Clinical trial results:
A phase III/IV, cluster-randomized, controlled study to evaluate the effectiveness of GlaxoSmithKline Biologicals' 10-valent pneumococcal and non-typeable Haemophilus influenzae protein D conjugate vaccine in reducing the incidence of invasive diseases.

Summary

EudraCT number	2008-005149-48
Trial protocol	FI
Global end of trial date	05 October 2013

Results information

Result version number	v3
This version publication date	15 November 2020
First version publication date	29 July 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	111442

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00861380
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Disclosure Advisor,, GlaxoSmithKline Biologicals,, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000673-PIP01-09
Does article 45 of REGULATION (EC) No 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	15 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the effectiveness of 10Pn-PD-DiT vaccine in preventing culture-confirmed IPD due to vaccine pneumococcal serotypes in children vaccinated with at least one dose of 10Pn-PD-DiT within the first 7 months of life in clusters assigned to a 3-dose primary vaccination course.
Criteria for effectiveness: Effectiveness (VE) in preventing culture-confirmed IPD due to the 10 vaccine serotypes will be demonstrated if the 2-sided p-value calculated for the null hypothesis H0 = {vaccine-type [VT] IPD VE = 0%} is lower than 5%.

Protection of trial subjects:

The nurses administering vaccines were instructed to observe the vaccinees closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed up for serious adverse events (SAEs) reported as occurring during the study up to study end. In addition, an Independent Data Monitoring Committee (IDMC) was set up, of which responsibilities included the following: (1) Review of data collection methods, safety/effectiveness monitoring procedures and making recommendations for additions or adjustments, as applicable; (2) Recommendations for maintaining, or breaking the blind where necessary, in the course of reviewing safety results; (3) Recommendations for stopping the trial for effectiveness or safety reasons when appropriate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 87165
Worldwide total number of subjects	87165
EEA total number of subjects	87165

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	87165
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study also served as basis for conducting a long-term evaluation of the impact of vaccination with GSK Biologicals' 10Pn-PD-DiT vaccine. 4796 subjects of the 10PN-PD-DIT-053 (112595) study (NCT00839254-EUDRACT:2008-006551-51) contributed to objectives of this study i.e.: a total of 45977 subjects.

Pre-assignment

Screening details:

41188 subjects were enrolled in 10PN-PD-DIT-043 study, 7 subjects didn't receive any vaccination, 41181 subjects started in the study.

Pre-assignment period milestones

Number of subjects started	87165
Number of subjects completed	41181

Pre-assignment subject non-completion reasons

Reason: Number of subjects	10PN043-053 subjects: 45977
Reason: Number of subjects	10PN-043 Subjects not vaccinated: 7

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn3+1-6W-6M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal and non-typeable H. influenzae protein D conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh.

Arm title	10Pn2+1-6W-6M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks, followed by a booster dose of the same vaccine with an interval of preferably 6

months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal and non-typeable H. influenzae protein D conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh.

Arm title	Ctrl-6W-6M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B vaccine (called also HBV vaccine) according to either a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule), or according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Arm type	Active comparator
Investigational medicinal product name	Engerix B-thio free
Investigational medicinal product code	
Other name	Engerix-B,HBV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh.

Arm title	10Pn7-11M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal and non-typeable H. influenzae protein D conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh.

Arm title	Ctrl7-11M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Engerix B (called also HBV) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Arm type	Active comparator

Investigational medicinal product name	Engerix B-thio free
Investigational medicinal product code	
Other name	Engerix-B,HBV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh.

Arm title	10Pn12-18M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Arm type	Experimental
Investigational medicinal product name	10-valent pneumococcal and non-typeable H. influenzae protein D conjugate vaccine
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn, Synflorix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Arm title	Ctrl12-18M/043 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Havrix (called also HAV) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Arm type	Active comparator
Investigational medicinal product name	Havrix-preservative free
Investigational medicinal product code	
Other name	HAV, Havrix 720 Junior
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscularly administration by injection in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Number of subjects in period 1[1]	10Pn3+1-6W-6M/043 Group	10Pn2+1-6W-6M/043 Group	Ctrl-6W-6M/043 Group
Started	8427	9112	8872
Completed	0	0	0
Not completed	8427	9112	8872
Withdrawal Information not recorded	8427	9112	8872

Number of subjects in period 1	10Pn7-11M/043 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group

[1]			
Started	3689	1812	6249
Completed	0	0	0
Not completed	3689	1812	6249
Withdrawal Information not recorded	3689	1812	6249

Number of subjects in period 1[1]	Ctrl12-18M/043 Group
Started	3020
Completed	0
Not completed	3020
Withdrawal Information not recorded	3020

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 4796 subjects of the 10PN-PD-DIT-053 (112595) study (NCT00839254-EUDRACT:2008-006551-51) contributed to objectives of this study i.e.: a total of 45977 subjects were part of objective analysis for both studies. 41188 subjects were planned to be vaccinated in the study. 41181 of these were actually vaccinated and included in baseline period of the study.

Baseline characteristics

Reporting groups

Reporting group title	10Pn3+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn2+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	Ctrl-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B vaccine (called also HBV vaccine) according to either a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule), or according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Engerix B (called also HBV) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Havrix (called also HAV) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group values	10Pn3+1-6W-6M/043 Group	10Pn2+1-6W-6M/043 Group	Ctrl-6W-6M/043 Group
Number of subjects	8427	9112	8872
Age Categorical Units: Participants			
28 days - 23 months	8427	9112	8872
Sex: Female, Male Units: Participants			
Female	4239	4399	4351
Male	4188	4713	4521
Unknown	0	0	0

Reporting group values	10Pn7-11M/043 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group
Number of subjects	3689	1812	6249
Age Categorical Units: Participants			
28 days - 23 months	3689	1812	6249
Sex: Female, Male Units: Participants			
Female	0	0	0
Male	0	0	0
Unknown	3689	1812	6249

Reporting group values	Ctrl12-18M/043 Group	Total	
Number of subjects	3020	41181	
Age Categorical Units: Participants			
28 days - 23 months	3020	41181	
Sex: Female, Male Units: Participants			
Female	0	12989	
Male	0	13422	
Unknown	3020	14770	

End points

End points reporting groups

Reporting group title	10Pn3+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn2+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	Ctrl-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B vaccine (called also HBV vaccine) according to either a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule), or according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Engerix B (called also HBV) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Havrix (called also HAV) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Subject analysis set title	10Pn3+1-6W-6M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 1846 subjects) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule). Refer to group description for 10Pn3+1-6W-6M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	Ctrl-6W-6M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 1329 subjects) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B vaccine (called also HBV vaccine) according to either a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule), or according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). Refer to group description for Ctrl6W-6M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	10Pn2+1-6W-6M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 942 subjects) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). Refer to group description for 10Pn2+1-6W-6M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	10Pn7-11M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 191 subjects) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). Refer to group description for 10Pn7-11M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	Ctrl7-11M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 96 subjects) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Engerix B (called also HBV) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). Refer to group description for Ctrl7-11M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	10Pn12-18M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 286 subjects) studies, pooled, aged 12 to 18 months at enrolment. Subjects received

the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). Refer to group description for 10Pn12-18M/043 Group for vaccine specifics and administration route in this group.

Subject analysis set title	Ctrl12-18M/043+053 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects analyzed among all subjects who were enrolled in this group in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) and 10PN-PD-DIT-053 (NCT00839254 - EUDRACT 2008-006551-51) (i.e. 106 subjects) studies, pooled, and aged 12 to 18 months at enrolment. Subjects received the Havrix (called also HAV) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). Refer to group description for Ctrl12-18M/043 Group for vaccine specifics and administration route in this group.

Primary: Person Year Rate as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes. In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes. In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

The PYAR (Person-Year Rate) as regards subjects with culture-confirmed invasive pneumococcal disease (IPD) due to any of the pneumococcal vaccine serotypes was tabulated (vaccine pneumococcal serotypes = serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F). PYAR was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Primary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10201		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	0.000 (0.000 to 0.172)	0.564 (0.291 to 0.984)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis aimed at providing an estimate of vaccine effectiveness (VE) at preventing culture-confirmed IPD by comparing PYARs between groups taking into account the following parameters: T, n, n+ (number of clusters with at least one event culture-confirmed ID), and n/T. VE of the 10Pn vaccine in preventing culture-confirmed IPD due to the 10 vaccine serotypes was demonstrated if the 2-sided p-value calculated for the null hypothesis H0 =(vaccine-type [VT] IPD VE = 0%) was lower than (<) 5%.

Comparison groups	Ctrl-6W-6M/043+053 Group v 10Pn3+1-6W-6M/043+053 Group

Number of subjects included in analysis	20474
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [1]
Method	Regression, Linear
Parameter estimate	VE (1-RR)
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	82.8
upper limit	100

Notes:

[1] - P-value was calculated using a classical log linear Poisson regression with strata, without taking into account the multiplicity of the endpoints.

Primary: Person Year Rate as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes. In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes. In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

The PYAR (Person-Year Rate) as regards subjects with culture-confirmed invasive pneumococcal disease (IPD) due to any of the pneumococcal vaccine serotypes was tabulated (vaccine pneumococcal serotypes = serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F). PYAR was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Primary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10201	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	0.564 (0.291 to 0.984)	0.048 (0.001 to 0.270)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis aimed at providing an estimate of vaccine effectiveness (VE) at preventing culture-confirmed IPD by comparing PYARs between groups taking into account the following parameters: T, n, n+

(number of clusters with at least one event culture-confirmed ID), and n/T. VE of the 10Pn vaccine in preventing culture-confirmed IPD due to the 10 vaccine serotypes was demonstrated if the 2-sided p-value calculated for the null hypothesis H0 = (vaccine-type [VT] IPD VE = 0%) was lower than (<) 5%.

Comparison groups	10Pn2+1-6W-6M/043+053 Group v Ctrl-6W-6M/043+053 Group
Number of subjects included in analysis	20255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009 [2]
Method	Regression, Linear
Parameter estimate	VE (1-RR)
Point estimate	91.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.3
upper limit	99.6

Notes:

[2] - p-value was calculated using a classical log linear Poisson regression with strata, without taking into account the multiplicity of the endpoints.

Secondary: Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course (till end of blinded ID FU period)

End point title	Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course (till end of blinded ID FU period)

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log- likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10201		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.093 (0.011 to 0.336)	0.845 (0.501 to 1.336)		
Pneumococcal invasive disease (IPD)	0.000 (0.000 to 0.172)	0.657 (0.359 to 1.103)		
Serotype 4	0.000 (0.000 to 0.172)	0.000 (0.000 to 0.173)		
Serotype 6B	0.000 (0.000 to 0.172)	0.235 (0.076 to 0.548)		

Serotype 7F	0.000 (0.000 to 0.172)	0.000 (0.000 to 0.173)		
Serotype 14	0.000 (0.000 to 0.172)	0.188 (0.051 to 0.481)		
Serotype 18C	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Serotype 19F	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Serotype 23F	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Cross-reactive serotypes	0.000 (0.000 to 0.172)	0.094 (0.011 to 0.339)		
Serotype 6A	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Serotype 19A	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Other pneumococcal serotypes	0.000 (0.000 to 0.172)	0.000 (0.000 to 0.173)		
Serotype 3	0.000 (0.000 to 0.172)	0.000 (0.000 to 0.173)		
Serotype 15C	0.000 (0.000 to 0.172)	0.000 (0.000 to 0.173)		
H. influenzae ID	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Non-typeable (NTHI)	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		
Other bacteria	0.093 (0.011 to 0.336)	0.188 (0.051 to 0.481)		
Neisseria meningitidis	0.093 (0.011 to 0.336)	0.047 (0.001 to 0.262)		
Streptococcus pyogenes	0.000 (0.000 to 0.172)	0.094 (0.011 to 0.339)		
Moraxella catarrhalis	0.000 (0.000 to 0.172)	0.047 (0.001 to 0.262)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course (till end of blinded ID FU period)

End point title	Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course (till end of blinded ID FU period)

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log- likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10201	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.845 (0.501 to 1.336)	0.194 (0.053 to 0.496)		
Pneumococcal invasive disease (IPD)	0.657 (0.359 to 1.103)	0.097 (0.012 to 0.350)		
Vaccine serotypes (vaccine type-IPD)	0.564 (0.291 to 0.984)	0.048 (0.001 to 0.270)		
Serotype 4	0.000 (0.000 to 0.173)	0.000 (0.000 to 0.179)		
Serotype 6B	0.235 (0.076 to 0.548)	0.000 (0.000 to 0.179)		
Serotype 7F	0.000 (0.000 to 0.173)	0.048 (0.001 to 0.270)		
Serotype 14	0.188 (0.051 to 0.481)	0.000 (0.000 to 0.179)		
Serotype 18C	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		
Serotype 19F	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		
Serotype 23F	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		
Cross-reactive serotypes	0.094 (0.011 to 0.339)	0.000 (0.000 to 0.179)		
Serotype 6A	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		
Serotype 19A	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		
Other pneumococcal serotypes	0.000 (0.000 to 0.173)	0.048 (0.001 to 0.270)		
Serotype 3	0.000 (0.000 to 0.173)	0.048 (0.001 to 0.270)		
Serotype 15C	0.000 (0.000 to 0.173)	0.000 (0.000 to 0.179)		
H. influenzae ID	0.047 (0.001 to 0.262)	0.048 (0.001 to 0.270)		
Non-typeable (NTHI)	0.047 (0.001 to 0.262)	0.048 (0.001 to 0.270)		
Other bacteria	0.188 (0.051 to 0.481)	0.048 (0.001 to 0.270)		
Neisseria meningitidis	0.047 (0.001 to 0.262)	0.048 (0.001 to 0.270)		
Streptococcus pyogenes	0.094 (0.001 to 0.339)	0.000 (0.000 to 0.179)		
Moraxella catarrhalis	0.047 (0.001 to 0.262)	0.000 (0.000 to 0.179)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination in the 7-11 months schedule

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log- likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1908		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.000 (0.000 to 0.410)	0.446 (0.054 to 1.612)		
Pneumococcal invasive disease (IPD)	0.000 (0.000 to 0.410)	0.446 (0.054 to 1.612)		
Vaccine serotypes (vaccine type-IPD)	0.000 (0.000 to 0.410)	0.446 (0.054 to 1.612)		
Serotype 4	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 6B	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 7F	0.000 (0.000 to 0.410)	0.223 (0.006 to 1.243)		
Serotype 14	0.000 (0.000 to 0.410)	0.223 (0.006 to 1.243)		
Serotype 18C	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 19F	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 23F	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Cross-reactive serotypes	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 6A	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 19A	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Other pneumococcal serotypes	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Serotype 3	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		

Serotype 15C	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
H. influenzae ID	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Non-typeable (NTHI)	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Other bacteria	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point title	Person Year Rate in the prevention of culture-confirmed invasive disease (ID)- In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log- likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6535	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.000 (0.000 to 0.240)	0.674 (0.219 to 1.572)		
Pneumococcal invasive disease (IPD)	0.000 (0.000 to 0.240)	0.674 (0.219 to 1.572)		
Vaccine serotypes (vaccine type-IPD)	0.000 (0.000 to 0.240)	0.404 (0.083 to 1.181)		
Serotype 4	0.000 (0.000 to 0.240)	0.135 (0.003 to 0.751)		
Serotype 6B	0.000 (0.000 to 0.240)	0.135 (0.003 to 0.751)		
Serotype 7F	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Serotype 14	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Serotype 18C	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		

Serotype 19F	0.000 (0.000 to 0.240)	0.135 (0.0003 to 0.751)		
Serotype 23F	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Cross-reactive serotypes	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Serotype 6A	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Serotype 19A	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Other pneumococcal serotypes	0.000 (0.000 to 0.240)	0.269 (0.033 to 0.974)		
Serotype 3	0.000 (0.000 to 0.240)	0.135 (0.003 to 0.751)		
Serotype 15C	0.000 (0.000 to 0.240)	0.135 (0.003 to 0.751)		
H. influenzae ID	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Non-typeable (NTHI)	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Other bacteria	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	14.657
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.229
upper limit	16.197

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	13.582
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.691
upper limit	15.693

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	8.452
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.376
upper limit	9.639

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	7.603

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.206
upper limit	9.221

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	1.637
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.185
upper limit	2.205

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	1.845
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.194
upper limit	2.724

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	3.997
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.269
upper limit	4.839

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	3.322
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.423
upper limit	4.445

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group

Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	14.487
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.071
upper limit	16.015

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	13.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.841
upper limit	15.857

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	7.813

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.782
upper limit	8.955

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	7.789
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.377
upper limit	9.42

Statistical analysis title	Statistical analysis 13

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	2.313
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	2.972

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	1.984
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.307
upper limit	2.886

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model without strata
Parameter estimate	PYAR
Point estimate	4.172
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.429
upper limit	5.028

Statistical analysis title	Statistical analysis 16

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model without strata
Parameter estimate	PYAR
Point estimate	3.968
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.981
upper limit	5.177

Statistical analysis title	Statistical analysis 17

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	14.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.628
upper limit	15.516

Statistical analysis title	Statistical analysis 18

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (any serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	15.066

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.079
upper limit	17.269

Statistical analysis title	Statistical analysis 19

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	5.916
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.026
upper limit	6.917

Statistical analysis title	Statistical analysis 20

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine serotype), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	8.557
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.077
upper limit	10.255

Statistical analysis title	Statistical analysis 21

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	2.977
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.357
upper limit	3.71

Statistical analysis title	Statistical analysis 22

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Linear
Parameter estimate	PYAR
Point estimate	2.048
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.361
upper limit	2.96

Statistical analysis title	Statistical analysis 23

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group

Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	5.011
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.196
upper limit	5.939

Statistical analysis title	Statistical analysis 24

Statistical analysis description:

For indirect effectiveness analysis at preventing Culture-confirmed IPD (non-vaccine & non-vaccine related), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9661
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	4.315
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.285
upper limit	5.566

Secondary: Person Year Rate in the prevention of probable culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate in the prevention of probable culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a probable or culture confirmed ID) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10201		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Probable cases of IPD	0.000 (0.000 to 0.172)	0.141 (0.029 to 0.412)		
Confirmed or probable cases of IPD	0.000 (0.000 to 0.172)	0.798 (0.465 to 1.278)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a probable or culture confirmed ID) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10201	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Probable cases of IPD	0.141 (0.029 to 0.412)	0.000 (0.000 to 0.179)		
Confirmed or probable cases of IPD	0.798 (0.465 to 1.278)	0.097 (0.012 to 0.350)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination in the 7-11 months schedule

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a probable or culture confirmed ID) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1908		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Probable cases of IPD	0.000 (0.000 to 0.410)	0.000 (0.000 to 0.823)		
Confirmed or probable cases of IPD	0.000 (0.000 to 0.410)	0.446 (0.054 to 1.612)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point title	Person Year Rate in the prevention of probable or culture-confirmed invasive disease (ID)- In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a probable or culture confirmed ID) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata. Data were not collected regarding indirect effects.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (The blinded ID Follow-up period lasted at least 30 months)

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6535	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Probable cases of IPD	0.000 (0.000 to 0.240)	0.000 (0.000 to 0.497)		
Confirmed or probable cases of IPD	0.000 (0.000 to 0.240)	0.674 (0.219 to 1.572)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

PYAR was calculated: n (=number of subjects with hospital-diagnosed pneumonia) divided by T (=sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. Hospital-diagnosed pneumonia (HDP) cases identified based on hospital discharge diagnosis using international Classification of Disease (ICD)-10 diagnosis codes: J10.0 (Influenza with HDP, other influenza virus identified), J11.0 (Influenza with HDP, virus not identified), J12 (Viral HDP, not elsewhere classified), J13 (HDP due to Sp.), J14 (for HDP due to Hi.), J15 (all HDP, not elsewhere classified), J16 (HDP due to other infectious organisms, not elsewhere classified), J17 (HDP in diseases classified elsewhere), J18 (HDP organism unspecified), J85.1 (Abscess of lung with HDP), and J86 (Pyothorax including empyema).

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10200		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	10.131 (8.804 to 11.601)	13.854 (12.287 to 15.566)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. Hospital-diagnosed pneumonia (HDP) cases identified based on hospital discharge diagnosis using international Classification of Disease (ICD)-10 diagnosis codes: J10.0 (Influenza with HDP, other influenza virus identified), J11.0 (Influenza with HDP, virus not identified), J12 (Viral HDP, not elsewhere classified), J13 (HDP due to Sp.), J14 (for HDP due to Hi.), J15 (all HDP, not elsewhere classified), J16 (HDP due to other infectious organisms, not elsewhere classified), J17 (HDP in diseases classified elsewhere), J18 (HDP organism unspecified), J85.1 (Abscess of lung with HDP), and J86 (Pyothorax including empyema).

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10200	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	13.854 (12.287 to 15.566)	10.155 (8.800 to 11.660)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia- In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia- In children starting vaccination in the 7-11 months schedule

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. Hospital-diagnosed pneumonia (HDP) cases identified based on hospital discharge diagnosis using international Classification of Disease (ICD)-10 diagnosis codes: J10.0 (Influenza with HDP, other influenza virus identified), J11.0 (Influenza with HDP, virus not identified), J12 (Viral HDP, not elsewhere classified), J13 (HDP due to Sp.), J14 (for HDP due to Hi.), J15 (all HDP, not elsewhere classified), J16 (HDP due to other infectious organisms, not elsewhere classified), J17 (HDP in diseases classified elsewhere), J18 (HDP organism unspecified), J85.1 (Abscess of lung with HDP), and J86 (Pyothorax including empyema).

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1907		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	10.263 (8.242 to 12.630)	15.572 (12.232 to 19.970)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. Hospital-diagnosed pneumonia (HDP) cases identified based on hospital discharge diagnosis using international Classification of Disease (ICD)-10 diagnosis codes: J10.0 (Influenza with HDP, other influenza virus identified), J11.0 (Influenza with HDP, virus not identified), J12 (Viral HDP, not elsewhere classified), J13 (HDP due to Sp.), J14 (for HDP due to Hi.), J15 (all HDP, not elsewhere classified), J16 (HDP due to other infectious organisms, not elsewhere classified), J17 (HDP in diseases classified elsewhere), J18 (HDP organism unspecified), J85.1 (Abscess of lung with HDP), and J86 (Pyothorax including empyema).

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6534	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	9.322 (7.832 to 11.013)	11.739 (9.363 to 14.533)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	9.218
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.103
upper limit	9.335

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	9.212
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.052
upper limit	9.375

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).	
Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.378
upper limit	10.624

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).	
Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	10.429
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.259
upper limit	10.601

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).	
Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	10.118
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.997
upper limit	10.239

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
For indirect effectiveness analysis at preventing Hospital-diagnosed Pneumonia, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).	
Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	9.921
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.755
upper limit	10.088

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia with Chest X-ray (CXR) reading according to WHO criteria- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia with Chest X-ray (CXR) reading according to WHO criteria- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia [HDP]) divided by T

(= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata for non-consolidated HDP and without strata for consolidated HDP). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. CXR HDP was defined as a HDP case with the presence of abnormal pulmonary infiltrates on the CXR as per independent review panel judgement using WHO methodology. Abnormal pulmonary infiltrates could be either with (Consolidated HDP) or without (Non-consolidated HDP) alveolar consolidation/pleural effusion. New cases of HDP and CXR HDP were based on a 30-day rule, i.e. a new episode was considered if at least a 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10200		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Consolidated pneumonia	2.181 (1.591 to 2.919)	3.965 (3.149 to 4.929)		
Non-consolidated pneumonia	2.908 (2.219 to 3.744)	2.937 (2.241 to 3.781)		
Consolidated or non- consolidated pneumonia	5.090 (4.163 to 6.161)	6.903 (5.810 to 8.141)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia [HDP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata for non-consolidated HDP and without strata for consolidated HDP). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. CXR HDP was defined as a HDP case with the presence of abnormal pulmonary infiltrates on the CXR as per independent review panel judgement using WHO methodology. Abnormal pulmonary infiltrates could be either with (Consolidated HDP) or without (Non-consolidated HDP) alveolar consolidation/pleural effusion. New cases of HDP and CXR HDP were based on a 30-day rule, i.e. a new episode was considered if at least a 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10200	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Consolidated pneumonia	3.965 (3.149 to 4.929)	2.273 (1.658 to 3.042)		
Non-consolidated pneumonia	2.937 (2.241 to 3.781)	2.627 (1.962 to 3.445)		
Consolidated or non- consolidated pneumonia	6.903 (5.810 to 8.141)	4.901 (3.974 to 5.978)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination in the 7-11 months schedule

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia [HDP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata for non-consolidated HDP and without strata for consolidated HDP). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. CXR HDP was defined as a HDP case with the presence of abnormal pulmonary infiltrates on the CXR as per independent review panel judgement using WHO methodology. Abnormal pulmonary infiltrates could be either with (Consolidated HDP) or without (Non-consolidated HDP) alveolar consolidation/pleural effusion. New cases of HDP and CXR HDP were based on a 30-day rule, i.e. a new episode was considered if at least a 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1907		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				

Consolidated pneumonia	1.960 (1.142 to 3.139)	4.401 (2.650 to 6.873)		
Non-consolidated pneumonia	3.344 (2.240 to 4.803)	4.865 (3.011 to 7.436)		
Consolidated or non- consolidated pneumonia	5.305 (3.884 to 7.076)	9.266 (6.620 to 12.618)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination in the 12-18 months schedule

End point title	Person Year Rate in reducing hospital-diagnosed pneumonia with CXR reading according to WHO criteria - In children starting vaccination in the 12-18 months schedule

End point description:

PYAR was calculated: n (= number of subjects with hospital-diagnosed pneumonia [HDP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata for non-consolidated HDP and without strata for consolidated HDP). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. CXR HDP was defined as a HDP case with the presence of abnormal pulmonary infiltrates on the CXR as per independent review panel judgement using WHO methodology. Abnormal pulmonary infiltrates could be either with (Consolidated HDP) or without (Non-consolidated HDP) alveolar consolidation/pleural effusion. New cases of HDP and CXR HDP were based on a 30-day rule, i.e. a new episode was considered if at least a 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6534	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Consolidated pneumonia	1.824 (1.202 to 2.654)	3.494 (2.261 to 5.157)		
Non-consolidated pneumonia	2.837 (2.045 to 3.835)	2.935 (1.817 to 4.486)		
Consolidated or non- consolidated pneumonia	4.661 (3.626 to 5.899)	6.428 (4.706 to 8.574)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all tympanostomy tube placements- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate in prevention of all tympanostomy tube placements- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with tympanostomy tube placement[TTP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. A TTP episode was defined as a TTP episode classified under the DCA 20 code in the Finnish National Institute of Health and Welfare (THL) and Social Insurance Institution of Finland (KELA) registers, using the Nordic Centre for Classifications in Health Care (NOMESCO) Classification of Surgical Procedures (NCSP), version 1.12 from January 2008, and could refer to either an unilateral or a bilateral TTP procedure. New episodes of TTP defined according to a 30-day rule meaning that a new episode was considered if at least 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10200		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	68.735 (65.203 to 72.408)	79.504 (75.683 to 83.467)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with tympanostomy tube placement[TTP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. A TTP episode was defined as a TTP episode classified under the DCA 20 code in the Finnish National Institute of Health and Welfare (THL) and Social Insurance Institution of Finland (KELA) registers, using the Nordic Centre for Classifications in Health Care (NOMESCO) Classification of Surgical Procedures (NCSP), version 1.12 from January 2008, and could refer to either an unilateral or a bilateral TTP procedure. New episodes of

TTP defined according to a 30-day rule meaning that a new episode was considered if at least 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10200	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	79.504 (75.683 to 83.467)	66.083 (62.550 to 69.764)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination in the 7-11 months schedule

End point description:

PYAR was calculated: n (= number of subjects with tympanostomy tube placement[TTP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. A TTP episode was defined as a TTP episode classified under the DCA 20 code in the Finnish National Institute of Health and Welfare (THL) and Social Insurance Institution of Finland (KELA) registers, using the Nordic Centre for Classifications in Health Care (NOMESCO) Classification of Surgical Procedures (NCSP), version 1.12 from January 2008, and could refer to either an unilateral or a bilateral TTP procedure. New episodes of TTP defined according to a 30-day rule meaning that a new episode was considered if at least 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1907		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	68.153 (62.769 to 73.876)	79.920 (71.708 to 88.814)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point title	Person Year Rate in prevention of all tympanostomy tube placements - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point description:

PYAR was calculated: n (= number of subjects with tympanostomy tube placement[TTP]) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. A TTP episode was defined as a TTP episode classified under the DCA 20 code in the Finnish National Institute of Health and Welfare (THL) and Social Insurance Institution of Finland (KELA) registers, using the Nordic Centre for Classifications in Health Care (NOMESCO) Classification of Surgical Procedures (NCSP), version 1.12 from January 2008, and could refer to either an unilateral or a bilateral TTP procedure. New episodes of TTP defined according to a 30-day rule meaning that a new episode was considered if at least 30-day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6534	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)	56.809 (53.034 to 60.782)	58.973 (53.480 to 64.877)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	22.624
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.02
upper limit	23.24

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	22.747
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.912
upper limit	23.606

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group

Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	24.503
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.852
upper limit	25.166

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).	
Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	26.236
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.308
upper limit	27.189

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).	
Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	27.502
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.81
upper limit	28.207

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).	
Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	26.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.171
upper limit	27.055

Statistical analysis title	Statistical analysis 7
Statistical analysis description:	
For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).	
Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	28.661
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.958
upper limit	29.377

Statistical analysis title	Statistical analysis 8
Statistical analysis description:	
For indirect effectiveness analysis at preventing Tympanostomy Tube Placements, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).	
Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	29.835
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.843
upper limit	30.85

Secondary: Person Year Rate in prevention of all antimicrobial prescriptions- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point title	Person Year Rate in prevention of all antimicrobial prescriptions- In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with antimicrobial prescriptions (APs)) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. An APs episode was an episode of APs to an infant/child falling under following Anatomic Therapeutic Chemical [ATC] codes: J01 (APs) and following codes for AP usually recommended for otitis media (OM) and respiratory tract infections (RTI). "For OM and RTI" category corresponds to following definition: APs for antibacterial usually recommended for OM and RTI (ATC codes: J01CA04, J01CR02, J01CE02, J01DC02, J01DC04, J01EE02, J01FA09 and J01FA10). New episodes of APs were analyzed according to a 2-day rule meaning new episode considered if at least 2 day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10273	10200		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Antimicrobial prescriptions (ATC code J01)	1592.585 (1575.411 to 1609.901)	1706.194 (1688.328 to 1724.202)		
For otitis media and respiratory infections	1451.141 (1434.749 to 1467.674)	1565.692 (1548.579 to 1582.947)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point title	Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course

End point description:

PYAR was calculated: n (= number of subjects with antimicrobial prescriptions (APs)) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. An APs episode was an episode of APs to an infant/child falling under following Anatomic Therapeutic Chemical [ATC] codes: J01 (APs) and following codes for AP usually recommended for otitis media (OM) and respiratory tract infections (RTI). "For OM and RTI" category corresponds to following definition: APs for antibacterial usually recommended for OM and RTI (ATC codes: J01CA04, J01CR02, J01CE02, J01DC02, J01DC04, J01EE02, J01FA09 and J01FA10). New episodes of APs were analyzed according to a 2-day rule meaning new episode considered if at least 2 day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=24 months

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10200	10054		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Antimicrobial prescriptions (ATC code J01)	1706.194 (1688.328 to 1724.202)	1552.493 (1535.183 to 1569.950)		
For otitis media and respiratory infections	1565.692 (1548.579 to 1582.947)	1415.983 (1399.453 to 1432.659)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination in the 7-11 months schedule

End point title	Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination in the 7-11 months schedule

End point description:

PYAR was calculated: n (= number of subjects with antimicrobial prescriptions (APs)) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. An APs episode was an episode of APs to

an infant/child falling under following Anatomic Therapeutic Chemical [ATC] codes: J01 (APs) and following codes for AP usually recommended for otitis media (OM) and respiratory tract infections (RTI). "For OM and RTI" category corresponds to following definition: APs for antibacterial usually recommended for OM and RTI (ATC codes: J01CA04, J01CR02, J01CE02, J01DC02, J01DC04, J01EE02, J01FA09 and J01FA10). New episodes of APs were analyzed according to a 2-day rule meaning new episode considered if at least 2 day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn7-11M/043+053 Group	Ctrl7-11M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3880	1907		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Antimicrobial prescriptions (ATC code J01)	1536.618 (1510.637 to 1562.934)	1649.360 (1611.269 to 1688.124)		
For otitis media and respiratory infections	1390.856 (1366.143 to 1415.903)	1499.713 (1463.401 to 1536.698)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point title	Person Year Rate in prevention of all antimicrobial prescriptions - In children starting vaccination in the 12-18 months schedule (+ indirect effects on the unvaccinated population)

End point description:

PYAR was calculated: n (= number of subjects with antimicrobial prescriptions (APs)) divided by T (= sum of follow-up (FU) period expressed in years) (per 1000) with 95% CI (2-sided profile log-likelihood ratio 95% CI-classical log linear Poisson regression with strata). FU period considered as period between Dose 1 administration and cut-off date of 31 December 2011. An APs episode was an episode of APs to an infant/child falling under following Anatomic Therapeutic Chemical [ATC] codes: J01 (APs) and following codes for AP usually recommended for otitis media (OM) and respiratory tract infections (RTI). "For OM and RTI" category corresponds to following definition: APs for antibacterial usually recommended for OM and RTI (ATC codes: J01CA04, J01CR02, J01CE02, J01DC02, J01DC04, J01EE02, J01FA09 and J01FA10). New episodes of APs were analyzed according to a 2-day rule meaning new episode considered if at least 2 day interval elapsed from the onset of the previous episode.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – FU mean time=27 months

End point values	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6534	3126		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Antimicrobial prescriptions (ATC code J01)	1315.936 (1297.521 to 1334.547)	1421.774 (1394.280 to 1449.675)		
For otitis media and respiratory infections	1177.729 (1160.312 to 1195.343)	1271.268 (1245.277 to 1297.665)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	816.813
Confidence interval	
level	95 %
sides	2-sided
lower limit	815.226
upper limit	818.392

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	841.176
Confidence interval	
level	95 %
sides	2-sided
lower limit	839.098
upper limit	843.239

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for Acute Otitis Media (AOM)/Respiratory Tract Infections (RTI), number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	702.245
Confidence interval	
level	95 %
sides	2-sided
lower limit	700.372
upper limit	704.114

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	720.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	718.355
upper limit	723.435

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	929.844
Confidence interval	
level	95 %
sides	2-sided
lower limit	928.755
upper limit	930.923

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	953.025
Confidence interval	
level	95 %
sides	2-sided
lower limit	951.77
upper limit	954.257

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI,

number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	804.703
Confidence interval	
level	95 %
sides	2-sided
lower limit	803.017
upper limit	806.38

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	818.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	816.391
upper limit	820.912

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	916.079

Confidence interval	
level	95 %
sides	2-sided
lower limit	914.891
upper limit	917.256

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	928.568
Confidence interval	
level	95 %
sides	2-sided
lower limit	927.038
upper limit	930.076

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	796.894
Confidence interval	
level	95 %
sides	2-sided
lower limit	795.175
upper limit	798.605

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	803.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	801.571
upper limit	806.25

Statistical analysis title	Statistical analysis 13

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	865.679
Confidence interval	
level	95 %
sides	2-sided
lower limit	864.227
upper limit	867.121

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group

Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	871.749
Confidence interval	
level	95 %
sides	2-sided
lower limit	869.771
upper limit	873.707

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any 10PN-PD-DIT vaccine - age stratum schedules).

Comparison groups	10Pn12-18M/043+053 Group v Ctrl12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	753.423
Confidence interval	
level	95 %
sides	2-sided
lower limit	751.591
upper limit	755.249

Statistical analysis title	Statistical analysis 16

Statistical analysis description:

For indirect effectiveness analysis at preventing Antimicrobial Prescriptions recommended for AOM/RTI, number of events in the unvaccinated cohort, which occurred around 6 months or more after study start was compared with treated group numbers (applicable to any control (HAV or HBV) vaccine - age stratum schedules).

Comparison groups	Ctrl12-18M/043+053 Group v 10Pn12-18M/043+053 Group
Number of subjects included in analysis	9660
Analysis specification	Pre-specified
Analysis type	
Method	Negative Binomial model with strata
Parameter estimate	PYAR
Point estimate	755.542

Confidence interval	
level	95 %
sides	2-sided
lower limit	753.008
upper limit	758.064

Secondary: Number of subjects classified by antimicrobial susceptiblity of IPD isolates in children starting vaccination within 7 months of life and assigned to a 2 or 3-dose primary vaccination course

End point title	Number of subjects classified by antimicrobial susceptiblity of IPD isolates in children starting vaccination within 7 months of life and assigned to a 2 or 3-dose primary vaccination course

End point description:

Antimicrobial susceptibility classification of IPD isolates reported during IPD follow-up with percentages for each serotype for the following categories: S= susceptible; I = intermediate ; R = resistant; N = not available.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end date of the follow-up (31 December 2011) – mean FU time=24 months

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[3]	24	2	
Units: Participants				
Serotype-4 -Pencillin-S		1	0	
Serotype-6A -Pencillin-S		1	0	
Serotype-6B -Pencillin-I		3	0	
Serotype-6B -Pencillin-R		1	0	
Serotype-6B -Pencillin-S		2	0	
Serotype-7F -Pencillin-S		1	1	
Serotype-14 -Pencillin-I		2	0	
Serotype-14 -Pencillin-R		1	0	
Serotype-14 -Pencillin-S		2	0	
Serotype-15C -Pencillin-S		1	0	
Serotype-18C -Pencillin-S		1	0	
Serotype-19A -Pencillin-I		1	0	
Serotype-19F -Pencillin-I		1	0	
Serotype-19F -Pencillin-S		1	0	
Serotype-23F -Pencillin-S		1	0	
Serotype-N -Pencillin-N		4	1	
Serotype-4 -Erythromycin-S		1	0	
Serotype-6A -Erythromycin-S		1	0	
Serotype-6B -Erythromycin-R		5	0	
Serotype-6B -Erythromycin-S		1	0	
Serotype-7F -Erythromycin-S		1	1	
Serotype-14 -Erythromycin-R		4	0	

Serotype-14 -Erythromycin-S		1	0	
Serotype-15C -Erythromycin-S		1	0	
Serotype-18C -Erythromycin-S		1	0	
Serotype-19A -Erythromycin-S		1	0	
Serotype-19F -Erythromycin-R		1	0	
Serotype-19F -Erythromycin-S		1	0	
Serotype-23F -Erythromycin-S		1	0	
Serotype-N -Erythromycin-N		4	1	
Serotype-4 -Tetracyclin-S		1	0	
Serotype-6A -Tetracyclin-S		1	0	
Serotype-6B -Tetracyclin-R		4	0	
Serotype-6B -Tetracyclin-S		2	0	
Serotype-7F -Tetracyclin-S		1	1	
Serotype-14 -Tetracyclin-S		5	0	
Serotype-15C -Tetracyclin-S		1	0	
Serotype-18C -Tetracyclin-S		1	0	
Serotype-19A -Tetracyclin-S		1	0	
Serotype-19F -Tetracyclin-R		1	0	
Serotype-19F -Tetracyclin-S		1	0	
Serotype-23F -Tetracyclin-S		1	0	
Serotype-N -Tetracyclin-N		4	1	
Serotype-4 -Levofloxacin-S		1	0	
Serotype-6A -Levofloxacin-S		1	0	
Serotype-6B -Levofloxacin-S		6	0	
Serotype-7F -Levofloxacin-S		1	1	
Serotype-14 -Levofloxacin-S		5	0	
Serotype-15C -Levofloxacin-S		1	0	
Serotype-18C -Levofloxacin-S		1	0	
Serotype-19A -Levofloxacin-S		1	0	
Serotype-19F -Levofloxacin-S		2	0	
Serotype-23F -Levofloxacin-S		1	0	
Serotype-N -Levofloxacin-N		4	1	
Serotype-4 -Ceftriaxone-S		1	0	
Serotype-6A -Ceftriaxone-S		1	0	
Serotype-6B -Ceftriaxone-S		6	0	
Serotype-7F -Ceftriaxone-S		1	1	
Serotype-14 -Ceftriaxone-I		1	0	
Serotype-14 -Ceftriaxone-S		4	0	
Serotype-15C -Ceftriaxone-S		1	0	
Serotype-18C -Ceftriaxone-S		1	0	
Serotype-19A -Ceftriaxone-S		1	0	
Serotype-19F -Ceftriaxone-S		2	0	
Serotype-23F -Ceftriaxone-S		1	0	
Serotype-N -Ceftriaxone-N		4	1	
Serotype-4 -Clindamycin-S		1	0	
Serotype-6A -Clindamycin-S		1	0	
Serotype-6B -Clindamycin-R		4	0	
Serotype-6B -Clindamycin-S		2	0	
Serotype-7F -Clindamycin-S		1	1	
Serotype-14 -Clindamycin-N		1	0	
Serotype-14 -Clindamycin-S		4	0	
Serotype-15C -Clindamycin-S		1	0	

Serotype-18C -Clindamycin-S		1	0	
Serotype-19A -Clindamycin-S		1	0	
Serotype-19F -Clindamycin-R		1	0	
Serotype-19F -Clindamycin-S		1	0	
Serotype-23F -Clindamycin-S		1	0	
Serotype-N -Clindamycin-N		4	1	

Notes:

[3] - No participants with results in this group

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Lower respiratory tract infections (LRTIs) (in a subset of 1500 subjects in Turku area)

End point title	Number of subjects with Lower respiratory tract infections (LRTIs) (in a subset of 1500 subjects in Turku area)

End point description:

Analysis of this outcome in the Turku area was not performed as no data was collected related to LRTIs.

End point type	Secondary

End point timeframe:

From the administration of the first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (at least 30 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group	10Pn7-11M/043+053 Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[4]	0[5]	0[6]	0[7]
Units: Participants				

Notes:

[4] - no data was collected related to LRTIs

[5] - no data was collected related to LRTIs

[6] - no data was collected related to LRTIs

[7] - no data was collected related to LRTIs

End point values	Ctrl7-11M/043+053 Group	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Participants				

Notes:

[8] - no data was collected related to LRTIs

[9] - no data was collected related to LRTIs

[10] - no data was collected related to LRTIs

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Upper respiratory tract infections (URTIs) (in a subset of 1500 subjects in Turku area)

End point title	Number of subjects with Upper respiratory tract infections (URTIs) (in a subset of 1500 subjects in Turku area)

End point description:

Analysis of this outcome in the Turku area was not performed as no data was collected related to URTIs.

End point type	Secondary

End point timeframe:

From the administration of the first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period (at least 30 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group	10Pn7-11M/043+053 Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: Participants				

Notes:

[11] - no data was collected related to URTIs.

[12] - no data was collected related to URTIs.

[13] - no data was collected related to URTIs.

[14] - no data was collected related to URTIs.

End point values	Ctrl7-11M/043+053 Group	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: Participants				

Notes:

[15] - no data was collected related to URTIs.

[16] - no data was collected related to URTIs.

[17] - no data was collected related to URTIs.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs reported during the blinded invasive disease phase, of the study

End point title	Number of subjects with SAEs reported during the blinded invasive disease phase, of the study

End point description:

An event is defined as 'serious' when it meets one of the pre-defined outcomes described below: results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation; results in disability/incapacity, or is a congenital anomaly/birth defect in the offspring of a study subject.
Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.

End point type	Secondary

End point timeframe:

For Month 0 till the end of the blinded ID Follow-Up, (at least 30 months from study start)

End point values	10Pn3+1-6W-6M/043 Group	10Pn2+1-6W-6M/043 Group	Ctrl-6W-6M/043 Group	10Pn7-11M/043 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8427	9112	8872	3689
Units: Participants	6	7	8	3

End point values	Ctrl7-11M/043 Group	10Pn12-18M/043 Group	Ctrl12-18M/043 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1812	6249	3020	
Units: Participants	2	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects enrolled and vaccinated in the 10PN-PD-DIT-043 and 10PN-PD-DIT-053 study with post-study SAEs reported via passive surveillance– Subjects enrolled aged 6 weeks to 6 months and 7 to 18 months

End point title	Number of subjects enrolled and vaccinated in the 10PN-PD-DIT-043 and 10PN-PD-DIT-053 study with post-study SAEs reported via passive surveillance– Subjects enrolled aged 6 weeks to 6 months and 7 to 18 months

End point description:

An event is defined as ‘serious’ when it meets one of the pre-defined outcomes described below: results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation; results in disability/incapacity, or is a congenital anomaly/birth defect in the offspring of a study subject.
Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.

End point type	Secondary

End point timeframe:

From the end of the blinded ID Follow-Up period(at least 30 months from study start) up to the end of 18-month period after study unblinding

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group	10Pn7-11M/043+053 Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10273	10201	10054	3880
Units: Participants	1	0	2	0

End point values	Ctrl7-11M/043+053 Group	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1908	6535	3126	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Culture-confirmed Invasive Disease (ID) Person Year Rate - In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course till end of LT FU period

End point title	Culture-confirmed Invasive Disease (ID) Person Year Rate - In children starting vaccination within 7 months of life and assigned to a 3-dose primary vaccination course till end of LT FU period

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the long-term Follow-up period (The Follow-up period lasted at least 77 months)

End point values	10Pn3+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10272	10201		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.046 (0.013 to 0.118)	0.268 (0.170 to 0.402)		
Pneumococcal invasive disease (IPD)	0.023 (0.003 to 0.084)	0.210 (0.124 to 0.331)		
Vaccine serotypes (vaccine type-IPD)	0.0 (0.0 to 0.043)	0.140 (0.072 to 0.244)		

Serotype 4	0.0 (0.0 to 0.043)	0.0 (0.0 to 0.043)		
Serotype 6B	0.0 (0.0 to 0.043)	0.058 (0.019 to 0.136)		
Serotype 7F	0.0 (0.0 to 0.043)	0.0 (0.0 to 0.043)		
Serotype 14	0.0 (0.0 to 0.043)	0.047 (0.013 to 0.119)		
Serotype 18C	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Serotype 19F	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Serotype 23F	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Cross-reactive serotypes	0.012 (0.0 to 0.064)	0.047 (0.013 to 0.119)		
Serotype 6A	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Serotype 19A	0.012 (0.0 to 0.064)	0.035 (0.007 to 0.102)		
Other pneumococcal serotypes	0.012 (0.0 to 0.064)	0.023 (0.003 to 0.084)		
Serotype 3	0.012 (0.0 to 0.064)	0.012 (0.0 to 0.065)		
Serotype 12F	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Serotype 15C	0.0 (0.0 to 0.043)	0.0 (0.0 to 0.043)		
H. influenzae ID	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Non-typeable (NTHI)	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		
Other bacteria	0.023 (0.003 to 0.084)	0.058 (0.019 to 0.136)		
Neisseria meningitidis	0.023 (0.003 to 0.084)	0.023 (0.003 to 0.084)		
Streptococcus pyogenes	0.0 (0.0 to 0.043)	0.023 (0.003 to 0.084)		
Moraxella catarrhalis	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.065)		

Statistical analyses

No statistical analyses for this end point

Secondary: Culture-confirmed Invasive Disease (ID) Person Year Rate - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course till end of LT FU period

End point title	Culture-confirmed Invasive Disease (ID) Person Year Rate - In children starting vaccination within 7 months of life and assigned to a 2-dose primary vaccination course till end of LT FU period

End point description:

The PYAR (Person-Year Rate) was calculated as follows n (= number of subjects reported with a culture confirmed IPD) divided by T (= sum of follow-up period expressed in years) (per 1000) as well as the corresponding 95% confidence interval (CI), calculated as a 2-sided profile log-likelihood ratio 95% CI using a classical log linear Poisson regression with strata.

End point type	Secondary

End point timeframe:

Period of follow-up was any time after the administration of first vaccine dose till the end of the long-term Follow-up period (The Follow-up period lasted at least 77 months)

End point values	Ctrl-6W-6M/043+053 Group	10Pn2+1-6W-6M/043+053 Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10201	10053		
Units: Participants per 1000 person-years				
number (confidence interval 95%)				
Culture confirmed ID	0.268 (0.170 to 0.402)	0.047 (0.013 to 0.122)		
Pneumococcal invasive disease (IPD)	0.21 (0.124 to 0.331)	0.024 (0.003 to 0.086)		
Vaccine serotypes (vaccine type-IPD)	0.140 (0.072 to 0.244)	0.012 (0.0 to 0.066)		
Serotype 4	0.0 (0.0 to 0.043)	0.0 (0.0 to 0.044)		
Serotype 6B	0.058 (0.019 to 0.136)	0.0 (0.0 to 0.044)		
Serotype 7F	0.0 (0.0 to 0.043)	0.012 (0.0 to 0.066)		
Serotype 14	0.047 (0.013 to 0.119)	0.0 (0.0 to 0.044)		
Serotype 18C	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		
Serotype 19F	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		
Serotype 23F	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		
Cross-reactive serotypes	0.047 (0.013 to 0.119)	0.0 (0.0 to 0.044)		
Serotype 6A	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		
Serotype 19A	0.035 (0.007 to 0.102)	0.0 (0.0 to 0.044)		
Other pneumococcal serotypes	0.023 (0.003 to 0.084)	0.012 (0.0 to 0.066)		
Serotype 3	0.012 (0.0 to 0.065)	0.012 (0.0 to 0.066)		
Serotype 12F	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		
Serotype 15C	0.0 (0.0 to 0.043)	0.0 (0.0 to 0.044)		
H. influenzae ID	0.012 (0.0 to 0.065)	0.012 (0.0 to 0.066)		
Non-typeable (NTHI)	0.012 (0.0 to 0.065)	0.012 (0.0 to 0.066)		
Other bacteria	0.058 (0.019 to 0.136)	0.012 (0.0 to 0.066)		
Neisseria meningitidis	0.023 (0.003 to 0.084)	0.012 (0.0 to 0.066)		
Streptococcus pyogenes	0.023 (0.003 to 0.084)	0.0 (0.0 to 0.044)		
Moraxella catarrhalis	0.012 (0.0 to 0.065)	0.0 (0.0 to 0.044)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

SAEs were reported from Month 0 to end of blinded invasive disease (ID) phase (at least 30 months from study start), in 10PN-PD-DIT-043 subjects.

Adverse event reporting additional description:

Solicited and unsolicited AEs were not collected in this study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	10Pn3+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn2+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks, followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	Ctrl-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B vaccine (called also HBV vaccine) according to either a 3-dose primary vaccination schedule with an interval of at least 4 weeks between doses followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (3+1 Infant Schedule), or according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (2+1 Infant Schedule). The vaccine was administered intramuscularly in the thigh.

Reporting group title	10Pn7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 7 to 11 months at enrolment. Subjects received the Engerix B (called also HBV) vaccine according to a 2-dose primary vaccination with an interval of at least 8 weeks followed by a booster dose of the same vaccine with an interval of preferably 6 months since the previous vaccine dose (minimum 4 months) (11-17M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Synflorix (called also 10Pn-PD-DiT, 10Pn or GSK1024850A) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Reporting group title	Ctrl12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (NCT00861380 - EUDRACT 2008-005149-48) study, aged 12 to 18 months at enrolment. Subjects received the Havrix (called also HAV) vaccine according to a 2-dose vaccination with an interval of at least and preferably 6 months between doses (12-18M Schedule). The vaccine was administered intramuscularly in the thigh or in the deltoid region of upper arm, provided the muscle size was adequate.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only SAEs events were collected as part of this study.

Serious adverse events	10Pn3+1-6W-6M/043 Group	10Pn2+1-6W-6M/043 Group	Ctrl-6W-6M/043 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8427 (0.07%)	7 / 9112 (0.08%)	8 / 8872 (0.09%)
number of deaths (all causes)	4	4	3
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Kawasaki’s disease			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Gaucher’s disease			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Krabbe's disease			
subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonic-hyporesponsive episode			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Death			

subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Injection site reaction			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 8427 (0.02%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatobiliary disorders			
Reye’s syndrome			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Parotitis			

subjects affected / exposed	0 / 8427 (0.00%)	1 / 9112 (0.01%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	1 / 8872 (0.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 8427 (0.01%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	10Pn7-11M/043 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3689 (0.08%)	2 / 1812 (0.11%)	2 / 6249 (0.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Kawasaki’s disease			

subjects affected / exposed	1 / 3689 (0.03%)	0 / 1812 (0.00%)	1 / 6249 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Gaucher’s disease			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Krabbe’s disease			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 3689 (0.00%)	1 / 1812 (0.06%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	1 / 3689 (0.03%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3689 (0.00%)	1 / 1812 (0.06%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonic-hyporesponsive episode			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site reaction			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	1 / 6249 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Reye’s syndrome			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			

subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 3689 (0.00%)	1 / 1812 (0.06%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 3689 (0.03%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ctrl12-18M/043 Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3020 (0.07%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
Kawasaki’s disease			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Gaucher’s disease			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Krabbe’s disease			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	1 / 3020 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonic-hyporesponsive episode			

subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injection site reaction			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Irritability			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden infant death syndrome			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 3020 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Reye’s syndrome			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 3020 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			

subjects affected / exposed	0 / 3020 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 3020 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parotitis				
subjects affected / exposed	0 / 3020 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	0 / 3020 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 3020 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 3020 (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	10Pn3+1-6W-6M/043 Group	10Pn2+1-6W-6M/043 Group	Ctrl-6W-6M/043 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 8427 (0.00%)	0 / 9112 (0.00%)	0 / 8872 (0.00%)

Non-serious adverse events	10Pn7-11M/043 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group
Total subjects affected by non-serious adverse events			

subjects affected / exposed	0 / 3689 (0.00%)	0 / 1812 (0.00%)	0 / 6249 (0.00%)

Non-serious adverse events	Ctrl12-18M/043 Group		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 3020 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2009	Amendment 1 of the 10PN-PD-DIT-043 (111442) study protocol was developed for the following reasons: (1) Addition of collection of data on respiratory tract infections (RTIs), including acute otitis media (AOM) in a subset of subjects in Turku area; (2) Addition of 6 clusters located in some selected municipalities where no collaboration with health care centres had been set up but where there was opportunity for parent(s) to let their child participate in nested study 10PNPD-DIT-053 (112595) and to receive the same vaccination as in the current study (i.e. Espoo, Vantaa and surroundings municipalities and municipalities surrounding Oulu); and (3) The National Public Health Institute (KTL) and the National Research and Development Centre for Welfare and Health (STAKES) were merged into the National Institute for Health and Welfare (THL).
22 August 2011	Amendment 2 was developed for the following reasons: (1) The study enrolment reached only 50% of the initial recruitment plan; therefore, there was a need to redefine the conditions for triggering IPD effectiveness analysis: (a) the study follow-up period for primary analysis on invasive disease (ID) cases was to end on 31 January 2012 (data lock point for ID cases), i.e. at least 30 months after study start. This would allow inclusion of an age-related IPD peak at 1119 months of age in the youngest enrolled subjects and an expected seasonal invasive pneumococcal disease (IPD) peak in the fall of 2011, thereby increasing the potential to accrue additional IPD cases; (b) Reaching a minimum number of 21 culture-confirmed vaccine-type IPD cases in the infant group was no longer a condition for triggering IPD effectiveness analysis because that minimum number was most probably not met due to the lower enrolment numbers. The estimated target number of vaccine-type IPD cases was adjusted accordingly, based on an assumed vaccine efficacy estimate and the currently available information on the total number of IPD cases by age cohort. Taking into account the lower than expected number of enrolled subjects, associated number of overall IPD cases reported so far and impact on power when considering 80% vaccine efficacy for the 2+1 vaccination schedule, it was decided to evaluate the effectiveness of the 10Pn-PD-DiT vaccine to prevent vaccine-type IPD in the infants assigned to a 2+1 vaccination course as a first secondary objective instead of the second primary objective (sequential) but to keep the predefined statistical criteria for success. (2) Following IDMC recommendation, it was decided to have the chest X-rays from the hospital-diagnosed pneumonia cases in the vaccinated population evaluated by an independent review panel according to World Health Organisation (WHO) guidelines for study purposes. The appropriate sections of the protocol were adjusted to reflect this.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported