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	v2
This version publication date	17 March 2016
First version publication date	29 July 2015
Version creation reason	• New data added to full data set Data for secondary endpoints have been added.
Summary attachment (see zip file)	10PN-PD-DIT-043 results summary (111442 (10PN-PD-DIT-043-CTRS.pdf)

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, B-1330, Belgium, Rixensart, Belgium, B-1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 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	22 April 2015
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: 2695198
Worldwide total number of subjects	2695198
EEA total number of subjects	2695198

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	41188
Children (2-11 years)	530802
Adolescents (12-17 years)	530802
Adults (18-64 years)	530802
From 65 to 84 years	530802
85 years and over	530802

Subject disposition

Recruitment

Recruitment details:

This study is linked with 10PN-PD-DIT-053 (112595) study (EudraCT: 2008-006551-51) with which primary objectives and endpoints are common. +/- 6000 subjects in 10PN-PD-DIT-053 study contributed to primary objectives and endpoints results of this 10PN-PD-DIT-043 study as well as some secondary efficacy and safety analyses.

Pre-assignment

Screening details:

Screening involved: check on inclusion/exclusion criteria & medical history, randomization, signing of informed consent forms by subjects' parent(s)/legally accepted representative(s) (LAR[s]) & check for enrolment of control unvaccinated subjects towards indirect effect analysis (up to maximum 2626735 subjects per year of analysis were assessed).

Pre-assignment period milestones

Number of subjects started	2695198
Number of subjects completed	41181

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Unvaccinated subject enrolled for Indirect effect: 2654010
Reason: Number of subjects	Subject not vaccinated: 7

Period 1

Period 1 title	Entire Study Period (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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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	10PN 7-11M/111442 Group

Arm description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

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 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

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 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Havrix-preservative free (or 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[1]	10PN 7-11M/111442 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group

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: Including unvaccinated subjects enrolled for indirect effect analysis (including results to year 2012 only), a total of 2695198 subjects were enrolled in the study. Out of these, 41188 were planned to be vaccinated. 41181 of these were actually vaccinated and included in baseline period for 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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	10PN 7-11M/111442 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Havrix-preservative free (or 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: Subjects			
Infants and toddlers (28 days-23 months)	8427	9112	8872
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Not recorded	0	0	0
Gender categorical			
Units: Subjects			
Female	4239	4399	4351
Male	4188	4713	4521
Not recorded	0	0	0

Reporting group values	10PN 7-11M/111442 Group	Ctrl7-11M/043 Group	10Pn12-18M/043 Group
Number of subjects	3689	1812	6249
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Not recorded	3689	1812	6249
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	0	0	0
Not recorded	3689	1812	6249

Reporting group values	Ctrl12-18M/043 Group	Total	
Number of subjects	3020	41181	
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	0	26411	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Not recorded	3020	14770	
Gender categorical			
Units: Subjects			
Female	0	12989	

Male	0	13422	
Not recorded	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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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	10PN 7-11M/111442 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Havrix-preservative free (or 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) vaccine according to either 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on 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 in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on vaccine specifics and administration route in this group.

Subject analysis set title	Ctrl3+1-6W-6M/043 Group
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or HBV 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 Ctrl6W-6M/043 Group for details on vaccine specifics and administration route in this group.

Subject analysis set title	Ctrl2+1-6W-6M/043 Group
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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) (2+1 Infant Schedule). Refer to group description for Ctrl6W-6M/043 Group for details on vaccine specifics and administration route in this group.

Subject analysis set title	Ind-10Pn/043+053 Y2010 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year 2010 (1st January to 31st December 2010) with the 10Pn vaccine and who lived in the study cluster areas, in which study participants received 10Pn vaccine.

Subject analysis set title	Ind-Ctrl/043+053 Y2010 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year 2010 (1st January to 31st December 2010) with the HBV or HAV vaccine and who lived in the study cluster areas, in which study participants received HBV or HAV vaccine.

Subject analysis set title	Ind-10Pn/043+053 Y2011 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year 2011 (1st January to 31st December 2011) with the 10Pn vaccine and who lived in the study cluster areas, in which study participants received 10Pn vaccine.

Subject analysis set title	Ind-Ctrl/043+053 Y2011 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year 2011 (1st January to 31st December 2011) with the HBV or HAV vaccine and who lived in the study cluster areas, in which study participants received HBV or HAV vaccine.

Subject analysis set title	Ind-10Pn/043+053 Y2012 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year 2010 (1st January to 31st December 2010) with the 10Pn vaccine and who lived in the study cluster areas, in which study participants received 10Pn vaccine.

Subject analysis set title	Ind-Ctrl/043+053 Y2012 Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 5 years and above at enrolment, who were unvaccinated in the civil year

2010 (1st January to 31st December 2010) with the 10Pn vaccine and who lived in the study cluster areas, in which study participants received 10Pn vaccine.

Primary: PYAR as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes.

End point title	PYAR as regards subjects with culture-confirmed IPD due to any of the 10 pneumococcal vaccine serotypes.

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 anytime after the administration of first vaccine dose till the end of the blinded invasive disease (ID) Follow-up period.

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: PYAR				
arithmetic mean (confidence interval 95%)				
PYAR IPD Pneumococcal	0 (0 to 1.172)	0.564 (0.291 to 0.984)		

Statistical analyses

Statistical analysis title	VE at preventing culture-confirmed IPD

Statistical analysis description:

The 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	10Pn3+1-6W-6M/043+053 Group v Ctrl-6W-6M/043+053 Group
Number of subjects included in analysis	20474
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001 [2]
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] - VE (defined as 1 minus Relative Risk (RR)) was calculated by comparing numbers of culture-confirmed IPD. The number of subjects with IPD in each cluster was compared between groups (10PN3+1 vs Control). This comparison was done using a negative binomial log-linear model with correction for dispersion group- and cluster-related effect. Over-dispersion being assessed was null, a standard Poisson model methodology was applied including the group and cluster stratification factors as covariates.

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

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Only SAEs were collected, based on 2 follow-up (FU) periods. First period assessed is from Month 0 to end of blinded invasive disease (ID) FU phase (31 Jan 2012), in 10PN-PD-DIT-043 subjects only, Events collected from this period are marked "M0-IDFU"

Adverse event reporting additional description:

Second period of assessment from the end of blinded ID FU phase to study end in 10PN-PD-DIT-043 study, 05 October 2013. Events from this period of assessment are marked "IDFU-SE" The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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	Ctrl2+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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) (2+1 Infant Schedule). Refer to group description for Ctrl6W-6M/043 Group for details on vaccine specifics and administration route in this group.

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 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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	Ctrl3+1-6W-6M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or HBV 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 Ctrl6W-6M/043 Group for details on vaccine specifics and administration route in this group.

Reporting group title	10Pn7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7 to 11 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) vaccine according to either 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.

Reporting group title	Ctrl7-11M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 7

to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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.

Reporting group title	10Pn12-18M/043 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 (111442) study only and aged 12 to 18 months at enrolment. Subjects received the Havrix-preservative free (or 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 title	10Pn3+1-6W-6M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on vaccine specifics and administration route in this group.

Reporting group title	10Pn2+1-6W-6M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on vaccine specifics and administration route in this group.

Reporting group title	Ctrl-6W-6M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 6 weeks to 6 months at enrolment. Subjects received the Engerix B-thio free vaccine (or 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 details on vaccine specifics and administration route in this group.

Reporting group title	10Pn7-11M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) vaccine according to either 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 details on vaccine specifics and administration route in this group.

Reporting group title	Ctrl7-11M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 7 to 11 months at enrolment. Subjects received the Engerix B-thio free (or HBV) vaccine according to either 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 details on vaccine specifics and administration route in this group.

Reporting group title	10Pn12-18M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on vaccine specifics and administration route in this group.

Reporting group title	Ctrl12-18M/043+053 Group

Reporting group description:

Subjects in this group were subjects enrolled in the 10PN-PD-DIT-043 (111442) and 10PN-PD-DIT (112595) studies, pooled, and aged 12 to 18 months at enrolment. Subjects received the Synflorix (or 10Pn-PD-DiT, or 10Pn) 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 details on vaccine specifics and administration route in this group.

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	10Pn2+1-6W-6M/043 Group	Ctrl2+1-6W-6M/043 Group	10Pn3+1-6W-6M/043 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 9112 (0.08%)	1 / 4399 (0.02%)	6 / 8427 (0.07%)
number of deaths (all causes)	4	0	4
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Road traffic accident M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Krabbe’s disease M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Quadriplegic infantile cerebral palsy IDFU-SE			

subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Nervous system disorders			
Convulsion M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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
Febrile convulsion M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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
Epilepsy IDFU-SE			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Injection site reaction M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	2 / 8427 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Sudden infant death syndrome M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Eye disorders			
Optic atrophy IDFU-SE			

subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Diarrhoea haemorrhagic M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Hepatobiliary disorders			
Reye’s syndrome M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Infections and infestations			
Cystitis M0-ID FU			

subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	1 / 4399 (0.02%)	0 / 8427 (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
Laryngitis M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Parotitis M0-ID FU			
subjects affected / exposed	1 / 9112 (0.01%)	0 / 4399 (0.00%)	0 / 8427 (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
Pneumococcal sepsis M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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
Sepsis M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	1 / 8427 (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
Tonsillitis M0-ID FU			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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 infection IDFU-SE			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (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	Ctrl3+1-6W-6M/043 Group	10Pn7-11M/043 Group	Ctrl7-11M/043 Group

Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 4473 (0.16%)	3 / 3689 (0.08%)	2 / 1812 (0.11%)
number of deaths (all causes)	3	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Congenital, familial and genetic disorders			
Gaucher’s disease M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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
Quadriplegic infantile cerebral palsy IDFU-SE			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	1 / 3689 (0.03%)	0 / 1812 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis M0-ID FU			

subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	1 / 1812 (0.06%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	1 / 3689 (0.03%)	0 / 1812 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	1 / 1812 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonic-hyporesponsive episode M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Epilepsy IDFU-SE			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Death M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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
Eye disorders			
Optic atrophy IDFU-SE			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Respiratory, thoracic and mediastinal disorders			
Asphyxia M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Infection M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			

subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	1 / 4473 (0.02%)	0 / 3689 (0.00%)	0 / 1812 (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
Sepsis M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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 M0-ID FU			
subjects affected / exposed	0 / 4473 (0.00%)	1 / 3689 (0.03%)	0 / 1812 (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 infection IDFU-SE			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (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	10Pn12-18M/043 Group	Ctrl12-18M/043 Group	10Pn3+1-6W-6M/043+053 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6249 (0.03%)	2 / 3020 (0.07%)	1 / 10273 (0.01%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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
Quadriplegic infantile cerebral palsy IDFU-SE			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	1 / 6249 (0.02%)	0 / 3020 (0.00%)	0 / 10273 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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
Febrile convulsion M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	1 / 3020 (0.03%)	0 / 10273 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope M0-ID FU			

subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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
Epilepsy IDFU-SE			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	1 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			

subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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
Eye disorders			
Optic atrophy IDFU-SE			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	1 / 6249 (0.02%)	0 / 3020 (0.00%)	0 / 10273 (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
Vomiting M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			

subjects affected / exposed	0 / 6249 (0.00%)	1 / 3020 (0.03%)	0 / 10273 (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
Skin and subcutaneous tissue disorders			
Eczema M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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
Sepsis M0-ID FU			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 M0-ID FU			

subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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 infection IDFU-SE			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (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	10Pn2+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn7-11M/043+053 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10054 (0.01%)	0 / 10201 (0.00%)	0 / 3880 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Quadriplegic infantile cerebral palsy IDFU-SE			

subjects affected / exposed	1 / 10054 (0.01%)	0 / 10201 (0.00%)	0 / 3880 (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
Vascular disorders			
Kawasaki's disease M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Febrile convulsion M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Syncope M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Epilepsy IDFU-SE			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Eye disorders			
Optic atrophy IDFU-SE			

subjects affected / exposed	1 / 10054 (0.01%)	0 / 10201 (0.00%)	0 / 3880 (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
Gastrointestinal disorders			
Diarrhoea M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			

subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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
Sepsis M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 M0-ID FU			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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 infection IDFU-SE			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (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	Ctrl7-11M/043+053 Group	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1908 (0.00%)	1 / 6535 (0.02%)	0 / 3126 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign body M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Quadriplegic infantile cerebral palsy IDFU-SE			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			

subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Febrile convulsion M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Syncope M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Epilepsy IDFU-SE			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Eye disorders			
Optic atrophy IDFU-SE			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			

subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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
Sepsis M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 M0-ID FU			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 infection IDFU-SE			
subjects affected / exposed	0 / 1908 (0.00%)	1 / 6535 (0.02%)	0 / 3126 (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

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

Non-serious adverse events	10Pn2+1-6W-6M/043 Group	Ctrl2+1-6W-6M/043 Group	10Pn3+1-6W-6M/043 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 9112 (0.00%)	0 / 4399 (0.00%)	0 / 8427 (0.00%)

Non-serious adverse events	Ctrl3+1-6W-6M/043 Group	10Pn7-11M/043 Group	Ctrl7-11M/043 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4473 (0.00%)	0 / 3689 (0.00%)	0 / 1812 (0.00%)

Non-serious adverse events	10Pn12-18M/043 Group	Ctrl12-18M/043 Group	10Pn3+1-6W-6M/043+053 Group
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	0 / 6249 (0.00%)	0 / 3020 (0.00%)	0 / 10273 (0.00%)

Non-serious adverse events	10Pn2+1-6W-6M/043+053 Group	Ctrl-6W-6M/043+053 Group	10Pn7-11M/043+053 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10054 (0.00%)	0 / 10201 (0.00%)	0 / 3880 (0.00%)

Non-serious adverse events	Ctrl7-11M/043+053 Group	10Pn12-18M/043+053 Group	Ctrl12-18M/043+053 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1908 (0.00%)	0 / 6535 (0.00%)	0 / 3126 (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 10PN-PD-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 pre-defined 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study population included subjects of nested study 2008-006551-51. Due to the technical complexity to present results for such study population, secondary outcomes are presented in the attached PDF file.

Notes: