Clinical trial results:
Assessment of long-term antibody persistence and immunological memory in children previously vaccinated with four pneumococcal conjugate vaccine doses and assessment of pneumococcal catch-up vaccination with GSK1024850A at 5 years of age.

Summary

EudraCT number	2007-005392-34
Trial protocol	PL
Global end of trial date	21 November 2011

Results information

Result version number	v3
This version publication date	08 July 2020
First version publication date	30 July 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	111345

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GSKClinicalSupportHD, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 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	14 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2011
Global end of trial reached?	Yes
Global end of trial date	21 November 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess antibody persistence in children previously vaccinated with four doses of pneumococcal conjugate vaccine in primary vaccination study 10PN-PD-DIT-001 and booster vaccination study 10PN-PD-DIT-007.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2008
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	Poland: 524
Worldwide total number of subjects	524
EEA total number of subjects	524

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	524
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:

Primed groups included Synflorix vaccinated subjects in study 10PN-PD-DIT-007. The Unprimed Group, added only in Year 4,included subjects unprimed with any pneumococcal vaccine age-matched with primed groups. The study included 3 sub-studies (111345, 111346, 111347) corresponding to Year 1, 2 and 4 time points post Dose 1 in Study 10PN-PD-DIT-001.

Pre-assignment

Screening details:

At screening, subjects with previous participation in 10PN-PD-DIT-007 study were invited to join this study. Informed consent was obtained and signed from subjects' parents/guardians, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected.

Period 1

Period 1 title	Follow-up Period: Year 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046);

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Arm title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046)

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Arm title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Control
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553)

Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046)

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Number of subjects in period 1	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Started	391	31	102
Completed	391	31	102

Period 2

Period 2 title	Follow-up Period: Year 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Arm type	Experimental

Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046);

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Arm title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046)

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Arm title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Control
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553)

Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix
Pharmaceutical forms	Powder for suspension for injection, Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046)

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

Investigational medicinal product name	Varilrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

Number of subjects in period 2[1]	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Started	370	31	96
Completed	370	31	96

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of 524 subjects enrolled in the Follow-up Period: Year 1, 11 subjects were lost to follow-up, 15 subjects did not consent to participate due to other reasons, and 1 subject died.

Period 3

Period 3 title	Follow-up Period: Year 4 Persistence
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

Arm title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Control
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046)

Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose at follow-up visit (Visit 3)

Arm title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses received in primary vaccination study 10PN-PD-DT-001 (1105553)

Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

Number of subjects in period 3[2]	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Started	316	25	85
Completed	316	25	85

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of 497 subjects enrolled in the Follow-up Period: Year 2, 23 subjects were lost to follow-up and 48 subjects did not consent to participate due to other reasons.
Out of 426 subjects enrolled in the Follow-up Period: Year 4 Persistency, 59 subjects were withdrawn due to invalid immunogenicity results and 9 were withdrawn due to protocol violation.

Period 4

Period 4 title	Follow-up Period: Year 4 Immunogenicity
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Arm type	Experimental
Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Route of administration not applicable

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

Arm title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Control
Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose at follow-up visit (Visit 3)

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046)

Arm title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Arm type	Experimental

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses received in primary vaccination study 10PN-PD-DT-001 (1105553)

Investigational medicinal product name	10Pn-PD-DiT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

Number of subjects in period 4[3]	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Started	264	20	65
Completed	263	19	64
Not completed	1	1	1
Parents' Decision	-	-	1
Lost to follow-up	1	1	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of 349 subjects enrolled in Follow-up Period: Year 4 Immunogenicity, 1 subject was withdrawn from the study period due to parent's decision and 2 subjects were lost to follow-up.

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group
Reporting group description:	
This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).	
Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group
Reporting group description:	
This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).	
Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Reporting group description:	
This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).	

Reporting group values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Number of subjects	391	31	102
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	391	31	102
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			
Data was presented for Follow-up Period: Year 1			
Units: Months			
arithmetic mean	29.1	29.0	29.1
standard deviation	± 0.88	± 0.75	± 0.81

Sex: Female, Male			
Data was presented for Follow-up Period Year 1			
Units: Participants			
Female	203	14	52
Male	188	17	50
Race/Ethnicity, Customized			
Data was presented for Follow-up Period: Year 1			
Units: Subjects			
White - caucasia/ european heritage	386	31	102
White arabic/ north african heritage	4	0	0
Other, not specified	1	0	0
Asian - Central/South Asian heritage	0	0	0

Reporting group values	Total		
Number of subjects	524		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	524		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Data was presented for Follow-up Period: Year 1			
Units: Months			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Data was presented for Follow-up Period Year 1			
Units: Participants			
Female	269		
Male	255		
Race/Ethnicity, Customized			
Data was presented for Follow-up Period: Year 1			
Units: Subjects			
White - caucasia/ european heritage	519		
White arabic/ north african heritage	4		
Other, not specified	1		
Asian - Central/South Asian heritage	0		

Subject analysis sets

Subject analysis set title	Unprimed Group
Subject analysis set type	Per protocol

Subject analysis set description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

Reporting group values	Unprimed Group		
Number of subjects	100		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	100		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Data was presented for Follow-up Period: Year 1			
Units: Months			
arithmetic mean	65.4		
standard deviation	± 1.31		
Sex: Female, Male			
Data was presented for Follow-up Period Year 1			
Units: Participants			
Female	53		
Male	47		
Race/Ethnicity, Customized			
Data was presented for Follow-up Period: Year 1			
Units: Subjects			
White - caucasia/ european heritage	98		
White arabic/ north african heritage	1		
Other, not specified	1		
Asian - Central/South Asian heritage	1		

End points

End points reporting groups

Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Subject analysis set title	Unprimed Group
Subject analysis set type	Per protocol

Subject analysis set description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations greater than or equal to (≥) the cut-off [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations greater than or equal to (≥) the cut-off [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)][1]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 microgram per milliliter (µg/mL) as seropositivity cut off.

End point type	Primary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This outcome was descriptive; hence no statistical analyses were required.

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	31	102	
Units: Participants				
Anti-1 antibodies, Y1 (N= 387, 29, 102)	372	7	99	
Anti-4 antibodies, Y1 (N= 387, 31, 102)	384	31	102	
Anti-5 antibodies, Y1 (N= 387, 30, 101)	386	19	101	
Anti-6B antibodies, Y1 (N= 389, 31, 102)	384	31	100	
Anti-7F antibodies, Y1 (N= 387, 31, 102)	387	17	102	
Anti-9V antibodies, Y1 (N= 388, 31, 102)	388	17	102	
Anti-14 antibodies, Y1 (N= 388, 31, 102)	387	31	102	
Anti-18C antibodies, Y1 (N= 384, 31, 102)	384	31	102	
Anti-19F antibodies, Y1 (N= 387, 31, 102)	387	31	102	
Anti-23F antibodies, Y1 (N= 388, 31, 102)	386	31	102	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)][2]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme -linked immunosorbent assay (ELISA), using 0.05 µg/mL as seropositivity cut off.

End point type	Primary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This outcome was descriptive; hence no statistical analyses were required.

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: Participants				
Anti-1 antibodies, Y2 (N= 367, 29, 96)	354	18	90	
Anti-4 antibodies, Y2 (N= 368, 30, 96)	356	30	96	
Anti-5 antibodies, Y2 (N= 368, 29, 95)	362	21	95	
Anti-6B antibodies, Y2 (N= 368, 30, 96)	355	30	95	
Anti-7F antibodies, Y2 (N= 368, 30, 96)	367	19	95	
Anti-9V antibodies, Y2 (N= 368, 30, 96)	362	30	96	
Anti-14 antibodies, Y2 (N= 368, 30, 96)	367	30	96	
Anti-18C antibodies, Y2 (N= 368, 30, 96)	365	30	96	
Anti-19F antibodies, Y2 (N= 368, 30, 95)	368	30	95	
Anti-23F antibodies, Y2 (N= 368, 30, 96)	357	30	95	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)][3]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 µg/mL as seropositivity cut off.

End point type	Primary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This outcome was descriptive; hence no statistical analyses were required.

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: Participants				
Anti-1 antibodies, Y4 (N= 263, 19, 75)	238	14	75	
Anti-4 antibodies, Y4 (N= 263, 18, 74)	238	18	74	
Anti-5 antibodies, Y4 (N= 263, 19, 74)	257	19	73	
Anti-6B antibodies, Y4 (N= 263, 19, 75)	258	19	74	
Anti-7F antibodies, Y4 (N= 263, 19,75)	260	13	73	
Anti-9V antibodies, Y4 (N= 263, 19, 75)	255	19	75	
Anti-14 antibodies, Y4 (N= 263, 19, 75)	2633	19	75	
Anti-18C antibodies, Y4 (N= 263, 19, 74)	256	19	73	
Anti-19F antibodies, Y4 (N= 263, 19, 75)	260	19	75	
Anti-23F antibodies, Y4 (N= 262, 19, 75)	254	19	74	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point title	Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point description:

Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL).The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	31	102	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, Y1 (N= 387, 29, 102)	0.29 (0.27 to 0.32)	0.04 (0.03 to 0.06)	0.26 (0.21 to 0.31)	
Anti-4 antibodies, Y1 (N= 387, 31, 102)	0.5 (0.45 to 0.55)	0.59 (0.46 to 0.75)	1.01 (0.84 to 1.21)	
Anti-5 antibodies, Y1 (N= 387, 30, 101)	0.59 (0.54 to 0.65)	0.07 (0.05 to 0.11)	0.42 (0.35 to 0.52)	
Anti-6B antibodies, Y1 (N= 389, 31, 102)	0.52 (0.45 to 0.6)	0.98 (0.63 to 1.53)	0.54 (0.42 to 0.69)	
Anti-7F antibodies, Y1 (N= 387, 31, 102)	0.71 (0.66 to 0.77)	0.08 (0.05 to 0.13)	0.83 (0.7 to 0.99)	
Anti-9V antibodies, Y1 (N= 388, 31, 102)	0.79 (0.71 to 0.89)	0.93 (0.7 to 1.22)	0.58 (0.49 to 0.68)	
Anti-14 antibodies, Y1 (N= 388, 31, 102)	1.27 (1.12 to 1.44)	1.79 (1.29 to 2.48)	1.47 (1.17 to 1.85)	
Anti-18C antibodies, Y1 (N= 384, 31, 102)	0.88 (0.81 to 0.96)	0.91 (0.71 to 1.16)	0.82 (0.69 to 0.98)	
Anti-19F antibodies, Y1 (N= 387, 31, 102)	1.43 (1.27 to 1.6)	0.83 (0.47 to 1.45)	1.51 (1.19 to 1.92)	
Anti-23F antibodies, Y1 (N= 388, 30, 102)	0.61 (0.54 to 0.69)	1.18 (0.84 to 1.68)	0.7 (0.56 to 0.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point title	Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point description:

Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, Y2 (N= 367, 29, 96)	0.19 (0.17 to 0.21)	0.07 (0.05 to 0.10)	0.17 (0.14 to 0.20)	
Anti-4 antibodies, Y2 (N= 368, 30, 96)	0.27 (0.24 to 0.3)	0.3 (0.24 to 0.38)	0.52 (0.43 to 0.64)	
Anti-5 antibodies, Y2 (N= 368, 29, 95)	0.41 (0.37 to 0.45)	0.09 (0.06 to 0.13)	0.33 (0.27 to 0.41)	
Anti-6B antibodies, Y2 (N= 368, 30, 96)	0.70 (0.58 to 0.83)	0.99 (0.57 to 1.71)	0.9 (0.63 to 1.29)	
Anti-7F antibodies, Y2 (N= 368, 30, 96)	0.53 (0.48 to 0.58)	0.1 (0.06 to 0.16)	0.59 (0.49 to 0.71)	
Anti-9V antibodies, Y2 (N= 368, 30, 96)	0.64 (0.54 to 0.75)	0.61 (0.37 to 1)	0.5 (0.37 to 0.68)	
Anti-14 antibodies, Y2 (N= 368, 30, 96)	1.73 (1.48 to 2.02)	1.94 (1.12 to 3.36)	1.7 (1.25 to 2.31)	
Anti-18C antibodies, Y2 (N= 368, 30, 96)	0.54 (0.48 to 0.62)	0.59 (0.39 to 0.88)	0.48 (0.38 to 0.59)	
Anti-19F antibodies, Y2 (N= 368, 30, 95)	2.16 (1.77 to 2.65)	0.99 (0.51 to 1.91)	2.41 (1.67 to 3.46)	
Anti-23F antibodies, Y2 (N= 368, 30, 96)	0.68 (0.56 to 0.82)	1.24 (0.83 to 1.85)	0.64 (0.48 to 0.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

Pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PDDIT- 007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, Y4 (N= 263, 19, 75)	0.2 (0.17 to 0.24)	0.17 (0.07 to 0.43)	0.23 (0.17 to 0.32)	
Anti-4 antibodies, Y4 (N= 263, 19, 74)	0.19 (0.16 to 0.22)	0.23 (0.12 to 0.41)	0.31 (0.25 to 0.38)	
Anti-5 antibodies, Y4 (N= 263, 19, 74)	0.36 (0.31 to 0.4)	0.19 (0.1 to 0.35)	0.35 (0.28 to 0.43)	
Anti-6B antibodies, Y4 (N= 263, 19, 75)	1.3 (1.1 to 1.55)	1.19 (0.68 to 2.07)	0.97 (0.74 to 1.27)	
Anti-7F antibodies, Y4 (N= 263, 19, 75)	0.44 (0.38 to 0.52)	0.16 (0.08 to 0.36)	0.49 (0.37 to 0.65)	
Anti-9V antibodies, Y4 (N= 263, 19, 75)	1.17 (0.92 to 1.47)	1.19 (0.43 to 3.27)	0.67 (0.46 to 0.99)	
Anti-14 antibodies, Y4 (N= 263, 19, 75)	3.66 (3.01 to 4.45)	2.57 (1.22 to 5.42)	2.94 (2.11 to 4.12)	
Anti-18C antibodies, Y4 (N= 263, 19, 74)	0.7 (0.58 to 0.84)	0.87 (0.4 to 1.88)	0.63 (0.45 to 0.89)	
Anti-19F antibodies, Y4 (N= 263, 19, 75)	4.17 (3.4 to 5.1)	4.74 (2.24 to 10)	4.05 (3.03 to 5.41)	
Anti-23F antibodies, Y4 (N= 262, 19, 75)	1.57 (1.26 to 1.96)	1.64 (1.15 to 2.34)	1.12 (0.79 to 1.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

Anti-pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F . Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	210	14	55	98
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, PRE (N=0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.1 (0.08 to 0.13)
Anti-1 antibodies, D7 (N= 208, 14, 54, 98)	5.36 (4.54 to 6.33)	3.04 (1.22 to 7.56)	5 (3.72 to 6.71)	1.35 (1.08 to 1.69)
Anti-1 antibodies, M3 (N=0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.39 (2.06 to 2.78)
Anti-4 antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.04 (0.03 to 0.05)
Anti-4 antibodies, D7 (N=208, 14, 54, 98)	12.11 (10.08 to 14.54)	10.45 (6.49 to 16.81)	7.13 (5.18 to 9.82)	4.74 (3.77 to 5.95)
Anti-4 antibodies, M3 (N=0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	7.32 (6.7 to 8)
Anti-5 antibodies, PRE (N=0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.1 (0.08 to 0.12)
Anti-5 antibodies, D7 (N=208, 14, 54, 98)	6.23 (5.19 to 7.49)	3.24 (1.44 to 7.29)	8.15 (5.71 to 11.63)	1.2 (0.97 to 1.49)
Anti-5 antibodies, M3 (N=0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	3.1 (2.7 to 3.55)
Anti-6B antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.21 (0.15 to 0.29)
Anti-6B antibodies, D7 (N= 208, 14, 54, 97)	3.68 (3.16 to 4.28)	2.85 (1.89 to 4.3)	2.15 (1.62 to 2.85)	0.53 (0.4 to 0.71)
Anti-6B antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1.25 (1.01 to 1.54)
Anti-7F antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.12 (0.09 to 0.16)
Anti-7F antibodies, D7 (N=208, 14, 54, 98)	7.16 (6.11 to 8.39)	3.26 (1.67 to 6.35)	7.57 (5.84 to 9.81)	1.67 (1.33 to 2.09)
Anti-7F antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4.55 (3.93 to 5.26)
Anti-9V antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.19 (0.12 to 0.28)
Anti-9V antibodies, D7 (N=208, 14, 54, 98)	9.94 (8.59 to 11.51)	9 (5.49 to 14.77)	5.32 (4.08 to 6.94)	0.9 (0.66 to 1.23)
Anti-9V antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.2 (1.85 to 2.62)
Anti-14 antibodies, PRE (N= 0, 0, 0, 96)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.58 (0.38 to 0.87)
Anti-14 antibodies, D7 (N= 208, 14, 54, 98)	19.38 (16.74 to 22.43)	13.26 (6.91 to 25.43)	18.61 (14.23 to 24.34)	1.72 (1.2 to 2.46)
Anti-14 antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	7.81 (6.34 to 9.63)
Anti-18C antibodies, PRE (N= 0, 0, 0, 96)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.1 (0.07 to 0.15)
Anti-18C antibodies, D7 (N=208, 14, 54, 98)	15.51 (13.06 to 18.43)	19.71 (11.87 to 32.74)	13.34 (9.34 to 19.05)	2.26 (1.66 to 3.09)
Anti-18C antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	13.21 (11.44 to 15.25)
Anti-19F antibodies, PRE (N= 0, 0, 0, 96)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.6 (0.4 to 0.89)
Anti-19F antibodies, D7 (N=208, 14, 54, 98)	11.63 (10 to 13.51)	16.44 (10.68 to 25.29)	8.09 (6.29 to 10.42)	5.12 (3.97 to 6.62)

Anti-19F antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	15.47 (13.08 to 18.29)
Anti-23F antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.1 (0.07 to 0.14)
Anti-23F antibodies, D7 (N= 208, 14, 54, 98)	6.5 (5.61 to 7.53)	9.34 (5.62 to 15.54)	4.7 (3.43 to 6.45)	0.42 (0.3 to 0.59)
Anti-23F antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1.63 (1.32 to 2.01)

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	27	94	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, Y1 (N=354, 27, 92)	16.2 (13.8 to 19)	4.8 (3.6 to 6.4)	7.3 (5.9 to 9)	
Anti-4 OPA Titers, Y1 (N= 340, 26, 86)	59.8 (45.7 to 78.3)	192.9 (82.4 to 452)	88.9 (54.6 to 144.6)	
Anti-5 OPA Titers, Y1 (N=335, 27, 89)	24.2 (20.8 to 28.2)	5.1 (3.6 to 7.4)	11.2 (8.7 to 14.3)	
Anti-6B OPA Titers, Y1 (N=354, 25, 88)	35.5 (26.5 to 47.5)	476.9 (175.3 to 1298)	44.7 (24 to 83.3)	
Anti-7F OPA Titers, Y1 (N= 346, 25, 89)	1855.7 (1644.4 to 2094.1)	350.4 (121.8 to 1008)	1617.2 (1152.9 to 2268.3)	
Anti-9V OPA Titers, Y1 (N=352, 26, 94)	791.5 (701.8 to 892.8)	1240.7 (829.4 to 1855.9)	370.5 (281.8 to 487.2)	
Anti-14 OPA Titers, Y1 (N= 343, 25, 91)	551.9 (486.5 to 626.2)	607.3 (385.3 to 957.1)	456.6 (361.1 to 577.3)	
Anti-18C OPA Titers, Y1 (N= 319, 24, 84)	23.5 (18.6 to 29.8)	15.5 (6.1 to 39.2)	10.4 (7.1 to 15.4)	

Anti-19F OPA Titers, Y1 (N= 359, 27, 94)	53.4 (44.7 to 63.9)	35.4 (15.9 to 78.6)	58 (41.6 to 80.7)	
Anti-23F OPA Titers, Y1 (N= 336, 27, 93)	784.9 (625.4 to 985)	3013.1 (1349.5 to 6727.2)	552.3 (362.1 to 842.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	354	27	92	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, Y2 (N= 354, 27, 92)	8.4 (7.3 to 9.7)	4 (4 to 4)	6.3 (4.9 to 8)	
Anti-4 OPA Titers, Y2 (N= 335, 27, 84)	29 (22.1 to 38)	33.5 (11.9 to 94.6)	39.3 (23.7 to 65.2)	
Anti-5 OPA Titers, Y2 (N= 351, 27, 91)	11.4 (10 to 13)	4.3 (3.9 to 4.7)	7.4 (6 to 9.1)	
Anti-6B OPA Titers, Y2 (N= 342, 27, 88)	167.2 (124.1 to 225.2)	526.1 (210.5 to 1314.4)	213.7 (117.8 to 387.6)	
Anti-7F OPA Titers, Y2 (N= 350, 27, 91)	1488.7 (1358.3 to 1631.6)	1068.3 (619.5 to 1842.4)	1387.8 (1096.2 to 1756.9)	
Anti-9V OPA Titers, Y2 (N= 349, 27, 92)	648.5 (570 to 737.7)	730.4 (457.7 to 1165.7)	391 (279.2 to 547.5)	
Anti-14 OPA Titers, Y2 (N= 341, 25, 90)	660.2 (567.2 to 768.4)	651 (348.6 to 1215.5)	391 (279.2 to 547.5)	
Anti-18C OPA Titers, Y2 (N= 325, 27, 83)	34.9 (26.6 to 45.7)	34.8 (11.7 to 103.2)	17.7 (10.7 to 29.2)	
Anti-19F OPA Titers, Y2 (N= 349, 27, 92)	78.1 (60.9 to 100.2)	49.2 (21.2 to 113.9)	105.4 (65.8 to 168.7)	
Anti-23F OPA Titers, Y2 (N= 342, 26, 91)	632 (483 to 827)	1923 (952.2 to 3883.7)	435 (250.5 to 755.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

Pneumococcal serotypes assessed were pneumococcal serotypes OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administrated in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	16	72	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, Y4 (N= 250, 16, 72)	8.8 (7.1 to 10.9)	4.6 (3.4 to 6.4)	8.9 (5.9 to 13.2)	
Anti-4 OPA Titers, Y4 (N= 232, 16, 63)	37.9 (27.2 to 52.8)	62.2 (13.6 to 284.7)	50.7 (26.5 to 97)	
Anti-5 OPA Titers, Y4 (N= 243, 15, 68)	7.7 (6.8 to 8.9)	5.3 (3.5 to 8.1)	5.5 (4.5 to 6.6)	
Anti-6B OPA Titers, Y4 (N= 250, 16, 68)	875.7 (658.7 to 1164.3)	978.3 (395.3 to 2421.3)	716.4 (417.4 to 1229.7)	
Anti-7F OPA Titers, Y4 (N= 249, 15, 71)	1693.1 (1489.3 to 1924.8)	965.8 (666.8 to 1398.9)	1602.2 (1286.9 to 1994.5)	
Anti-9V OPA Titers, Y4 (N= 250, 15, 70)	747.4 (624.9 to 894.1)	563.8 (220.2 to 1444)	558.6 (403 to 774.2)	
Anti-14 OPA Titers, Y4 (N= 250, 15, 71)	1139.8 (961.9 to 1350.5)	687.9 (267.8 to 1767.4)	849.4 (645.4 to 1117.8)	
Anti-18C OPA Titers, Y4 (N= 226, 16, 63)	46.4 (33.3 to 64.5)	35.3 (8.8 to 142.5)	26.6 (14.3 to 49.3)	
Anti-19F OPA Titers, Y4 (N= 247, 16, 69)	151.7 (115.9 to 198.4)	178.8 (64.6 to 495.1)	129.3 (83.1 to 201.4)	
Anti-23F OPA Titers, Y4 (N= 239, 15, 65)	1518.4 (1107.9 to 2080.9)	3366.1 (1599.2 to 7085.1)	1146.2 (596.8 to 2201.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	204	13	54	96
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, PRE (N= 0, 0, 0, 94)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	5 (4.2 to 5.9)
Anti-1 OPA Titers, D7 (N= 197, 13, 50, 92)	2920.8 (2353.5 to 3624.7)	1331 (586.7 to 3019.5)	1816.1 (1090 to 3025.8)	605 (462.7 to 791.2)
Anti-1 OPA Titers, M3 (N= 0, 0, 0, 95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	128.3 (97.3 to 169.1)
Anti-4 OPA Titers, PRE (N= 0, 0, 0, 81)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	11.5 (7.2 to 18.3)
Anti-4 OPA Titers, D7 (N=196, 13, 51, 93)	23633.7 (19118.5 to 29215.3)	10650.3 (3969.2 to 28577.6)	8592.8 (5609.3 to 13163.1)	18262.1 (15571.6 to 21417.4)
Anti-4 OPA Titers, M3 (N= 0, 0, 0, 94)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4451.3 (3962.4 to 5000.6)
Anti-5 OPA Titers, PRE (N= 0, 0, 0, 91)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4.9 (4.3 to 5.7)
Anti-5 OPA Titers, D7 (N= 193, 13, 48, 91)	822.3 (662.7 to 1020.3)	375.6 (217.4 to 648.9)	683.6 (428.6 to 1090.2)	295.6 (219.4 to 398.3)
Anti-5 OPA Titers, M3 (N= 0, 0, 0, 92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	93.2 (73.7 to 117.8)

Anti-6B OPA Titers, PRE (N= 0, 0, 0, 79)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	70.7 (33.5 to 149.2)
Anti-6B OPA Titers, D7 (N= 198, 13, 50, 93)	3513.1 (2858.1 to 4318.1)	3566.6 (2446.1 to 5200.3)	1590.5 (942.8 to 2683.3)	1971.4 (1238 to 3139.2)
Anti-6B OPA Titers, M3 (N= 0, 0, 0, 95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2536.9 (2014.1 to 3195.5)
Anti-7F OPA Titers, PRE (N= 0, 0, 0, 74)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1368.2 (849.6 to 2185.8)
Anti-7F OPA Titers, D7 (N= 199, 13, 50, 93)	25196.4 (21149.5 to 30017.6)	17828.8 (10270.4 to 30949.7)	13098.6 (9715.5 to 17659.8)	19243.4 (15701.4 to 23584.5)
Anti-7F OPA Titers, M3 (N= 0, 0, 0, 93)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	9692 (8299.3 to 11318.4)
Anti-9V OPA Titers, PRE (N= 0, 0, 0, 87)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	398.2 (253.8 to 624.9)
Anti-9V OPA Titers, D7 (N=201, 13, 51, 93)	9419.4 (7586 to 11695.9)	12234.7 (8280.5 to 18077.3)	7730.3 (5361.8 to 11145.2)	8322.7 (6605.7 to 10486.1)
Anti-9V OPA Titers, M3 (N= 0, 0, 0, 94)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	6456.1 (5458.1 to 7636.6)
Anti-14 OPA Titers, PRE (N= 0, 0, 0, 83)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	586.5 (439 to 783.6)
Anti-14 OPA Titers, D7 (N= 197, 13, 51, 94)	8572.3 (7145.4 to 10284.3)	4192.8 (2218.6 to 7923.7)	6883.1 (5057.3 to 9368)	4678.2 (3788 to 5777.5)
Anti-14 OPA Titers, M3 (N= 0, 0, 0, 95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4891.1 (4178.8 to 5724.8)
Anti-18C OPA Titers, PRE (N= 0, 0, 0, 89)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	5.3 (4.2 to 6.6)
Anti-18C OPA Titers, D7 (N= 194, 13, 50, 92)	3378.9 (2652.2 to 4304.8)	3478.6 (1788.5 to 6765.8)	1663.2 (970.5 to 2850.2)	2503.1 (1692.6 to 3701.6)
Anti-18C OPA Titers, M3 (N= 0, 0, 0, 92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2255.9 (1876.9 to 2711.4)
Anti-19F OPA Titers, PRE (N= 0, 0, 0, 92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	12 (8.3 to 17.5)
Anti-19F OPA Titers, D7 (N= 196, 13, 50, 93)	1346.4 (1068.6 to 1696.5)	2340.4 (654.8 to 8365.2)	662.3 (430 to 1020.1)	700.2 (456.1 to 1074.9)
Anti-19F OPA Titers, M3 (N= 0, 0, 0, 93)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1437.7 (1146.9 to 1802.3)
Anti-23F OPA Titers, PRE (N= 0, 0, 0, 83)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	176.4 (83.4 to 373.2)
Anti-23F OPA Titers, D7 (N= 199, 13, 50, 96)	8700.4 (7021.7 to 10780.5)	11341.1 (5374.6 to 23931)	7871.9 (4965.3 to 12480.1)	6813.9 (5249.5 to 8844.6)
Anti-23F OPA Titers, M3 (N= 0, 0, 0, 95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	5586.1 (4666.1 to 6687.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)]

End point description:

The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	31	102	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, Y1 (N= 390, 31, 102)	0.28 (0.24 to 0.32)	0.44 (0.28 to 0.7)	0.27 (0.21 to 0.36)	
Anti-19A antibodies, Y1 (N= 390, 31, 102)	0.28 (0.25 to 0.32)	0.21 (0.13 to 0.33)	0.23 (0.17 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) – Follow-Up Period: Persistence analysis in Year 2 (111346 sub-study)

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) – Follow-Up Period: Persistence analysis in Year 2 (111346 sub-study)

End point description:

The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PDDIT- 007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, Y2 (N= 368, 30, 96)	0.33 (0.28 to 0.4)	0.57 (0.3 to 1.11)	0.4 (0.27 to 0.58)	
Anti-19A antibodies, Y2 (N= 368, 30, 96)	0.37 (0.31 to 0.44)	0.25 (0.14 to 0.44)	0.35 (0.25 to 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administrated in study 10PN-PD-DIT- 007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, Y4 (N= 263, 19, 74)	0.92 (0.77 to 1.1)	0.69 (0.34 to 1.38)	0.75 (0.55 to 1.03)	
Anti-19A antibodies, Y4 (N= 263, 19, 75)	1.3 (1.07 to 1.59)	1.08 (0.5 to 2.33)	1.14 (0.77 to 1.68)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	210	14	55	98
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.2 (0.15 to 0.27)
Anti-6A antibodies, D7 (N= 208, 14, 55, 98)	2.2 (1.85 to 2.6)	1.67 (1 to 2.8)	1.33 (0.96 to 1.83)	0.44 (0.33 to 0.58)
Anti-6A antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.92 (0.73 to 1.16)
Anti-19A antibodies, PRE (N= 0, 0, 0, 97)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.44 (0.32 to 0.6)
Anti-19A antibodies, D7 (N= 208, 14, 54, 98)	2.79 (2.33 to 3.35)	2.44 (1.2 to 4.96)	1.72 (1.14 to 2.61)	1.1 (0.84 to 1.45)
Anti-19A antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.39 (1.9 to 3.01)

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	352	26	93	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, Y1 (N= 323, 25, 75)	59 (45.9 to 76)	610.2 (317.7 to 1171.9)	46.6 (28.3 to 76.8)	
Anti-19A OPA Titers, Y1 (N= 155, 26, 93)	6 (5.2 to 6.8)	5.9 (3.7 to 9.5)	5.5 (4.5 to 6.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	351	27	91	
Units: Titers				

geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, Y2 (N= 314, 25, 82)	121.8 (95.2 to 156)	356.5 (134.6 to 944.6)	133.7 (81.8 to 218.7)	
Anti-19A OPA Titers, Y2 (N= 351, 27, 91)	12.8 (10.4 to 15.7)	10.9 (5.2 to 22.8)	11.1 (7.6 to 16.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	251	16	71	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, Y4 (N= 231, 14, 66)	213.5 (165.4 to 275.7)	227.8 (72.1 to 720)	153.5 (90.5 to 260.2)	
Anti-19A OPA Titers, Y4 (N= 246, 15, 68)	31.2 (23.6 to 41.3)	14.3 (5.6 to 36.8)	21.8 (13.3 to 35.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A [Follow-up Period: Immunogenicity

	Analysis in Year 4 (111347 sub-study)]

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	201	13	50	92
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, PRE (N= 0, 0, 0, 82)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	102.6 (61.5 to 171.2)
Anti-6A OPA Titers, D7 (N= 189, 12, 49, 90)	1217.7 (957.8 to 1548.2)	1490.2 (681.6 to 3257.8)	467.7 (293.8 to 744.5)	826.5 (593.9 to 1150.2)
Anti-6A OPA Titers, M3 (N= 0, 0, 0, 91)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	943.4 (691.3 to 1287.4)
Anti-19A OPA Titers, PRE (N= 0, 0, 0, 92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	9.9 (7 to 13.8)
Anti-19A OPA Titers, D7 (N= 194, 13, 48, 90)	467 (335 to 651.1)	437.6 (81.3 to 2356.3)	106.1 (54.1 to 208.3)	431.2 (269.4 to 689.9)
Anti-19A OPA Titers, M3 (N= 0, 0, 0, 91)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	376.4 (256.3 to 552.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) - Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)

End point title	Antibody concentrations to protein D (Anti-PD) - Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	30	102	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, Y1 (N= 390, 30, 102)	822.1 (731.5 to 923.9)	93.9 (66.6 to 132.3)	193.6 (155.9 to 240.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) – Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)

End point title	Antibody concentrations to protein D (Anti-PD) – Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT- 007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	29	96	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, Y2 (N= 368, 29, 96)	573.2 (509.6 to 644.8)	116.7 (80.9 to 168.3)	157.5 (128.7 to 192.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT- 007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, Y4 (N= 261, 19, 74)	372.4 (329.6 to 420.9)	144.9 (86.3 to 243.2)	161.4 (128.4 to 203)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	208	14	54	98
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, PRE (N= 0, 0, 0, 95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	106 (91.1 to 123.4)
Anti-PD antibodies, D7 (N= 208, 14, 54, 98)	2106 (1806.7 to 2454.9)	718.2 (442.5 to 1165.7)	680.7 (522.9 to 886.2)	382.9 (320.7 to 457.2)
Anti-PD antibodies, M3 (N= 0, 0, 0, 98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	708.6 (604.6 to 830.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with solicited local symptoms

End point title	Number of subjects reported with solicited local symptoms

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any occurrence of symptom regardless of intensity grade. Any Redness or any Swelling symptom = any symptom greater than (>) 0 millimeter (mm). Grade 3 pain = maximum intensity of local injection defined as subject crying when limb was moved/spontaneously painful. Grade 3 redness/swelling= maximum intensity of local injection >30 mm. Follow-up period was of 4 days (Days 0-3) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) period(s) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	64	100
Units: Participants				
Pain, Any (N= 264, 20, 64, 100)	157	9	34	54
Redness, Any (N= 264, 20, 64, 100)	90	5	14	21
Swelling, Any (N= 264, 20, 64, 100)	67	4	15	20
Pain, Grade 3 (N= 264, 20, 64, 100)	7	1	5	3
Redness, Grade 3 (> 30 mm) (N= 264, 20, 64, 100)	7	0	0	1
Swelling, Grade 3 (> 30 mm) (N= 264, 20, 64, 100)	5	0	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with solicited general symptoms

End point title	Number of subjects reported with solicited general symptoms

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever (any fever defined as temperature by axillary measurement of 37.5°C and above). Grade 3 drowsiness was defined as drowsiness that prevented normal activity; Grade 3 irritability was defined as crying that could not be comforted/prevented normal activity. Grade 3 loss of appetite was defined as subject not eating at all. Grade 3 fever was defined as axillary temperature >39.5°C. Related AE was defined as any AE assessed by investigators to be causally related to administration of the study vaccine. Follow-up period was of 4 days (Days 0-3) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) period(s) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	263	20	64	100
Units: Participants				
Drowsiness, Any (N= 263, 20, 64, 100)	49	2	12	12
Drowsiness, Grade 3 (N= 263, 20, 64, 100)	1	0	0	0
Drowsiness, Related (N= 263, 20, 64, 100)	48	2	11	11
Irritability, Any (N= 263, 20, 64, 100)	35	4	6	8
Irritability, Related (N= 263, 20, 64, 100)	35	4	6	8
Irritability, Grade 3 (N= 263, 20, 64, 100)	0	0	0	0
Loss of appetite, Any (N= 263, 20, 64, 100)	30	3	6	13
Loss of appetite, Grade 3 (N= 263, 20, 64, 100)	1	0	1	0
Loss of appetite, Related (N= 263, 20, 64, 100)	30	3	5	11
Fever, Any (N= 263, 20, 64, 100)	13	0	2	5
Fever, >39,5°C (N= 263, 20, 64, 100)	0	0	0	0
Fever, Related (N= 263, 20, 64, 100)	13	0	1	5

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" was defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. Follow-up period was of 31 days (Days 0-30) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 31 days for primed subjects and 2 periods of 31 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	65	100
Units: Participants				
Any Unsolicited AEs (N= 264, 20, 65, 100)	25	0	3	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) related to study procedures [Follow-up Period: Year 1 (111345 sub-study)]

End point title	Number of subjects with serious adverse events (SAEs) related to study procedures [Follow-up Period: Year 1 (111345 sub-study)]

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" was defined an incidence of a SAE regardless of intensity/severity.

End point type	Secondary

End point timeframe:

During Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007) i.e. for each primed subject: from the time the subject was enrolled in the 111345 study until he/she completed the same study (approximatively 12 months)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	31	102	
Units: Participants				
Any Related SAEs, Y1 (N=391, 31, 102)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) related to study procedures [(Follow-up Period: Year 2 (111346 sub-study) until Year 4 (111347 sub-study)]

End point title	Number of subjects with serious adverse events (SAEs) related to study procedures [(Follow-up Period: Year 2 (111346 sub-study) until Year 4 (111347 sub-study)]

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. “Any” is defined an incidence of a SAE regardless of intensity/severity.

End point type	Secondary

End point timeframe:

From Year (Y) 2 to Y4 FU visit (post booster vaccination administered in 10PN-PD-DIT-007) i.e. for each subject(S): when S was enrolled in 111346 study until S completed the same study visit or the 111347 study visit (range of 1 to 3 years for each S))

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	370	31	96	
Units: Participants				
Any Related SAEs, Y2 to Y4, (N= 370, 31, 96)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) [Follow-up Period: Vaccination Period in Year 4 (111347 sub-study)]

End point title	Number of subjects with serious adverse events (SAEs) [Follow-up Period: Vaccination Period in Year 4 (111347 sub-study)]

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity.

End point type	Secondary

End point timeframe:

For primed groups: from Months 48-49 (additional vaccination period); for unprimed group: from Day 0 up to Month 3 (catch-up vaccination period)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	65	100
Units: Participants				
Any Related SAEs, Y4 (N= 264, 20, 65, 100)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	27	94	
Units: Participants				
Anti-1 OPA, Y1 (N= 354, 27, 92)	188	2	26	
Anti-4 OPA, Y1 (N= 340, 26, 86)	201	21	65	
Anti-5 OPA, Y1 (N= 335, 27, 89	241	2	46	
Anti-6B OPA, Y1 (N= 354, 25, 88)	164	23	44	
Anti-7F OPA, Y1 (N= 346, 25, 89)	343	20	85	
Anti-9V OPA, Y1 (N= 352, 26, 94)	351	26	90	
Anti-14 OPA, Y1 (N= 343, 25, 91)	336	25	89	
Anti-18C OPA, Y1 (N= 319, 24, 84)	173	10	25	
Anti-19F OPA, Y1 (N= 359, 27, 93)	306	19	83	
Anti-23F OPA, Y1 (N=336, 27, 93)	301	26	82	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: persistence analysis in Year 2 (111346 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: persistence analysis in Year 2 (111346 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	354	27	92	
Units: Participants				
Anti-1 OPA, Y2 (N= 354, 27, 92)	92	0	15	
Anti-4 OPA, Y2 (N= 335, 27, 84)	146	12	48	
Anti-5 OPA, Y2 (N= 351, 27, 91)	169	2	31	
Anti-6B OPA, Y2 (N= 342, 27, 88)	241	24	67	
Anti-7F OPA Titers, Y2 (N= 350, 27, 91)	350	26	90	

Anti-9V OPA, Y2 (N= 349, 27, 92)	247	27	87	
Anti-14 OPA, Y2 (N= 341, 25, 90)	333	24	85	
Anti-18C OPA, Y2 (N= 325, 27, 83)	165	11	29	
Anti-19F OPA, Y2 (N= 349, 27, 92)	279	21	78	
Anti-23F OPA, Y2 (N= 342, 26, 91)	285	25	72	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	16	72	
Units: Participants				
Anti-1 OPA, Y4 (N= 250, 16, 72)	55	1	17	
Anti-4 OPA, Y4 (N= 232, 16, 63)	107	8	33	
Anti-5 OPA, Y4 (N= 243, 15, 68)	80	2	11	
Anti-6B OPA, Y4 (N= 250, 16, 68)	223	15	62	
Anti-7F OPA, Y4 (N= 249, 15, 71)	248	15	71	
Anti-9V OPA, Y4 (N= 250, 15, 70)	242	14	68	
Anti-14 OPA, Y4 (N= 250, 15, 71)	247	14	70	
Anti-18C OPA, Y4 (N= 226, 16, 63)	121	8	27	
Anti-19F OPA, Y4 (N= 247, 16, 69)	211	14	62	
Anti-23F OPA, Y4 (N= 239, 15, 65)	209	15	55	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsophagocytic activity against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for opsophagocytic activity against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Analysis was performed with Unprimed group included. The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	201	13	51	96
Units: Participants				
Anti-1 OPA, PRE (N= 0, 0, 0, 94)	0	0	0	8
Anti-1 OPA, D7 (N= 197, 13, 50, 92)	193	13	48	90
Anti-1 OPA, M3 (N= 0, 0, 0, 95)	0	0	0	87
Anti-4 OPA, PRE (N= 0, 0, 0, 81)	0	0	0	17
Anti-4 OPA, D7 (N= 196, 13, 51, 93)	194	13	50	93
Anti-4 OPA, M3 (N= 0, 0, 0, 94)	0	0	0	94
Anti-5 OPA, PRE (N= 0, 0, 0, 92)	0	0	0	8
Anti-5 OPA, D7 (N= 193, 13, 48, 91)	186	13	47	87
Anti-5 OPA, M3 (N= 0, 0, 0, 92)	0	0	0	89
Anti-6B OPA, PRE (N= 0, 0, 0, 79)	0	0	0	35
Anti-6B OPA, D7 (N= 198, 13, 50, 93)	196	13	48	84
Anti-6B OPA, M3 (N= 0, 0, 0, 95)	0	0	0	94
Anti-7F OPA, PRE (N= 0, 0, 0, 74)	0	0	0	67
Anti-7F OPA, D7 (N= 199, 13, 50, 93)	199	13	50	93
Anti-7F OPA, M3 (N= 0, 0, 0, 93)	0	0	0	93
Anti-9V OPA, PRE (N= 0, 0, 0, 87)	0	0	0	87
Anti-9V OPA, D7 (N= 201, 13, 51, 93)	201	13	51	93
Anti-9V OPA, M3 (N= 0, 0, 0, 94)	0	0	0	94
Anti-14 OPA, PRE (N= 0, 0, 0, 83)	0	0	0	81
Anti-14 OPA, D7 (N= 197, 13, 51, 94)	197	13	51	94
Anti-14 OPA, M3 (N= 0, 0, 0, 95)	0	0	0	95
Anti-18C OPA, PRE (N= 0, 0, 0, 89)	0	0	0	7
Anti-18C OPA, D7 (N= 194, 13, 50, 92)	190	13	48	88
Anti-18C OPA, M3 (N= 0, 0, 0, 92)	0	0	0	92
Anti-19F OPA, PRE (N= 0, 0, 0, 92)	0	0	0	30
Anti-19F OPA, D7 (N= 196, 13, 50, 93)	194	13	50	91
Anti-19F OPA, M3 (N= 0, 0, 0, 93)	0	0	0	93
Anti-23F OPA, PRE (N= 0, 0, 0, 83)	0	0	0	47

Anti-23F OPA, D7 (N= 199, 13, 50, 96)	197	13	49	95
Anti-23F OPA, M3 (N= 0, 0, 0, 95)	0	0	0	95

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: persistence analysis in Year 1 (111345 sub-study)]

End point title	Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: persistence analysis in Year 1 (111345 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The results for the immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	31	102	
Units: Participants				
Anti-6A antibodies, Y1 (N= 390, 31, 102)	376	31	97	
Anti-19A antibodies, Y1 (N= 390, 31, 102)	366	29	93	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

End point title	Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were

measured by 22F-inhibation ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: Participants				
Anti-6A antibodies, Y2 (N= 368, 30, 96)	330	30	86	
Anti-19A antibodies, Y2 (N= 368, 30, 96)	319	25	83	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	263	19	75	
Units: Participants				
Anti-6A antibodies, Y4 (N= 263, 31, 75)	256	18	72	
Anti-19A antibodies, Y4 (N= 263, 31, 75)	260	18	74	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	208	14	54	98
Units: Participants				
Anti-6A antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	76
Anti-6A antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	92
Anti-6A antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	97
Anti-19A antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	88
Anti-19A antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	97
Anti-19A antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against

pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were mesured by Opsonophagocytic activity (OPA). The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	352	26	93	
Units: Participants				
Anti-6A OPA, Y1 (N= 323, 25, 75)	196	24	45	
Anti-19A OPA, Y1 (352, 26, 93)	45	3	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic activity (OPA). The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	351	27	91	
Units: Participants				
Anti-6A OPA, Y2 (N= 314, 25, 82)	235	21	62	
Anti-19A OPA, Y2 (N= 351, 27, 91)	115	8	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic Activity (OPA). The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	246	15	68	
Units: Participants				
Anti-6A OPA Titers, Y4 (N= 231, 14, 66)	194	12	51	
Anti-19A OPA Titers, Y4 (N= 246, 15, 68)	135	7	34	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic Activity (OPA). The seropositivity cut-off for the assay was 8.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	194	13	49	92
Units: Participants				
Anti-6A OPA, PRE (N= 0, 0, 0, 82)	0	0	0	57
Anti-6A OPA, D7 (N= 189, 12, 49, 92)	185	12	46	88
Anti-6A OPA, M3 (N= 0, 0, 0, 91)	0	0	0	87
Anti-19A OPA, PRE (N= 0, 0, 0, 92)	0	0	0	25
Anti-19A OPA, D7 (N= 194, 13, 48, 90)	173	11	36	81
Anti-19A OPA, M3 (N= 0, 0, 0, 91)	0	0	0	87

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point title	Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	30	102	
Units: Participants				
Anti-PD antibodies, Y1 (N= 390, 30, 102)	373	11	71	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 2 (111345 sub-study)]

End point title	Number of seropositive subjects for anti protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 2 (111345 sub-study)]

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

End point type	Secondary

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	29	96	
Units: Participants				
Anti-PD antibodies, Y2 (N= 368, 29, 96)	340	15	65	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

End point type	Secondary

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	261	19	74	
Units: Participants				
Anti-PD antibodies, Y4 (N= 261, 19, 74)	241	12	54	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	208	14	54	98
Units: Participants				
Anti-PD antibodies, PRE (N= 0, 0, 0, 95)	0	0	0	54
Anti-PD antibodies, D7 (N= 208, 14, 54, 96)	207	14	45	92
Anti-PD antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-vaccine pneumococcal serotypes antibodies [Follow-up Period: Immunogenicity analysis in Year 4 (111347 sub-study)]

End point title	Number of seropositive subjects for anti-vaccine pneumococcal serotypes antibodies [Follow-up Period: Immunogenicity analysis in Year 4 (111347 sub-study)]

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 microgram per milliliter (µg/mL) as seropositivity cut off.

End point type	Secondary

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

End point values	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	208	14	54	98
Units: Participants				
Anti-1 antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	69
Anti-1 antibodies, D7 (N= 208, 14, 54, 98)	207	14	54	97
Anti-1 antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-4 antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	29
Anti-4 antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	98
Anti-4 antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-5 antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	72
Anti-5 antibodies, D7 (N= 208, 14, 54, 98)	207	14	54	98
Anti-5 antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-6B antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	77
Anti-6B antibodies, D7 (N= 208, 14, 54, 97)	207	14	54	94
Anti-6B antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-7F antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	64
Anti-7F antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	98
Anti-7F antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-9V antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	67
Anti-9V antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	94
Anti-9V antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-14 antibodies, PRE (N= 0, 0, 0, 96)	0	0	0	90
Anti-14 antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	97

Anti-14 antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-18C antibodies, PRE (N= 0, 0, 0, 96)	0	0	0	52
Anti-18C antibodies, D7 (N= 208, 14, 54, 98)	207	14	54	97
Anti-18C antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-19F antibodies, PRE (N= 0, 0, 0, 96)	0	0	0	75
Anti-19F antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	97
Anti-19F antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98
Anti-23F antibodies, PRE (N= 0, 0, 0, 97)	0	0	0	98
Anti-23F antibodies, D7 (N= 208, 14, 54, 98)	208	14	54	90
Anti-23F antibodies, M3 (N= 0, 0, 0, 98)	0	0	0	98

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Solicited and Unsolicited AEs: within 4 days and 31 days post Synflorix vaccination in 111347 study for all subjects. Related SAEs: at Year 1 (111345 study), Year 2 up to Year 4 (111346-11347 study). Any SAEs: during the 111347 study vaccination period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Synflorix + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Infanrix + Havrix and/or Varilrix Group

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

Reporting group title	Unprimed Group

Reporting group description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

Serious adverse events	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 391 (0.26%)	0 / 31 (0.00%)	0 / 102 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Broncopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 391 (0.26%)	0 / 31 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Unprimed Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Broncopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Synflorix + Infanrix + Havrix and/or Varilrix Group	Prevenar + Infanrix + Havrix and/or Varilrix Group	Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 391 (40.15%)	9 / 31 (29.03%)	34 / 102 (33.33%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	157 / 264 (59.47%)	9 / 20 (45.00%)	34 / 64 (53.13%)
occurrences (all)	157	9	34
Redness			
subjects affected / exposed[2]	90 / 264 (34.09%)	5 / 20 (25.00%)	14 / 64 (21.88%)
occurrences (all)	90	5	14
Swelling			
subjects affected / exposed[3]	67 / 264 (25.38%)	4 / 20 (20.00%)	15 / 64 (23.44%)
occurrences (all)	67	4	15

Drowsiness			
subjects affected / exposed[4]	49 / 263 (18.63%)	2 / 20 (10.00%)	12 / 64 (18.75%)
occurrences (all)	49	2	12
Irritability			
subjects affected / exposed[5]	35 / 263 (13.31%)	4 / 20 (20.00%)	6 / 64 (9.38%)
occurrences (all)	35	4	6
Loss of appetite			
subjects affected / exposed[6]	30 / 263 (11.41%)	3 / 20 (15.00%)	6 / 64 (9.38%)
occurrences (all)	30	3	6
Fever (Axillary temperature ≥ 37.5° C)			
subjects affected / exposed[7]	13 / 263 (4.94%)	0 / 20 (0.00%)	2 / 64 (3.13%)
occurrences (all)	13	0	2

Non-serious adverse events	Unprimed Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 100 (54.00%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	54 / 100 (54.00%)		
occurrences (all)	54		
Redness			
subjects affected / exposed[2]	21 / 100 (21.00%)		
occurrences (all)	21		
Swelling			
subjects affected / exposed[3]	20 / 100 (20.00%)		
occurrences (all)	20		
Drowsiness			
subjects affected / exposed[4]	12 / 100 (12.00%)		
occurrences (all)	12		
Irritability			
subjects affected / exposed[5]	8 / 100 (8.00%)		
occurrences (all)	8		
Loss of appetite			
subjects affected / exposed[6]	13 / 100 (13.00%)		
occurrences (all)	13		
Fever (Axillary temperature ≥ 37.5°			

C)			
subjects affected / exposed[7]	5 / 100 (5.00%)		
occurrences (all)	5		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This analysis was based only on those subjects from the Total Vaccinated cohort who completed symptom sheets.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2010	Amendment 1 Some aspects of study design, endpoints and study conclusion regarding the immunological memory and assessment of immune response following a second-dose of the vaccine have been added for the clarity of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported