix II Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were previously given 3 primary vaccination doses of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107017 (NCT00370318) and one booster dose of Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study one dose of Synflorix vaccine at Month 9 (40-48 months of age), administered intramuscularly in the deltoid muscle. At the time of both primary and booster vaccinations, subjects did not receive any prophylactic antipyretic (AP) treatment.

Reporting group title	Synflorix III Group

Reporting group description:

Healthy male or female subjects between and including 31 and 44 months of age at the time of enrolment, who were not previously primed with Synflorix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), but vaccinated with Nimenrix vaccine co-administered with Infanrix Hexa vaccine in study 107137 (NCT00496015), additionally received in the current study 2 doses of Synflorix vaccine at Month 9 (40-48 months of age) and at Month 11 (42-50 months of age), administered intramuscularly in the deltoid muscle.

Serious adverse events	Synflorix I Group	Synflorix II Group	Synflorix III Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 112 (0.00%)	0 / 108 (0.00%)	0 / 223 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Synflorix I Group	Synflorix II Group	Synflorix III Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 112 (85.71%)	86 / 108 (79.63%)	190 / 223 (85.20%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	75 / 112 (66.96%)	67 / 108 (62.04%)	167 / 223 (74.89%)
occurrences (all)	75	67	167
Redness			
subjects affected / exposed	58 / 112 (51.79%)	60 / 108 (55.56%)	127 / 223 (56.95%)
occurrences (all)	58	60	127
Swelling			
subjects affected / exposed	43 / 112 (38.39%)	41 / 108 (37.96%)	101 / 223 (45.29%)
occurrences (all)	43	41	101
Drowsiness			
subjects affected / exposed	41 / 112 (36.61%)	34 / 108 (31.48%)	102 / 223 (45.74%)
occurrences (all)	41	34	102
Irritability			
subjects affected / exposed	33 / 112 (29.46%)	26 / 108 (24.07%)	98 / 223 (43.95%)
occurrences (all)	33	26	98
Loss of appetite			
subjects affected / exposed	23 / 112 (20.54%)	15 / 108 (13.89%)	61 / 223 (27.35%)
occurrences (all)	23	15	61
Fever/(Axillary ≥ 37.5°C)			
subjects affected / exposed	12 / 112 (10.71%)	8 / 108 (7.41%)	30 / 223 (13.45%)
occurrences (all)	12	8	30

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2011	The primary objective of the current study is to demonstrate the immunological memory induced following primary vaccination in study 10PN-PD-DIT-010 (107017) and booster vaccination in study 10PN-PD-DIT-014 (107137) with the 10Pn-PD-DiT vaccine, through evaluation of early antibody responses after an additional dose of 10Pn-PD-DiT at 40-48 months of age. In addition, as secondary objective, the antibody persistence 25-36 months following vaccination with GSK Biologicals' MenACWYTT conjugate vaccine in study 10PN-PD-DIT-014 (107137) will be evaluated in terms of the percentage of subjects with N. meningitidis serogroup A, C, W-135 and Y titers ≥ 8 as measured by a serum bactericidal assay using rabbit complement (rSBA). In addition, to support the data obtained by rSBA testing, antibody concentrations against meningococcal polysaccharides are planned to be assessed by ELISA. However, the sponsor has decided not to perform the ELISA testing against meningococcal polysaccharides for this study for the following reasons: ● the World Health Organization (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines [WHO, 2006; WHO, 1999] ● circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than antibodies against meningococcal polysaccharides [CDC, 2011; WHO, 2006]. Although antibody concentrations will not be determined by ELISA, all subjects will be informed of their antibody titers measured by rSBA when statistical analyses have been completed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported