



Clinical trial results:

Prophylactic Antipyretic Treatment in Children Receiving Booster Dose of Pneumococcal Vaccine GSK1024850A and DTPa-HBV-IPV/Hib Vaccine (Infanrix Hexa) and Assessment of Impact of Pneumococcal Vaccination on Nasopharyngeal Carriage

Summary

EudraCT number	2006-001481-17
Trial protocol	CZ
Global end of trial date	17 February 2009

Results information

Result version number	v3 (current)
This version publication date	22 July 2022
First version publication date	30 July 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	107137
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00496015
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 July 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 March 2008
Global end of trial reached?	Yes
Global end of trial date	17 February 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the percentage reduction in febrile reactions [rectal temperature greater than or equal to ($\geq$) 38.0 degrees celsius($^{\circ}$ C) or oral/axillary/tympanic $\geq$ 37.5 $^{\circ}$ C] when prophylactic antipyretic treatment is administered compared to no prophylactic antipyretic treatment, after booster vaccination with GSK Biologicals' 10-valent pneumococcal conjugate vaccine and routine Diphtheria-tetanus-acellular pertussis-hepatitis B virus-inactivated poliovirus and Haemophilus influenzae type b vaccine (DTPa-HBV-IPV/Hib) (Infanrix hexa) vaccination in children at 12-15 months of age.

Protection of trial subjects:

The vaccines 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 vaccine(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2007
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: 750
Worldwide total number of subjects	750
EEA total number of subjects	750

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)	750
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:

This was a multicenter study with the same centers as the primary vaccination study 10PN-PD-DIT-010 (107017) and all subjects enrolled in the primary vaccination study and received 10Pn-PD-DIT (Synflorix) vaccine were invited to participate in the study. In addition, an age-matched pneumococcal vaccine unprimed control group has been enrolled.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	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:

Subjects were vaccinated with 3 primary vaccination doses of Synflorix (10Pn) vaccine with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa along with prophylactic antipyretic treatment.

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	GSK1024850A
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 booster dose at 12-15 months of age, into the right thigh or deltoid region.

Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One booster dose at 12-15 months of age, into the left thigh or deltoid region.

Investigational medicinal product name	PANADOL 125 mg
Investigational medicinal product code	
Other name	Panadol 125
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

The prophylactic antipyretic treatment was administered as rectal suppositories according to the subject's body weight.

Arm title	Synflorix II Group
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Arm description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	GSK1024850A
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 booster dose at 12-15 months of age, into the right thigh or deltoid region.

Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One booster dose at 12-15 months of age, into the left thigh or deltoid region.

Arm title	Synflorix PRE Group
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Arm description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (before the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Arm type	Active comparator
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	GSK1024850A
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 booster dose at 12-15 months of age, into the right thigh or deltoid region.

Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One booster dose at 12-15 months of age, into the left thigh or deltoid region.

Arm title	Synflorix POST Group
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Arm description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (after the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Arm type	Active comparator
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Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	GSK1024850A
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 booster dose at 12-15 months of age, into the right thigh or deltoid region.

Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One booster dose at 12-15 months of age, into the left thigh or deltoid region.

Arm title	Mencevax + Infanrix Hexa Group
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Arm description:

Age-matched pneumococcal vaccine unprimed group received a single dose of Mencevax vaccine co-administered with Infanrix hexa vaccine.

Arm type	Active comparator
Investigational medicinal product name	Mencevax vaccine
Investigational medicinal product code	GSK134612
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose at 12-15 months of age, into the right thigh or deltoid region.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose at 12-15 months of age, into the left thigh or deltoid region.

Number of subjects in period 1	Synflorix I Group	Synflorix II Group	Synflorix PRE Group
Started	178	27	172
Completed	177	27	172
Not completed	1	0	0
Unspecified	1	-	-

Number of subjects in period 1	Synflorix POST Group	Mencevax + Infanrix Hexa Group
Started	37	336
Completed	36	336
Not completed	1	0

Unspecified	1	-
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Baseline characteristics

Reporting groups

Reporting group title	Synflorix I Group
Reporting group description:	
Subjects were vaccinated with 3 primary vaccination doses of Synflorix (10Pn) vaccine with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa along with prophylactic antipyretic treatment.	
Reporting group title	Synflorix II Group
Reporting group description:	
Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.	
Reporting group title	Synflorix PRE Group
Reporting group description:	
Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (before the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.	
Reporting group title	Synflorix POST Group
Reporting group description:	
Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (after the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.	
Reporting group title	Mencevax + Infanrix Hexa Group
Reporting group description:	
Age-matched pneumococcal vaccine unprimed group received a single dose of Mencevax vaccine co-administered with Infanrix hexa vaccine.	

Reporting group values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group
Number of subjects	178	27	172
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)	178	27	172
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	12.6	13.2	12.7
standard deviation	± 0.77	± 0.74	± 0.77

Gender categorical Units: Subjects			
Female	90	11	79
Male	88	16	93

Reporting group values	Synflorix POST Group	Mencevax + Infanrix Hexa Group	Total
Number of subjects	37	336	750
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)	37	336	750
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	13.1	13.1	
standard deviation	± 1.15	± 1.1	-
Gender categorical Units: Subjects			
Female	18	155	353
Male	19	181	397

Subject analysis sets

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

Subject analysis set description:

For carriage analyses the Synforix I, Synforix II, Synflorix PRE Group and Synflorix POST Group were pooled.

Subject analysis set title	Pooled Synflorix PRE and POST Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pooled group with subjects from both, Synflorix PRE Group and Synflorix POST Group, that received in this study (before and after the implementation of the protocol amendment) a booster dose of Synforix vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group values	Pooled Synflorix Group	Pooled Synflorix PRE and POST Group	
Number of subjects	414	209	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	414	209	

Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: months			
arithmetic mean	12.73	12.8	
standard deviation	± 0.83	± 0.86	
Gender categorical			
Units: Subjects			
Female	198	97	
Male	216	112	

End points

End points reporting groups

Reporting group title	Synflorix I Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of Synflorix (10Pn) vaccine with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa along with prophylactic antipyretic treatment.

Reporting group title	Synflorix II Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Synflorix PRE Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (before the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Synflorix POST Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study (after the implementation of the protocol amendment) at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Mencevax + Infanrix Hexa Group
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Reporting group description:

Age-matched pneumococcal vaccine unprimed group received a single dose of Mencevax vaccine co-administered with Infanrix hexa vaccine.

Subject analysis set title	Pooled Synflorix Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

For carriage analyses the Synforix I, Synforix II, Synflorix PRE Group and Synflorix POST Group were pooled.

Subject analysis set title	Pooled Synflorix PRE and POST Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Pooled group with subjects from both, Synflorix PRE Group and Synflorix POST Group, that received in this study (before and after the implementation of the protocol amendment) a booster dose of Synforix vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Primary: Number of subjects reported with core fever (rectal temperature) $\geq$ the cut-off

End point title	Number of subjects reported with core fever (rectal temperature) $\geq$ the cut-off
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End point description:

The cut-off for core fever was 38.0°C.

End point type	Primary
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End point timeframe:

Within 4 days (Day 0-Day 3) after primary vaccine dose

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Fever $\geq 38.0^{\circ}\text{C}$	64	14	100	16

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Fever $\geq 38.0^{\circ}\text{C}$	146			

Statistical analyses

Statistical analysis title	Difference between groups (core fever $\geq 38.0^{\circ}\text{C}$)
Comparison groups	Synflorix PRE Group v Synflorix I Group
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
Parameter estimate	Difference in percentages
Point estimate	22.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.78
upper limit	32.11

Notes:

[1] - Superiority was demonstrated if the lower limit (LL) computed standardized asymptotic 95 percent (%) CI was above 0%.

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

End point title	Number of subjects reported with core fever (rectal temperature) greater than (>) the cut-off
End point description:	
The cut-off value for core fever (rectal temperature) was 39.0°C .	
End point type	Secondary
End point timeframe:	
Within 4 days (Day 0-Day 3) after primary vaccination dose	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Fever (rectal temperature) > 39.0°C	4	0	14	1

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Fever (rectal temperature) > 39.0°C	16			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with any and Grade 3 solicited local symptoms
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End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any occurrence of the specified symptom regardless of intensity. Grade 3 pain was defined as cried when limb was moved/spontaneously painful. Grade 3 redness/swelling was defined as redness/swelling > 30 millimeters (mm) from injection site

End point type	Secondary
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End point timeframe:

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

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Any Pain	54	10	79	19
Grade 3 Pain	2	2	10	3
Any Redness	89	9	74	12
Grade 3 Redness	7	1	14	1
Any Swelling	52	8	50	13
Grade 3 Swelling	2	1	9	3

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Any Pain	114			
Grade 3 Pain	4			
Any Redness	146			
Grade 3 Redness	16			
Any Swelling	71			
Grade 3 Swelling	12			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with any, Grade 3 and related solicited general symptoms
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End point description:

Solicited general symptoms assessed were drowsiness, fever (rectal temperature $\geq 38.5^{\circ}\text{C}$), irritability and loss of appetite. Any was defined as any occurrence of the specified symptom regardless of intensity and relation to vaccination. Grade 3 drowsiness was defined as drowsiness that prevented normal activity. Grade 3 fever was defined as rectal temperature $>40.0^{\circ}\text{C}$. Grade 3 irritability was defined as crying that could not be comforted/ prevented normal activity. Grade 3 loss of appetite was defined as not eating at all. Related was defined as solicited symptoms assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Any Drowsiness	91	11	84	18
Grade 3 Drowsiness	0	0	1	1
Related Drowsiness	84	11	79	18
Any Fever (rectal temperature $\geq 38.0^{\circ}\text{C}$)	64	14	100	16
Grade 3 Fever (rectal temperature $> 40.0^{\circ}\text{C}$)	1	0	1	0
Related Fever (rectal temperature $> 40.0^{\circ}\text{C}$)	62	14	99	16
Any Irritability	86	17	105	19
Grade 3 Irritability	1	0	2	2
Related Irritability	80	17	98	18

Any Loss of appetite	47	8	46	10
Grade 3 Loss of appetite	0	0	4	1
Related Loss of appetite	42	7	41	10

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Any Drowsiness	146			
Grade 3 Drowsiness	2			
Related Drowsiness	120			
Any Fever (rectal temperature $\geq$ 38.0°C)	146			
Grade 3 Fever (rectal temperature > 40.0°C)	3			
Related Fever (rectal temperature > 40.0°C)	140			
Any Irritability	147			
Grade 3 Irritability	2			
Related Irritability	129			
Any Loss of appetite	88			
Grade 3 Loss of appetite	3			
Related Loss of appetite	71			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with unsolicited adverse events (AEs) ^[2]
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End point description:

The outcome measure was not reporting statistics for all the arms in the baseline period. Results were tabulated on baseline groups except for the Synforix PRE and Synforix POST groups, for which results were presented for the Pooled Synforix PRE and POST Group. 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.

End point type	Secondary
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End point timeframe:

Within 31 days (Day 0-Day 30) after primary vaccine dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Synforix I Group, Synforix II Group, Mencevax + Infanrix Hexa Group and the Pooled Synforix PRE and POST Group.

End point values	Synflorix I Group	Synflorix II Group	Mencevax + Infanrix Hexa Group	Pooled Synflorix PRE and POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	178	27	336	209
Units: Subjects				
Subject(s) with any AE(s)	22	3	64	30

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with serious adverse events (SAEs)
End point description: SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.	
End point type	Secondary
End point timeframe: Throughout the entire study period (Month 0-Month 12)	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Subject(s) with any SAE(s)	13	5	13	4

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Subject(s) with any SAE(s)	30			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with AEs resulting in rash, new onset of chronic illness (NOCI), emergency room (ER) visits and non-routine physician office

visits

End point title	Number of subjects reported with AEs resulting in rash, new onset of chronic illness (NOCI), emergency room (ER) visits and non-routine physician office visits ^[3]
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End point description:

Results were tabulated only on Mencevax + Infanrix Hexa Group, according to the outcome measure specification of the protocol.

End point type	Secondary
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End point timeframe:

Up to 6 months after vaccination with Mencevax

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting values for the Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Subject(s) with any rash(es)	7			
Subject(s) with any NOCI(s)	1			
Subject(s) with any ER visit(s)	0			
Subject(s) with any visit(s) at physician office	53			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against pneumococcal serotypes >= the cut-off

End point title	Number of subjects with antibody concentrations against pneumococcal serotypes >= the cut-off
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End point description:

Certain pneumococcal serotypes includes 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). Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA). The seroprotection cut-off for the assay was >= 0.2 microgram per milliliter (µg/mL).

End point type	Secondary
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End point timeframe:

Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	25	168	37
Units: Subjects				
ANTI-1 PRE(N=132,25,163,37,284)	74	14	115	27
ANTI-1 M1(N=140,24,167,36,244)	140	24	167	36
ANTI-1 M12(N=138,25,167,36,263)	89	11	122	30
ANTI-4 PRE(N=139,25,160,35,289)	123	15	147	31
ANTI-4 M1(N=141,24,167,37,261)	141	24	167	37
ANTI-4 M12(N=139,25,168,36,288)	103	14	147	27
ANTI-5 PRE(N=131,25,156,37,277)	102	15	142	30
ANTI-5 M1(N=140,24,167,36,256)	140	23	167	36
ANTI-5 M12(N=139,25,168,36,281)	113	18	159	30
ANTI-6B PRE(N=139,25,164,37,282)	110	13	143	32
ANTI-6B M1(N=140,24,167,36,282)	134	21	166	35
ANTI-6B M12(N=139,25,168,36,289)	97	18	148	30
ANTI-7F PRE(N=136,24,159,35,281)	130	21	156	34
ANTI-7F M1(N=140,25,167,37,265)	140	25	167	37
ANTI-7F M12(N=139,25,168,36,283)	132	21	165	36
ANTI-9V PRE(N=127,24,154,35,279)	117	20	152	34
ANTI-9V M1(N=141,25,167,37,266)	141	24	167	37
ANTI-9V M12(N=139,25,168,36,285)	129	20	166	35
ANTI-14 PRE(N=136,25,164,37,274)	131	22	159	35
ANTI-14 M1(N=140,24,167,36,261)	140	24	166	36
ANTI-14 M12(N=139,25,168,36,277)	131	21	166	34
ANTI-18C PRE(N=135,25,163,35,275)	118	14	154	29
ANTI-18C M1(N=141,25,167,37,269)	141	25	167	37
ANTI-18C M12(N=139,25,168,36,281)	113	18	157	35
ANTI-19F PRE(N=137,25,165,37,278)	128	21	163	36
ANTI-19F M1(N=141,25,167,37,269)	138	25	165	37
ANTI-19F M12(N=138,25,168,36,283)	135	22	165	36
ANTI-23F PRE(N=136,25,155,35,275)	103	14	132	30
ANTI-23F M1(N=140,24,167,37,259)	135	21	163	36
ANTI-23F M12(N=139,25,168,36,289)	115	16	154	33

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Subjects				
ANTI-1 PRE(N=132,25,163,37,284)	6			
ANTI-1 M1(N=140,24,167,36,244)	5			
ANTI-1 M12(N=138,25,167,36,263)	11			
ANTI-4 PRE(N=139,25,160,35,289)	6			
ANTI-4 M1(N=141,24,167,37,261)	6			
ANTI-4 M12(N=139,25,168,36,288)	20			
ANTI-5 PRE(N=131,25,156,37,277)	6			
ANTI-5 M1(N=140,24,167,36,256)	10			

ANTI-5 M12(N=139,25,168,36,281)	31			
ANTI-6B PRE(N=139,25,164,37,282)	1			
ANTI-6B M1(N=140,24,167,36,282)	1			
ANTI-6B M12(N=139,25,168,36,289)	21			
ANTI-7F PRE(N=136,24,159,35,281)	5			
ANTI-7F M1(N=140,25,167,37,265)	9			
ANTI-7F M12(N=139,25,168,36,283)	20			
ANTI-9V PRE(N=127,24,154,35,279)	5			
ANTI-9V M1(N=141,25,167,37,266)	10			
ANTI-9V M12(N=139,25,168,36,285)	30			
ANTI-14 PRE(N=136,25,164,37,274)	25			
ANTI-14 M1(N=140,24,167,36,261)	29			
ANTI-14 M12(N=139,25,168,36,277)	63			
ANTI-18C PRE(N=135,25,163,35,275)	8			
ANTI-18C M1(N=141,25,167,37,269)	9			
ANTI-18C M12(N=139,25,168,36,281)	29			
ANTI-19F PRE(N=137,25,165,37,278)	17			
ANTI-19F M1(N=141,25,167,37,269)	24			
ANTI-19F M12(N=138,25,168,36,283)	90			
ANTI-23F PRE(N=136,25,155,35,275)	2			
ANTI-23F M1(N=140,24,167,37,259)	4			
ANTI-23F M12(N=139,25,168,36,289)	24			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes >= the cut-off

End point title	Antibody concentrations against pneumococcal serotypes >= the cut-off
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End point description:

Certain pneumococcal serotypes included 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). Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA). Seropositivity cut-off for the assay was >= 0.05 microgram per milliliter (µg/mL).

End point type	Secondary
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End point timeframe:

Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	25	168	37
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 PRE(N=132,25,163,37,284)	0.22 (0.19 to 0.25)	0.18 (0.12 to 0.27)	0.31 (0.27 to 0.35)	0.26 (0.19 to 0.35)

ANTI-1 M1(N=140,24,167,36,244)	1.67 (1.47 to 1.9)	1.64 (1.08 to 2.47)	2.62 (2.3 to 2.99)	2.97 (2.21 to 3.99)
ANTI-1 M12(N=138,25,167,36,263)	0.26 (0.22 to 0.31)	0.18 (0.12 to 0.29)	0.39 (0.34 to 0.45)	0.41 (0.31 to 0.56)
ANTI-4 PRE(N=139,25,160,35,289)	0.4 (0.35 to 0.45)	0.24 (0.17 to 0.35)	0.6 (0.52 to 0.69)	0.45 (0.35 to 0.58)
ANTI-4 M1(N=141,24,167,37,261)	3.01 (2.69 to 3.36)	2.84 (1.98 to 4.08)	4.21 (3.72 to 4.76)	3.95 (2.97 to 5.26)
ANTI-4 M12(N=139,25,168,36,288)	0.34 (0.29 to 0.39)	0.21 (0.13 to 0.33)	0.5 (0.43 to 0.56)	0.55 (0.39 to 0.78)
ANTI-5 PRE(N=131,25,156,37,277)	0.36 (0.32 to 0.42)	0.31 (0.18 to 0.52)	0.59 (0.52 to 0.68)	0.53 (0.36 to 0.78)
ANTI-5 M1(N=140,24,167,36,256)	2.3 (2.04 to 2.6)	2 (1.31 to 3.06)	3.68 (3.26 to 4.15)	3.03 (2.16 to 4.26)
ANTI-5 M12(N=139,25,168,36,281)	0.42 (0.36 to 0.48)	0.35 (0.23 to 0.52)	0.72 (0.63 to 0.83)	0.58 (0.42 to 0.81)
ANTI-6B PRE(N=139,25,164,37,282)	0.35 (0.3 to 0.41)	0.18 (0.1 to 0.32)	0.55 (0.48 to 0.63)	0.5 (0.35 to 0.72)
ANTI-6B M1(N=140,24,167,36,282)	1.35 (1.12 to 1.61)	0.89 (0.46 to 1.72)	2.45 (2.17 to 2.77)	2.25 (1.51 to 3.33)
ANTI-6B M12(N=139,25,168,36,289)	0.4 (0.32 to 0.5)	0.36 (0.19 to 0.66)	0.56 (0.47 to 0.68)	0.54 (0.37 to 0.81)
ANTI-7F PRE(N=136,24,159,35,281)	0.74 (0.65 to 0.84)	0.55 (0.4 to 0.76)	1.05 (0.93 to 1.18)	0.87 (0.66 to 1.13)
ANTI-7F M1(N=140,25,167,37,265)	2.9 (2.59 to 3.25)	2.37 (1.86 to 3.03)	4.13 (3.69 to 4.63)	4.38 (3.35 to 5.72)
ANTI-7F M12(N=139,25,168,36,283)	0.68 (0.6 to 0.78)	0.45 (0.32 to 0.63)	0.91 (0.82 to 1.02)	0.96 (0.74 to 1.24)
ANTI-9V PRE(N=127,24,154,35,279)	0.61 (0.53 to 0.7)	0.59 (0.33 to 1.05)	1 (0.88 to 1.13)	0.99 (0.78 to 1.26)
ANTI-9V M1(N=141,25,167,37,266)	2.86 (2.52 to 3.23)	2.57 (1.73 to 3.81)	4.39 (3.91 to 4.94)	4.35 (3.3 to 5.73)
ANTI-9V M12(N=139,25,168,36,285)	0.67 (0.56 to 0.8)	0.55 (0.33 to 0.92)	0.97 (0.85 to 1.12)	0.86 (0.64 to 1.17)
ANTI-14 PRE(N=136,25,164,37,274)	0.82 (0.69 to 0.96)	0.52 (0.36 to 0.74)	1.57 (1.32 to 1.86)	1.27 (0.86 to 1.88)
ANTI-14 M1(N=140,24,167,36,261)	4.58 (4.05 to 5.18)	4.37 (3.01 to 6.33)	5.95 (5.28 to 6.71)	5.86 (4.35 to 7.89)
ANTI-14 M12(N=139,25,168,36,277)	0.89 (0.73 to 1.09)	0.94 (0.48 to 1.84)	1.54 (1.3 to 1.81)	1.25 (0.9 to 1.76)
ANTI-18C PRE(N=135,25,163,35,275)	0.47 (0.41 to 0.54)	0.29 (0.2 to 0.43)	0.78 (0.69 to 0.89)	0.54 (0.39 to 0.76)
ANTI-18C M1(N=141,25,167,37,269)	4.96 (4.4 to 5.6)	3.46 (2.35 to 5.09)	7 (6.28 to 7.79)	6.13 (4.85 to 7.75)
ANTI-18C M12(N=139,25,168,36,281)	0.56 (0.47 to 0.66)	0.44 (0.27 to 0.72)	1.05 (0.92 to 1.21)	0.92 (0.69 to 1.21)
ANTI-19F PRE(N=137,25,165,37,278)	0.98 (0.81 to 1.19)	0.63 (0.39 to 1.02)	1.48 (1.27 to 1.73)	1.4 (1 to 1.97)
ANTI-19F M1(N=141,25,167,37,269)	6 (5.08 to 7.08)	4.84 (3.47 to 6.77)	7.55 (6.48 to 8.79)	8.77 (6.68 to 11.53)
ANTI-19F M12(N=138,25,168,36,283)	1.46 (1.18 to 1.82)	0.82 (0.56 to 1.2)	1.8 (1.52 to 2.13)	2.04 (1.41 to 2.94)
ANTI-23F PRE(N=136,25,155,35,275)	0.38 (0.31 to 0.46)	0.3 (0.16 to 0.58)	0.54 (0.45 to 0.64)	0.45 (0.31 to 0.65)
ANTI-23F M1(N=140,24,167,37,259)	1.99 (1.67 to 2.38)	1.33 (0.64 to 2.78)	2.92 (2.5 to 3.4)	3.86 (2.52 to 5.91)
ANTI-23F M12(N=139,25,168,36,289)	0.46 (0.38 to 0.56)	0.29 (0.16 to 0.52)	0.8 (0.67 to 0.95)	0.98 (0.69 to 1.39)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 PRE(N=132,25,163,37,284)	0.03 (0.03 to 0.03)			
ANTI-1 M1(N=140,24,167,36,244)	0.03 (0.03 to 0.03)			
ANTI-1 M12(N=138,25,167,36,263)	0.04 (0.04 to 0.04)			
ANTI-4 PRE(N=139,25,160,35,289)	0.03 (0.03 to 0.03)			
ANTI-4 M1(N=141,24,167,37,261)	0.03 (0.03 to 0.03)			
ANTI-4 M12(N=139,25,168,36,288)	0.04 (0.03 to 0.04)			
ANTI-5 PRE(N=131,25,156,37,277)	0.04 (0.03 to 0.04)			
ANTI-5 M1(N=140,24,167,36,256)	0.04 (0.03 to 0.04)			
ANTI-5 M12(N=139,25,168,36,281)	0.06 (0.05 to 0.06)			
ANTI-6B PRE(N=139,25,164,37,282)	0.03 (0.03 to 0.03)			
ANTI-6B M1(N=140,24,167,36,282)	0.03 (0.03 to 0.03)			
ANTI-6B M12(N=139,25,168,36,289)	0.04 (0.04 to 0.04)			
ANTI-7F PRE(N=136,24,159,35,281)	0.03 (0.03 to 0.03)			
ANTI-7F M1(N=140,25,167,37,265)	0.03 (0.03 to 0.03)			
ANTI-7F M12(N=139,25,168,36,283)	0.04 (0.04 to 0.04)			
ANTI-9V PRE(N=127,24,154,35,279)	0.03 (0.03 to 0.03)			
ANTI-9V M1(N=141,25,167,37,266)	0.03 (0.03 to 0.03)			
ANTI-9V M12(N=139,25,168,36,285)	0.04 (0.04 to 0.05)			
ANTI-14 PRE(N=136,25,164,37,274)	0.04 (0.04 to 0.05)			
ANTI-14 M1(N=140,24,167,36,261)	0.05 (0.04 to 0.05)			
ANTI-14 M12(N=139,25,168,36,277)	0.11 (0.09 to 0.13)			
ANTI-18C PRE(N=135,25,163,35,275)	0.03 (0.03 to 0.03)			
ANTI-18C M1(N=141,25,167,37,269)	0.03 (0.03 to 0.03)			
ANTI-18C M12(N=139,25,168,36,281)	0.04 (0.04 to 0.05)			
ANTI-19F PRE(N=137,25,165,37,278)	0.03 (0.03 to 0.04)			
ANTI-19F M1(N=141,25,167,37,269)	0.05 (0.04 to 0.05)			
ANTI-19F M12(N=138,25,168,36,283)	0.12 (0.1 to 0.14)			

ANTI-23F PRE(N=136,25,155,35,275)	0.03 (0.03 to 0.03)			
ANTI-23F M1(N=140,24,167,37,259)	0.03 (0.03 to 0.03)			
ANTI-23F M12(N=139,25,168,36,289)	0.04 (0.03 to 0.04)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F
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End point description:

OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8 .

End point type	Secondary
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End point timeframe:

Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	131	25	161	35
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 PRE(N=125,25,152,31,26)	6.1 (5 to 7.4)	5.6 (4 to 8)	8.1 (6.6 to 10)	6 (4.2 to 8.5)
OPSONO-1 M1(N=130,23,156,34,39)	144.6 (109.6 to 190.6)	193.4 (95.8 to 390.8)	417 (330.6 to 526.2)	325 (178.8 to 590.7)
OPSONO-1 M12(N=129,21,153,34,126)	12.8 (10 to 16.5)	12.5 (6.8 to 23.2)	23.1 (18.2 to 29.2)	20.5 (13.1 to 32.3)
OPSONO-4 PRE(N=121,22,148,31,31)	23.8 (16.5 to 34.2)	8.8 (5.2 to 14.9)	44.9 (33.2 to 60.8)	29.7 (14.3 to 61.6)
OPSONO-4 M1(N=130,22,158,32,23)	1547.9 (1357.9 to 1764.4)	971.6 (615.8 to 1532.7)	2297 (2005.8 to 2630.4)	1303.2 (918.6 to 1849)
OPSONO-4 M12(N=125,21,152,33,119)	19.9 (13.9 to 28.6)	14.9 (6.4 to 34.8)	51.2 (36.2 to 72.4)	72.5 (33.7 to 156.1)
OPSONO-5 PRE(N=121,24,146,31,26)	8.5 (7 to 10.4)	10.4 (6.2 to 17.4)	16.6 (13.2 to 20.9)	15.1 (8.8 to 25.9)
OPSONO-5 M1(N=130,23,156,34,45)	134.3 (109.8 to 164.2)	105 (55.9 to 196.9)	289.3 (243.5 to 343.7)	227.7 (130.7 to 396.6)
OPSONO-5 M12(N=124,21,154,32,135)	10.3 (8.3 to 12.9)	10.5 (5.9 to 18.7)	23.7 (18.9 to 29.8)	15.4 (10.2 to 23.2)
OPSONO-6B PRE(N=126,22,154,31,25)	32.5 (21.6 to 48.9)	15.9 (6 to 42.1)	45.2 (32.9 to 62.2)	49.7 (23 to 107.3)
OPSONO-6B M1(N=130,22,157,34,29)	496.7 (351.4 to 702.2)	148.3 (46.5 to 472.5)	985.7 (807.1 to 1203.9)	718.3 (445.7 to 1157.5)

OPSONO-6B M12(N=123,22,145,31,113)	46.9 (29.6 to 74.2)	97.7 (27.7 to 345.1)	53.9 (36.1 to 80.4)	29.4 (13.2 to 65.2)
OPSONO-7F PRE(N=115,22,148,32,23)	413.6 (266.1 to 642.9)	221.4 (65.7 to 745.9)	584.7 (426.1 to 802.3)	258.4 (119.9 to 556.7)
OPSONO-7F M1(N=130,23,158,34,28)	4025.8 (3457.3 to 4687.9)	1749 (1144.2 to 2673.4)	4674.7 (4102.2 to 5327)	2212.2 (1569.1 to 3118.7)
OPSONO-7F M12(N=130,25,159,34,118)	1503.3 (1209.1 to 1869.2)	1606.4 (1101.4 to 2343)	1285.7 (1050.8 to 1573)	1738.3 (1330.6 to 2271)
OPSONO-9V PRE(N=119,21,147,31,23)	420.7 (342.7 to 516.5)	472.9 (255.6 to 874.7)	407.7 (340.3 to 488.4)	365.7 (240.6 to 555.8)
OPSONO-9V M1(N=129,23,157,34,31)	2234.8 (1905.7 to 2620.7)	752.9 (476.9 to 1188.8)	2403.7 (2092.3 to 2761.4)	1155.5 (733.4 to 1820.4)
OPSONO-9V M12(N=131,25,161,35,124)	791.6 (647.4 to 967.9)	552.2 (337.1 to 904.6)	906.7 (757.6 to 1085.2)	716.8 (481 to 1068.2)
OPSONO-14 PRE(N=118,21,152,29,12)	189.7 (141.7 to 254)	150.2 (81.5 to 276.8)	293.2 (235.3 to 365.5)	227.4 (115.1 to 449.4)
OPSONO-14 M1(N=130,22,154,34,19)	1581.7 (1381.1 to 1811.4)	1515 (911.2 to 2519)	1865.2 (1633.4 to 2129.9)	1964.5 (1359.9 to 2837.9)
OPSONO-14 M12(N=117,15,147,32,98)	434.5 (353 to 534.8)	438.4 (137.7 to 1396)	447.5 (376 to 532.6)	558 (425 to 732.5)
OPSONO-18C PRE(N=124,23,148,24,38)	6.1 (5.2 to 7.2)	6 (3.7 to 9.7)	11.7 (9.2 to 15.1)	9.5 (4.9 to 18.5)
OPSONO-18C M1(N=128,22,154,34,42)	652.9 (553.5 to 770.1)	269.7 (128.9 to 564.3)	737.8 (633.6 to 859.1)	537.6 (370.9 to 779.3)
OPSONO-18C M12(N=121,23,154,28,124)	11.9 (8.9 to 16.1)	24.7 (9 to 67.5)	27.7 (21.3 to 36)	23.5 (11 to 50.3)
OPSONO-19F PRE(N=121,24,149,32,39)	21.2 (16.1 to 28)	17.4 (10.5 to 28.7)	35.1 (28 to 44)	36.4 (22 to 60.3)
OPSONO-19F M1(N=130,23,156,34,42)	629.4 (496.6 to 797.7)	372.9 (180.1 to 772.5)	1062.2 (871.8 to 1294.3)	1198.8 (807.1 to 1780.5)
OPSONO-19F M12(N=130,25,155,35,132)	64.3 (47.6 to 86.7)	39.4 (17.3 to 89.5)	101.3 (80.7 to 127)	121.3 (67.5 to 218.1)
OPSONO-23F PRE(N=122,20,149,31,25)	288.7 (192.1 to 434)	310.1 (85.9 to 1119.4)	408 (288.6 to 576.6)	305.3 (135 to 690.5)
OPSONO-23F M1(N=130,23,157,34,28)	2335.7 (2016.2 to 2705.7)	1223.1 (910.6 to 1642.8)	3154 (2658 to 3742.4)	1808.7 (1381.1 to 2368.7)
OPSONO-23F M12(N=122,20,152,33,124)	386.4 (250 to 597.2)	433.8 (110.1 to 1709.8)	857.5 (634 to 1159.7)	670.2 (331.9 to 1353.3)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 PRE(N=125,25,152,31,26)	4.9 (3.7 to 6.5)			
OPSONO-1 M1(N=130,23,156,34,39)	5.1 (4.1 to 6.4)			
OPSONO-1 M12(N=129,21,153,34,126)	4.7 (4.3 to 5.1)			
OPSONO-4 PRE(N=121,22,148,31,31)	5.9 (3.4 to 10.2)			

OPSONO-4 M1(N=130,22,158,32,23)	7.8 (3.6 to 16.8)			
OPSONO-4 M12(N=125,21,152,33,119)	6.8 (5 to 9.3)			
OPSONO-5 PRE(N=121,24,146,31,26)	4.2 (3.8 to 4.7)			
OPSONO-5 M1(N=130,23,156,34,45)	4.3 (3.8 to 4.8)			
OPSONO-5 M12(N=124,21,154,32,135)	4 (4 to 4)			
OPSONO-6B PRE(N=126,22,154,31,25)	9.9 (3.5 to 27.7)			
OPSONO-6B M1(N=130,22,157,34,29)	20.9 (6.6 to 65.9)			
OPSONO-6B M12(N=123,22,145,31,113)	19.1 (12 to 30.5)			
OPSONO-7F PRE(N=115,22,148,32,23)	90 (23.2 to 349.8)			
OPSONO-7F M1(N=130,23,158,34,28)	267.3 (89.1 to 801.2)			
OPSONO-7F M12(N=130,25,159,34,118)	681.1 (499.7 to 928.3)			
OPSONO-9V PRE(N=119,21,147,31,23)	69.2 (22.9 to 208.9)			
OPSONO-9V M1(N=129,23,157,34,31)	87.4 (45.2 to 169)			
OPSONO-9V M12(N=131,25,161,35,124)	127.2 (86.8 to 186.2)			
OPSONO-14 PRE(N=118,21,152,29,12)	11.5 (3.3 to 40.1)			
OPSONO-14 M1(N=130,22,154,34,19)	158 (59.4 to 420.2)			
OPSONO-14 M12(N=117,15,147,32,98)	287.8 (203.2 to 407.6)			
OPSONO-18C PRE(N=124,23,148,24,38)	4.5 (3.5 to 5.8)			
OPSONO-18C M1(N=128,22,154,34,42)	4 (4 to 4)			
OPSONO-18C M12(N=121,23,154,28,124)	4.6 (4 to 5.3)			
OPSONO-19F PRE(N=121,24,149,32,39)	5.3 (3.7 to 7.7)			
OPSONO-19F M1(N=130,23,156,34,42)	4.5 (3.7 to 5.6)			
OPSONO-19F M12(N=130,25,155,35,132)	6.4 (5.1 to 8.1)			
OPSONO-23F PRE(N=122,20,149,31,25)	20.2 (7.2 to 56.2)			
OPSONO-23F M1(N=130,23,157,34,28)	261.8 (97.9 to 700.5)			
OPSONO-23F M12(N=122,20,152,33,124)	147.1 (86.7 to 249.9)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against protein D (Anti-PD)
End point description: The seropositivity cut-off for the assay was ≥ 100 Enzyme-Linked ImmunoSorbent Assay (ELISA) units per milliliter (EL.U/mL).	
End point type	Secondary

End point timeframe:

Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	25	167	37
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD-PRE (N=135,25,158,37,260)	365.1 (302.1 to 441.1)	356.5 (247 to 514.4)	685.5 (585.4 to 802.9)	584.3 (393.1 to 868.4)
Anti-PD-M1 (N=140,24,166,36,258)	1654 (1399.9 to 1954.4)	1813.5 (1111.5 to 2958.9)	3134.2 (2765.4 to 3552.1)	2612.3 (1804.4 to 3782.1)
Anti-PD-M12 (N=138,25,167,36,270)	468.1 (381.8 to 573.8)	418 (259.9 to 672.3)	834.6 (720 to 967.5)	713.4 (476.9 to 1067.4)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	270			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD-PRE (N=135,25,158,37,260)	65.6 (60.9 to 70.8)			
Anti-PD-M1 (N=140,24,166,36,258)	64.6 (59.9 to 69.5)			
Anti-PD-M12 (N=138,25,167,36,270)	74.4 (67.8 to 81.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes 6A and 19A (anti-6A and 19A)

End point title	Antibody concentrations against pneumococcal serotypes 6A and 19A (anti-6A and 19A)
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End point description:

Anti-6A and 19A antibody concentrations were measured by 22F-inhibition ELISA.

End point type	Secondary
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End point timeframe:

Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	139	25	168	37
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A-PRE N(=136,25,161,37,278)	0.12 (0.1 to 0.15)	0.08 (0.05 to 0.12)	0.21 (0.18 to 0.26)	0.19 (0.12 to 0.29)
Anti-6A-M1 (N=138,25,166,36,288)	0.4 (0.31 to 0.51)	0.29 (0.15 to 0.55)	0.86 (0.69 to 1.07)	0.75 (0.43 to 1.3)
Anti-6A-M12 (N=139,25,167,36,279)	0.14 (0.11 to 0.18)	0.1 (0.07 to 0.16)	0.24 (0.2 to 0.3)	0.2 (0.13 to 0.29)
Anti-19A-PRE (n=138,25,165,36,277)	0.15 (0.13 to 0.18)	0.12 (0.07 to 0.19)	0.23 (0.19 to 0.27)	0.2 (0.14 to 0.29)
Anti-19A-M1 (N=138,25,166,37,276)	0.84 (0.67 to 1.05)	0.56 (0.29 to 1.09)	1.34 (1.09 to 1.66)	1.54 (0.98 to 2.43)
Anti-19A-M12 (N=139,25,168,36,284)	0.22 (0.17 to 0.28)	0.13 (0.08 to 0.22)	0.36 (0.3 to 0.44)	0.41 (0.26 to 0.65)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	288			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A-PRE N(=136,25,161,37,278)	0.03 (0.03 to 0.03)			
Anti-6A-M1 (N=138,25,166,36,288)	0.03 (0.03 to 0.03)			
Anti-6A-M12 (N=139,25,167,36,279)	0.04 (0.03 to 0.04)			
Anti-19A-PRE (n=138,25,165,36,277)	0.03 (0.03 to 0.04)			
Anti-19A-M1 (N=138,25,166,37,276)	0.04 (0.03 to 0.04)			
Anti-19A-M12 (N=139,25,168,36,284)	0.06 (0.05 to 0.07)			

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
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End point description:

OPA titers against pneumococcal serotypes 6A and 19A (Opsono-6A and 19A) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8 .

End point type	Secondary
End point timeframe:	
Prior to booster vaccination (PRE), 1 month (M1) and 12 months (M12) post-booster vaccination	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	22	153	33
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-6A-PRE (N=116,19,139,20,24)	72.4 (48.3 to 108.4)	35.6 (12.2 to 104.1)	65.4 (45.7 to 93.7)	66 (25.7 to 169.5)
OPSONO-6A-M1 (N=124,21,149,31,16)	251.5 (180.2 to 351)	105.1 (40.6 to 271.8)	401.7 (319.5 to 505.2)	403.7 (253.5 to 642.9)
OPSONO-6A-M12 (N=111,17,131,29,115)	59.4 (38.8 to 91)	23 (8.4 to 62.6)	52.1 (35.6 to 76.3)	37.2 (17.5 to 79)
OPSONO-19A-PRE (N=118,21,141,28,36)	5 (4.3 to 5.7)	4.9 (3.2 to 7.3)	4.8 (4.3 to 5.4)	5 (3.6 to 6.9)
OPSONO-19A-M1 (N=129,18,151,31,45)	39.2 (26.4 to 58.2)	39.7 (11.5 to 137.4)	89.7 (61.2 to 131.6)	99.6 (40.8 to 243.1)
OPSONO-19A-M12 (N=127,22,153,33,131)	7 (5.5 to 8.8)	4.8 (3.6 to 6.5)	8.9 (7.1 to 11.1)	9.5 (5.6 to 16.1)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-6A-PRE (N=116,19,139,20,24)	9.7 (4.7 to 20)			
OPSONO-6A-M1 (N=124,21,149,31,16)	16.1 (5 to 52)			
OPSONO-6A-M12 (N=111,17,131,29,115)	17.1 (11.7 to 24.9)			
OPSONO-19A-PRE (N=118,21,141,28,36)	4 (4 to 4)			
OPSONO-19A-M1 (N=129,18,151,31,45)	4 (4 to 4)			
OPSONO-19A-M12 (N=127,22,153,33,131)	4.7 (4.2 to 5.2)			

Statistical analyses

Secondary: Number of subjects with serum bactericidal antibodies, using baby rabbit complement for assay (rSBA) titres $\geq$ the cut-off values

End point title	Number of subjects with serum bactericidal antibodies, using baby rabbit complement for assay (rSBA) titres $\geq$ the cut-off values ^[4]
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End point description:

The cut-off values assessed were 1:8 and 1:128 for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY). Results were only tabulated for subjects who received a vaccine including the respective antigens (Mencevax + Infanrix Hexa Group).

End point type	Secondary
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End point timeframe:

Prior to vaccination (PRE), 1 month (M1) and 12 months (M12) post-vaccination

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting values for the Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	301			
Units: Subjects				
rSBA-MenA,Pre, $\geq$ 1:8 [N=244]	69			
rSBA-MenA, Pre, $\geq$ 1:128 [N=244]	44			
rSBA-MenA, M1, $\geq$ 1:8 [N=299]	298			
rSBA-MenA, M1, $\geq$ 1:128 [N=299]	298			
rSBA-MenA, M12, $\geq$ 1:8 [N=136]	136			
rSBA-MenA, M12, $\geq$ 1:128 [N=136]	134			
rSBA-MenC,Pre, $\geq$ 1:8 [N=295]	50			
rSBA-MenC, Pre, $\geq$ 1:128 [N=295]	17			
rSBA-MenC, M1, $\geq$ 1:8 [N=301]	300			
rSBA-MenC, M1, $\geq$ 1:128 [N=301]	294			
rSBA-MenC, M12, $\geq$ 1:8 [N=161]	154			
rSBA-MenC, M12, $\geq$ 1:128 [N=161]	105			
rSBA-MenW-135,Pre, $\geq$ 1:8 [N=287]	114			
rSBA-MenW-135, Pre, $\geq$ 1:128 [N=287]	59			
rSBA-MenW-135, M1, $\geq$ 1:8 [N=301]	301			
rSBA-MenW-135, M1, $\geq$ 1:128 [N=301]	301			
rSBA-MenW-135, M12, $\geq$ 1:8 [N=139]	138			
rSBA-MenW-135, M12, $\geq$ 1:128 [N=139]	129			
rSBA-MenY,Pre, $\geq$ 1:8 [N=297]	167			
rSBA-MenY, Pre, $\geq$ 1:128 [N=297]	93			
rSBA-MenY, M1, $\geq$ 1:8 [N=301]	300			
rSBA-MenY, M1, $\geq$ 1:128 [N=301]	300			
rSBA-MenY, M12, $\geq$ 1:8 [N=138]	137			
rSBA-MenY, M12, $\geq$ 1:128 [N=138]	127			

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers in the Mencevax + Infanrix Hexa Group

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers in the Mencevax + Infanrix Hexa Group ^[5]
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End point description:

Results were only tabulated for subjects who received a vaccine including the respective antigens (Mencevax + Infanrix Hexa Group).

End point type	Secondary
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End point timeframe:

Prior to vaccination (PRE), 1 month (M1) and 12 months (M12) post vaccination

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	301			
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA,Pre [N=244]	11.5 (9.2 to 14.3)			
rSBA-MenA, M1 [N=299]	2151.3 (1927.4 to 2401.2)			
rSBA-MenA, M12 [N=136]	677.6 (579.9 to 791.8)			
rSBA-MenC,Pre [N=295]	6.9 (6 to 8)			
rSBA-MenC, M1 [N=301]	811.2 (728 to 904)			
rSBA-MenC, M12 [N=161]	191.1 (153.5 to 238)			
rSBA-MenW-135,Pre [N=287]	16.3 (13.2 to 20.1)			
rSBA-MenW-135, M1 [N=301]	5393.6 (4888.2 to 5951.1)			
rSBA-MenW-135, M12 [N=139]	573.1 (479.3 to 685.3)			
rSBA-MenY,Pre [N=297]	30.2 (24.2 to 37.7)			
rSBA-MenY, M1 [N=301]	2863.7 (2537.8 to 3231.4)			

rSBA-MenY, M12 [N=138]	665.2 (547.9 to 807.7)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide N (anti-PS) concentrations $\geq$ the cut-off value

End point title	Number of subjects with anti-polysaccharide N (anti-PS) concentrations $\geq$ the cut-off value ^[6]
End point description: Anti-PS assessed were anti-PS meningitidis serogroup A (anti-PSA), C (anti-PSC), W (anti-PSW-135) and Y (anti-PSY). The cut-offs for anti-PS concentrations were 0.3 µg/mL and 2.0 µg/mL, tabulated for subjects who received a vaccine including the respective antigens (Mencevax + Infanrix Hexa Group).	
End point type	Secondary
End point timeframe: Prior to vaccination (PRE), 1 month (M1) and 12 months (M12) post vaccination	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for the Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	278			
Units: Subjects				
ANTI-PSA PRE(N=246) $\geq$ 0.3 µg/mL	12			
ANTI-PSA PRE(N=246) $\geq$ 2.0 µg/mL	1			
ANTI-PSA M1(N=272) $\geq$ 0.3 µg/mL	271			
ANTI-PSA M1(N=272) $\geq$ 2.0 µg/mL	271			
ANTI-PSA M12(N=153) $\geq$ 0.3 µg/mL	133			
ANTI-PSA M12(N=153) $\geq$ 2.0 µg/mL	47			
ANTI-PSC PRE(N=269) $\geq$ 0.3 µg/mL	3			
ANTI-PSC PRE(N=269) $\geq$ 2.0 µg/mL	0			
ANTI-PSC M1(N=278) $\geq$ 0.3 µg/mL	278			
ANTI-PSC M1(N=278) $\geq$ 2.0 µg/mL	277			
ANTI-PSC M12(N=157) $\geq$ 0.3 µg/mL	94			
ANTI-PSC M12(N=157) $\geq$ 2.0 µg/mL	9			
ANTI-PSW-135 PRE(N=236) $\geq$ 0.3 µg/mL	1			
ANTI-PSW-135 PRE(N=236) $\geq$ 2.0 µg/mL	0			
ANTI-PSW-135 M1(N=259) $\geq$ 0.3 µg/mL	258			
ANTI-PSW-135 M1(N=259) $\geq$ 2.0 µg/mL	234			
ANTI-PSW-135 M12(N=132) $\geq$ 0.3 µg/mL	117			
ANTI-PSW-135 M12(N=132) $\geq$ 2.0 µg/mL	45			
ANTI-PSY PRE(N=261) $\geq$ 0.3 µg/mL	3			
ANTI-PSY PRE(N=261) $\geq$ 2.0 µg/mL	0			
ANTI-PSY M1(N=263) $\geq$ 0.3 µg/mL	261			

ANTI-PSY M1(N=263)≥2.0 µg/mL	249			
ANTI-PSY M12(N=135)≥0.3 µg/mL	131			
ANTI-PSY M12(N=135)≥2.0 µg/mL	59			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean antibody concentration (GMCs) for anti-polysaccharide N (anti-PS) antibody concentrations

End point title	Geometric mean antibody concentration (GMCs) for anti-polysaccharide N (anti-PS) antibody concentrations ^[7]
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End point description:

Anti-PS assessed were Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY. Results were only tabulated for subjects who received a vaccine including the respective antigens (Mencevax + Infanrix Hexa Group).

End point type	Secondary
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End point timeframe:

Prior to vaccination (PRE), 1 month (M1) and 12 months (M12) post vaccination

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting values for the Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	278			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, Pre [N=246]	0.16 (0.15 to 0.17)			
Anti-PSA, M1 [N=272]	36.28 (32.8 to 40.15)			
Anti-PSA, M12 [N=153]	0.99 (0.82 to 1.19)			
Anti-PSC, Pre [N=269]	0.15 (0.15 to 0.16)			
Anti-PSC, M1 [N=278]	14.12 (13 to 15.32)			
Anti-PSC, M12 [N=157]	0.42 (0.36 to 0.49)			
Anti-PSW-135, Pre [N=236]	0.15 (0.15 to 0.15)			
Anti-PSW-135, M1 [N=259]	6.11 (5.45 to 6.86)			
Anti-PSW-135, M12 [N=132]	1.21 (0.98 to 1.48)			
Anti-PSY, Pre [N=261]	0.15 (0.15 to 0.16)			
Anti-PSY, M1 [N=263]	8.03 (7.17 to 8.99)			
Anti-PSY, M12 [N=135]	1.81 (1.5 to 2.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-tetanus toxoids (anti-T) antibody concentrations in the Mencevax + Infanrix Hexa Group

End point title	Anti-tetanus toxoids (anti-T) antibody concentrations in the Mencevax + Infanrix Hexa Group ^[8]
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End point description:

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

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre)

Notes:

[8] - 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 Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	266			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, Pre [266]	0.512 (0.456 to 0.575)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations in the Mencevax + Infanrix Hexa Group

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations in the Mencevax + Infanrix Hexa Group ^[9]
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End point description:

The seroprotection cut-off for the assay was ≥ 10 mIU/mL. Results were only tabulated for subjects who received a vaccine including the respective antigens (Mencevax + Infanrix Hexa Group).

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre)

Notes:

[9] - 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 Mencevax + Infanrix Hexa Group.

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, Pre [2]	1336.1 (52.3 to 34160.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T)

End point title	Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T)
End point description: The seroprotection cut-off for the assay was ≥ 0.1 IU/mL.	
End point type	Secondary
End point timeframe: 1 month post-vaccination (M1)	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	24	167	37
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, M1 (N=140,24,166,37,245)	10.112 (9.042 to 11.309)	9.839 (7.475 to 12.95)	12.285 (11.18 to 13.5)	11 (8.786 to 13.77)
Anti-T, M1 (N=139,24,167,37,245)	7.382 (6.639 to 8.208)	8.684 (6.37 to 11.839)	9.583 (8.927 to 10.287)	8.196 (6.829 to 9.837)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	245			
Units: IU/mL				

geometric mean (confidence interval 95%)				
Anti-D, M1 (N=140,24,166,37,245)	7.291 (6.592 to 8.064)			
Anti-T, M1 (N=139,24,167,37,245)	11.79 (10.684 to 13.011)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations
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End point description:

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

End point type	Secondary
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End point timeframe:

1 month post-vaccination (M1)

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	24	167	37
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, M1 (N=138,24,166,36,248)	83.3 (73.8 to 94)	81.6 (62.2 to 106.9)	82 (73.4 to 91.7)	76.7 (62.2 to 94.4)
Anti-FHA, M1 (N=140,24,167,37,251)	467.9 (422.4 to 518.3)	431.1 (318.8 to 582.9)	453.8 (412.6 to 499.1)	400.4 (321.8 to 498.2)
Anti-PRN, M1 (N=140,24,167,36,246)	222.8 (193.9 to 256)	153.4 (97.5 to 241.2)	254.9 (225.8 to 287.8)	220.4 (168.7 to 288)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	251			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, M1 (N=138,24,166,36,248)	163.1 (143 to 185.9)			
Anti-FHA, M1 (N=140,24,167,37,251)	580.8 (532.2 to 633.8)			

Anti-PRN, M1 (N=140,24,167,36,246)	350.7 (316.8 to 388.3)			
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Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations
End point description: The seroprotection cut-off for the assay was ≥ 10 mIU/mL. Dummy LL (0.0) and UL (99999.9) are entered when number of subjects analysed = 1.	
End point type	Secondary
End point timeframe: 1 month post-vaccination (M1)	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	105	16	130	26
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M1	1883.9 (1332.9 to 2662.7)	1460.6 (816.4 to 2613.2)	2133 (1615 to 2817.1)	1818.5 (1142.8 to 2893.6)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M1	20610 (0 to 99999.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations

End point title	Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations
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End point description:

The seroprotection cut-off for the assay was ≥ 0.15 $\mu\text{g/mL}$.

End point type	Secondary
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End point timeframe:

1 month post-vaccination (M1)

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	24	167	36
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP, M1	23.066 (18.806 to 28.291)	26.006 (15.56 to 43.463)	27.373 (22.915 to 32.697)	22.011 (16.288 to 29.745)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	269			
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP, M1	20.985 (17.966 to 24.511)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus (Anti-Polio) types 1, 2 and 3 titers

End point title	Anti-poliovirus (Anti-Polio) types 1, 2 and 3 titers
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End point description:

The seroprotection cut-off for the assay was ≥ 8 . Dummy LL (0.0) and UL (99999.9) are entered when number of subjects analysed = 1.

End point type	Secondary
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End point timeframe:

1 month post-vaccination (M1)

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	12	114	23
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, M1 (N=93,12,114,23,1)	1193 (993.8 to 1432.2)	1534.2 (952 to 2472.5)	1058.7 (870.2 to 1288)	1208.6 (764.2 to 1911.2)
Anti-Polio 2, M1 (N=93,12,113,22,1)	1354.1 (1115.8 to 1643.3)	2047.9 (1246 to 3365.9)	1413.2 (1174.3 to 1700.7)	2215.8 (1544.4 to 3178.9)
Anti-Polio 3, M1 (N=92,12,114,23,1)	2354.2 (1946.1 to 2847.9)	2233.3 (1300.9 to 3834)	2647.5 (2221.5 to 3155.3)	3576.5 (2617.3 to 4887.2)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, M1 (N=93,12,114,23,1)	4096 (0 to 99999.9)			
Anti-Polio 2, M1 (N=93,12,113,22,1)	8192 (0 to 99999.9)			
Anti-Polio 3, M1 (N=92,12,114,23,1)	8192 (0 to 99999.9)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-hepatitis B surface antigen (Anti-HBs) antibody concentrations
End point description:	
The seroprotection cut-off for the assay was ≥ 10 mIU/mL.	
End point type	Secondary
End point timeframe:	
12 month post-vaccination (M12)	

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	16	133	20
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M12	219.3 (164.8 to 291.7)	147.3 (62.6 to 346.9)	231.2 (179.7 to 297.6)	139.2 (74.3 to 260.9)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M12	535.1 (277.8 to 1030.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus (Anti-Polio) type 1, 2 and 3 titers

End point title	Anti-poliovirus (Anti-Polio) type 1, 2 and 3 titers
End point description:	The seroprotection cut-off for the assay was ≥ 8 . Dummy lower limit (LL) (0.0) and upper limit UL (99999.9) were entered when number of subjects analysed = 1.
End point type	Secondary
End point timeframe:	12 month post-vaccination (M12)

End point values	Synflorix I Group	Synflorix II Group	Synflorix PRE Group	Synflorix POST Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	13	122	14
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, M12 (N=97,13,122,14,9)	208.2 (164.7 to 263.2)	150.4 (87.2 to 259.3)	234.5 (189.5 to 290.3)	220.8 (92.3 to 528.2)
Anti-Polio 2, M12 (N=96,13,122,14,9)	311.2 (241.5 to 401)	212.4 (100.5 to 449)	310.6 (256 to 376.9)	400 (218.6 to 732.1)
Anti-Polio 3, M12 (N=97,13,122,14,9)	431.3 (332.4 to 559.5)	301 (125.8 to 720.4)	506.3 (406.3 to 630.7)	672.2 (330 to 1369.4)

End point values	Mencevax + Infanrix Hexa Group			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, M12 (N=97,13,122,14,9)	335.4 (146.4 to 768.2)			
Anti-Polio 2, M12 (N=96,13,122,14,9)	322.7 (172.9 to 602.3)			
Anti-Polio 3, M12 (N=97,13,122,14,9)	203.3 (63.7 to 649.2)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of nasopharyngeal swabs with S.pneumoniae (vaccine serotypes) ^[10]
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End point description:

Results were tabulated on Pooled Synflorix Group and on Mencevax + Infanrix Hexa Group.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre), 1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

Notes:

[10] - 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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Swabs				
Pre (N=330,407)	53	43		
M1 (N=332,408)	47	45		
M3 (N=332,408)	55	49		
M7 (N=334,406)	50	42		
M12 (N=334,409)	43	34		
Overall (N=336,414)	115	111		

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) ^[11]
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End point description:

Results were tabulated on Pooled Synflorix Group and on Mencevax + Infanrix Hexa Group.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre), 1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

Notes:

[11] - 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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Swabs				
Pre (N=330,407)	13	15		
M1 (N=332,408)	19	22		
M3 (N=332,408)	21	27		
M7 (N=334,406)	19	21		
M12 (N=334,409)	19	18		
Overall (N=336,414)	55	59		

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) ^[12]
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End point description:

Results were tabulated on Mencevax + Infanrix Hexa Group and on Pooled Synflorix Group.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre), 1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Swabs				
Pre (N=330,407)	26	27		
M1 (N=332,408)	30	42		
M3 (N=332,408)	32	45		
M7 (N=334,406)	29	42		
M12 (N=334,409)	22	39		
Overall (N=336,414)	82	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with H. influenzae

End point title	Number of nasopharyngeal swabs with H. influenzae ^[13]
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End point description:

Results were tabulated on Mencevax + Infanrix Hexa Group and on Pooled Synflorix Group.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre), 1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Swabs				
Pre (N=312,397)	41	48		
M1 (N=318,402)	39	56		
M3 (N=328,403)	34	62		
M7 (N=332,403)	49	64		
M12 (N=333,406)	57	46		

Overall (N=336,414)	124	160		
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of nasopharyngeal swabs with *S. pneumoniae* and *H. influenzae*

End point title	Number of nasopharyngeal swabs with <i>S. pneumoniae</i> and <i>H. influenzae</i> ^[14]
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End point description:

Results were tabulated on Mencevax + Infanrix Hexa Group and on Pooled Synflorix Group.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre), 1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Swabs				
Pre (N=312,397)	19	21		
M1 (N=318,402)	20	30		
M3 (N=328,403)	17	31		
M7 (N=332,403)	22	28		
M12 (N=333,406)	22	19		
Overall (N=336,414)	61	86		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new acquisition associated to *S. pneumoniae* detected in nasopharyngeal swabs

End point title	Number of subjects with new acquisition associated to <i>S. pneumoniae</i> detected in nasopharyngeal swabs ^[15]
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End point description:

Results were tabulated on Mencevax + Infanrix Hexa Group and on Pooled Synflorix Group.

End point type	Secondary
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End point timeframe:

1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
M1 (N=332,408)	43	56		
M3 (N=332,408)	63	76		
M7 (N=334,406)	70	73		
M12 (N=334,409)	65	70		
Overall (N=336,414)	161	195		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with new acquisition associated to H. influenzae detected in nasopharyngeal swabs ^[16]
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End point description:

Results were tabulated on Mencevax + Infanrix Hexa Group and on Pooled Synflorix Group.

End point type	Secondary
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End point timeframe:

1 month post-vaccination (M1), 3 months post-vaccination (M3), 7 months post-vaccination (M7), 12 months post-vaccination (M12) and across all time points (Overall)

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 Mencevax + Infanrix Hexa Group and Pooled Synflorix Group.

End point values	Mencevax + Infanrix Hexa Group	Pooled Synflorix Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
M1 (N=318,402)	21	32		
M3 (N=328,403)	22	40		
M7 (N=332,403)	37	42		
M12 (N=333,406)	39	35		
Overall (N=336,414)	104	129		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited symptoms: during the 31-day (Day 0-Day 30) follow-up periods after vaccination. SAEs: Entire study period (Month 0- Month 12).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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Reporting groups

Reporting group title	Synflorix I Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of Synflorix vaccine with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa along with prophylactic antipyretic treatment.

Reporting group title	Synflorix II Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of Synflorix vaccine with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Synflorix PRE Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of Synflorix vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Synflorix POST Group
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Reporting group description:

Subjects were vaccinated with 3 primary vaccination doses of 10Pn vaccine without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of 10Pn vaccine, co-administered with Infanrix hexa without prophylactic antipyretic treatment.

Reporting group title	Mencevax + Infanrix Hexa Group
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Reporting group description:

Age-matched pneumococcal vaccine unprimed group receiving a single dose of Mencevax co-administered with Infanrix hexa vaccine.

Serious adverse events	Synflorix I Group	Synflorix II Group	Synflorix PRE Group
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 178 (7.30%)	5 / 27 (18.52%)	13 / 172 (7.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 178 (1.12%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body trauma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caustic injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pharyngeal injury alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 178 (0.00%) 0 / 0 0 / 0	1 / 27 (3.70%) 0 / 1 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0
Poisoning alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 178 (0.00%) 0 / 0 0 / 0	0 / 27 (0.00%) 0 / 0 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0
Skull fracture alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 178 (0.00%) 0 / 0 0 / 0	0 / 27 (0.00%) 0 / 0 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0
Congenital, familial and genetic disorders Arteriovenous malformation alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 178 (0.00%) 0 / 0 0 / 0	0 / 27 (0.00%) 0 / 0 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0
Nervous system disorders Febrile convulsion alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 178 (0.56%) 0 / 1 0 / 0	0 / 27 (0.00%) 0 / 0 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0
General disorders and administration site conditions Pyrexia alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 178 (0.56%) 0 / 1 0 / 0	0 / 27 (0.00%) 0 / 0 0 / 0	0 / 172 (0.00%) 0 / 0 0 / 0

Blood and lymphatic system disorders			
Lymphadenopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular retraction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dyspepsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermal cyst			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 178 (1.12%)	1 / 27 (3.70%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Salmonellosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulvitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Synflorix POST Group	Mencevax + Infanrix Hexa Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)	30 / 336 (8.93%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 37 (0.00%)	2 / 336 (0.60%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Foreign body trauma				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Accidental exposure				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 37 (2.70%)	1 / 336 (0.30%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Head injury				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Thermal burn				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Caustic injury				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Pharyngeal injury				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arteriovenous malformation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Testicular retraction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dyspepsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermal cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations Gastroenteritis alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 37 (2.70%) 0 / 1 0 / 0	 4 / 336 (1.19%) 0 / 4 0 / 0		
Laryngitis alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 37 (0.00%) 0 / 0 0 / 0	 4 / 336 (1.19%) 0 / 4 0 / 0		
Bronchopneumonia alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 37 (0.00%) 0 / 0 0 / 0	 2 / 336 (0.60%) 0 / 2 0 / 0		
Gastroenteritis rotavirus alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 37 (2.70%) 0 / 1 0 / 0	 3 / 336 (0.89%) 0 / 3 0 / 0		
Viral infection alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 37 (0.00%) 0 / 0 0 / 0	 4 / 336 (1.19%) 0 / 4 0 / 0		
Bronchitis alternative assessment type: Non-systematic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 37 (0.00%) 0 / 0 0 / 0	 4 / 336 (1.19%) 0 / 4 0 / 0		
Tonsillitis alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 37 (2.70%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary tract infection alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulvitis alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Synflorix I Group	Synflorix II Group	Synflorix PRE Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 178 (85.96%)	23 / 27 (85.19%)	154 / 172 (89.53%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	54 / 178 (30.34%)	10 / 27 (37.04%)	79 / 172 (45.93%)
occurrences (all)	54	10	79
Redness			
subjects affected / exposed	89 / 178 (50.00%)	9 / 27 (33.33%)	74 / 172 (43.02%)
occurrences (all)	89	9	74
Swelling			
subjects affected / exposed	52 / 178 (29.21%)	8 / 27 (29.63%)	50 / 172 (29.07%)
occurrences (all)	52	8	50
Drowsiness alternative assessment type: Non-systematic			

subjects affected / exposed	91 / 178 (51.12%)	11 / 27 (40.74%)	84 / 172 (48.84%)
occurrences (all)	91	11	84
Irritability			
subjects affected / exposed	86 / 178 (48.31%)	17 / 27 (62.96%)	105 / 172 (61.05%)
occurrences (all)	86	17	105
Loss of appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	47 / 178 (26.40%)	8 / 27 (29.63%)	46 / 172 (26.74%)
occurrences (all)	47	8	46
Pyrexia			
subjects affected / exposed	64 / 178 (35.96%)	14 / 27 (51.85%)	100 / 172 (58.14%)
occurrences (all)	64	14	100
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 178 (1.12%)	3 / 27 (11.11%)	4 / 172 (2.33%)
occurrences (all)	2	3	4
Bronchitis			
subjects affected / exposed	3 / 178 (1.69%)	0 / 27 (0.00%)	2 / 172 (1.16%)
occurrences (all)	3	0	2
Viral infection			
subjects affected / exposed	2 / 178 (1.12%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Synflorix POST Group	Mencevax + Infanrix Hexa Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 37 (94.59%)	290 / 336 (86.31%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	19 / 37 (51.35%)	114 / 336 (33.93%)	
occurrences (all)	19	114	
Redness			
subjects affected / exposed	12 / 37 (32.43%)	146 / 336 (43.45%)	
occurrences (all)	12	146	
Swelling			

subjects affected / exposed	13 / 37 (35.14%)	71 / 336 (21.13%)	
occurrences (all)	13	71	
Drowsiness			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 37 (48.65%)	146 / 336 (43.45%)	
occurrences (all)	18	146	
Irritability			
subjects affected / exposed	19 / 37 (51.35%)	147 / 336 (43.75%)	
occurrences (all)	19	147	
Loss of appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 37 (27.03%)	88 / 336 (26.19%)	
occurrences (all)	10	88	
Pyrexia			
subjects affected / exposed	16 / 37 (43.24%)	146 / 336 (43.45%)	
occurrences (all)	16	147	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 37 (2.70%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Bronchitis			
subjects affected / exposed	2 / 37 (5.41%)	12 / 336 (3.57%)	
occurrences (all)	2	12	
Viral infection			
subjects affected / exposed	2 / 37 (5.41%)	5 / 336 (1.49%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2007	The amendment was written in response to comments given by the Czech Republic Authorities. In addition the following changes have been included : • Change in Central Study Coordinator. • The microbiological procedures to assess the occurrence of other bacteriological pathogens have been described in more detail. • To avoid confusion regarding the administration of DTPa-HBV-IPV/Hib vaccine, this section has been rewritten. • Clarification of attribution of subject and treatment numbers to the subjects in the unprimed group. • Estimation of sample size of unprimed group has been clarified. • Analysis of carriage has been updated in accordance with the microbiological procedures used to assess the occurrence of other bacteriological pathogens. • Update of literature references.
19 July 2007	As groups were defined as primed and unprimed with regard to pneumococcal vaccination it seemed obvious that the unprimed group was supposed not to have been vaccinated with any pneumococcal vaccine before enrolment. To ensure that the subjects that had previously received a pneumococcal vaccine would not be enrolled or that subjects that received a pneumococcal vaccine during the study would be eliminated, this criterium was added. • Serology testing with regard to pneumococcal antibodies for the unprimed group was considered scientifically relevant to set a baseline for the interpretation of the carriage results of the primed group. In addition serology testing with regard to antibodies against the co-administered vaccine was added for both groups. • As GSK Biologicals is considering an extension study, the possibility to participate in a long-term follow-up study should be addressed at the concluding visit of this study. • For the unprimed group the power to detect group difference in carriage of <i>S. pneumoniae</i> and <i>H. influenzae</i> was adjusted to better reflect what was already observed in POET (study Undeca-Pn-010 [347414/010]) • Update of literature references.

24 September 2007	The results of the primary vaccination study 10PN-PD-DIT-010 have shown that paracetamol (acetaminophen) given as a prophylactic treatment at the time of vaccination significantly reduced the incidence of febrile reactions following vaccination with GSK Biologicals. 10-valent pneumococcal conjugate vaccine coadministered with DTPa-HBV-IPV/Hib (Infanrix hexa) vaccine at 3, 4 and 5 months of age and GSK Biologicals. oral live attenuated HRV (Rotarix) vaccine at 3 and 4 months of age [41.6% of subjects experienced fever $\geq 38^{\circ}\text{C}$ (rectal temperature) in the antipyretic group versus 66.1% of subjects in the non-antipyretic group]. In addition, the study also showed that the use of prophylactic paracetamol seemed to interfere with the primary immune response. The reason for a decrease in the immune response may relate to a reduction of the inflammatory signals that attract the dendritic cells to the injection sites, such that fewer and/or less activated dendritic cells reach the draining lymph nodes, resulting in a reduced B cell stimulation and lower antibody concentrations. In addition, it cannot be excluded that the induction of memory cells (T cells and B cells) is also affected by the prophylactic administration of paracetamol, which may prevent children from developing an adequate booster immune response. Therefore, the prophylactic administration of paracetamol during the booster phase will be stopped. Approximately 50% of the subjects were already enrolled and vaccinated according to the protocol (with or without prophylactic administration of paracetamol). The immune responses of all vaccinated children will be carefully monitored and the need for additional doses will be evaluated after the booster dose. Additional doses of vaccines will be made available, when necessary.
18 January 2008	• Details about the planned interim analysis. • Planning of a second interim analysis. • Correction in the EudraCT number. In addition, strikethrough text related to previous amendments has been removed. Furthermore, all bold italic text related to previous amendments has been changed into normal text. Those additional changes are documented below following the changes for which this fourth amendment has been developed.
03 February 2009	The study protocol has been amended for the following reason: - The availability of the results of the microbiological assessments on nasopharyngeal carriage up to Visit 3 has been delayed. Therefore there is a need to cancel second interim analysis on carriage based on the time point V3 and to involve additional other laboratories designated by GSK Biologicals to speed up the microbiological work. • The fact that microbial assessments can be performed not only at the regional laboratory in the Czech Republic, but also at a laboratory designated by GSK Biologicals, was added. • The planned second interim analysis will not be performed anymore.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported