Clinical trial results:
Immunogenicity and Safety of a Booster Dose of Polysaccharide Pneumococcal vaccine (Pneumo 23®) in 12 to 18 Months-Old Children Primed with Three Doses of Pneumococcal Conjugate Vaccine (Prevnar®) in Thailand

Summary

EudraCT number	2015-005337-45
Trial protocol	Outside EU/EEA
Global end of trial date	08 March 2008

Results information

Result version number	v1 (current)
This version publication date	25 March 2016
First version publication date	25 March 2016

Trial information

Trial identification

Sponsor protocol code	PNA19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00594347
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon Cedex 07, France, F-69367
Public contact	Franchise Medical Director, Sanofi Pasteur SA, 33 4 37 37 73 84, eric.desauziers@sanofipasteur.com
Scientific contact	Franchise Medical Director, Sanofi Pasteur SA, 33 4 37 37 73 84, eric.desauziers@sanofipasteur.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 March 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity
- To assess and describe the immunogenicity for 12 serotypes of the study vaccines one month after the booster vaccination in both groups
Safety
- To describe the safety of the study vaccines after the booster vaccination

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Children enrolled in this study completed a three-dose primary vaccination of Pneumococcal Conjugate Vaccine (Prevnar®) in a hexavalent combined vaccine study (2011-004457-87).

Evidence for comparator:

Not applicable

Actual start date of recruitment	25 November 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Thailand: 339
Worldwide total number of subjects	339
EEA total number of subjects	0

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)	339

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

Subject disposition

Recruitment

Recruitment details:

The study subjects were enrolled from 25 November 2007 to 09 February 2008 at 4 clinic centers in Thailand.

Pre-assignment

Screening details:

A total of 339 subjects who met all of the inclusion and none of the exclusion criteria were randomized and vaccinated in this study.

Period 1

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

Blinding implementation details:

A blind observer study design was used in this study and neither the Investigator nor the subject knew which vaccine was administered. To maintain the blind, the product preparation and administration, and the assessment of safety was performed by two different individuals (a nurse and an Investigator, respectively) in two different rooms. In the event of an emergency (i.e., SAE), a scratchable emergency randomization list was provided to the Investigator for unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pneumo23

Arm description:

Children 12 to 18 months of age received Pneumo23® vaccine as a booster dose.

Arm type	Experimental
Investigational medicinal product name	The 23-valent polysaccharide pneumococcal vaccine, Pneumo23®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the right deltoid, 1 booster injection on Day 0.

Arm title	Prevnar

Arm description:

Children 12 to 18 months of age received Prevnar® vaccine as a booster dose.

Arm type	Active comparator
Investigational medicinal product name	The 7-valent pneumococcal conjugate vaccine, Prevnar®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the right deltoid, 1 booster injection on Day 0.

Number of subjects in period 1	Pneumo23	Prevnar
Started	170	169
Completed	169	167
Not completed	1	2
Consent withdrawn by subject	1	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Pneumo23
Reporting group description:	
Children 12 to 18 months of age received Pneumo23® vaccine as a booster dose.	
Reporting group title	Prevnar
Reporting group description:	
Children 12 to 18 months of age received Prevnar® vaccine as a booster dose.	

Reporting group values	Pneumo23	Prevnar	Total
Number of subjects	170	169	339
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	170	169	339
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	14.8	14.8	
standard deviation	± 1.5	± 1.5	-
Gender categorical Units: Subjects			
Female	91	88	179
Male	79	81	160

End points

End points reporting groups

Reporting group title	Pneumo23
Reporting group description:	
Children 12 to 18 months of age received Pneumo23® vaccine as a booster dose.	
Reporting group title	Prevnar
Reporting group description:	
Children 12 to 18 months of age received Prevnar® vaccine as a booster dose.	

Primary: Summary of Geometric Mean Titers for all Vaccine Serotypes Before and Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Summary of Geometric Mean Titers for all Vaccine Serotypes Before and Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[1]
End point description:	
Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) and Day 30 post-vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	169		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serotype 1; Pre-dose	0.14 (0.121 to 0.162)	0.118 (0.105 to 0.132)		
Serotype 1; Post-dose	7.16 (6.1 to 8.41)	0.145 (0.128 to 0.165)		
Serotype 1; Post/Pre ratio	52.5 (43.1 to 63.8)	1.24 (1.12 to 1.37)		
Serotype 3; Pre-dose	0.365 (0.309 to 0.43)	0.303 (0.263 to 0.348)		
Serotype 3; Post-dose	6.82 (5.51 to 8.44)	0.666 (0.428 to 1.04)		
Serotype 3; Post/Pre ratio	15.7 (12.3 to 20)	1.6 (1.26 to 2.01)		
Serotype 4; Pre-dose	0.582 (0.519 to 0.651)	0.562 (0.498 to 0.635)		
Serotype 4; Post-dose	8.93 (7.77 to 10.3)	5.71 (5.02 to 6.51)		
Serotype 4; Post/Pre ratio	15.4 (13 to 18.2)	10.3 (8.9 to 11.8)		
Serotype 5; Pre-dose	0.406 (0.353 to 0.466)	0.381 (0.33 to 0.44)		

Serotype 5; Post-dose	2.02 (1.75 to 2.32)	0.435 (0.379 to 0.5)		
Serotype 5; Post/Pre ratio	4.97 (4.31 to 5.74)	1.12 (1.07 to 1.18)		
Serotype 6B; Pre-dose	0.616 (0.52 to 0.729)	0.562 (0.48 to 0.657)		
Serotype 6B; Post-dose	11.1 (9.43 to 13.1)	9.35 (7.91 to 11.1)		
Serotype 6B; Post/Pre ratio	17.9 (14.9 to 21.6)	16.5 (13.9 to 19.6)		
Serotype 7F; Pre-dose	0.115 (0.103 to 0.13)	0.115 (0.102 to 0.129)		
Serotype 7F; Post-dose	2.34 (2 to 2.73)	0.135 (0.12 to 0.153)		
Serotype 7F; Post/Pre ratio	20.3 (17.3 to 23.7)	1.18 (1.09 to 1.27)		
Serotype 9V; Pre-dose	0.533 (0.47 to 0.604)	0.551 (0.485 to 0.625)		
Serotype 9V; Post-dose	8.04 (7 to 9.24)	5.37 (4.7 to 6.13)		
Serotype 9V; Post/Pre ratio	15.1 (12.9 to 17.6)	9.76 (8.59 to 11.1)		
Serotype 14; Pre-dose	2.4 (2.05 to 2.8)	2.22 (1.91 to 2.57)		
Serotype 14; Post-dose	16.1 (13.7 to 18.9)	15.3 (13.2 to 17.6)		
Serotype 14; Post/Pre ratio	6.72 (5.65 to 7.98)	6.85 (5.87 to 7.99)		
Serotype 18C; Pre-dose	0.342 (0.302 to 0.387)	0.345 (0.306 to 0.39)		
Serotype 18C; Post-dose	5.99 (5.24 to 6.85)	3.11 (2.7 to 3.58)		
Serotype 18C; Post/Pre ratio	17.3 (15 to 20.1)	9.31 (8.26 to 10.5)		
Serotype 19A; Pre-dose	0.592 (0.522 to 0.672)	0.573 (0.502 to 0.655)		
Serotype 19A; Post-dose	1.94 (1.65 to 2.27)	1.46 (1.27 to 1.68)		
Serotype 19A; Post/Pre ratio	3.26 (2.79 to 3.8)	2.53 (2.24 to 2.86)		
Serotype 19F; Pre-dose	1.1 (0.971 to 1.26)	1.14 (0.988 to 1.31)		
Serotype 19F; Post-dose	14.7 (12.7 to 17)	5.89 (5.2 to 6.67)		
Serotype 19F; Post/Pre ratio	13.2 (11.1 to 15.6)	5.16 (4.49 to 5.94)		
Serotype 23F; Pre-dose	0.684 (0.581 to 0.805)	0.581 (0.497 to 0.68)		
Serotype 23F; Post-dose	9.74 (8.09 to 11.7)	8.74 (7.37 to 10.4)		
Serotype 23F; Post/Pre ratio	14.4 (12 to 17.3)	15.2 (13.1 to 17.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with at Least a 2-Fold Increase in Antibody Titers

Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with at Least a 2-Fold Increase in Antibody Titers Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[2]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	161		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1	98.8	11.9		
Serotype 3	93.1	17.1		
Serotype 4	95.9	96.4		
Serotype 5	84.6	4.8		
Serotype 6B	93.2	92.4		
Serotype 7F	98.2	6		
Serotype 9V	96.4	96.4		
Serotype 14	84.6	91		
Serotype 18C	98.2	97		
Serotype 19A	61.3	57.8		
Serotype 19F	93.5	84.4		
Serotype 23F	92.7	97		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with at Least a 4-Fold Increase in Antibody Titers Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with at Least a 4-Fold Increase in Antibody Titers Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[3]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	154		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1	97.5	3.1		
Serotype 3	91.7	5.7		
Serotype 4	87	83.8		
Serotype 5	52.1	1.2		
Serotype 6B	89.4	88		
Serotype 7F	92.9	1.8		
Serotype 9V	92.3	88		
Serotype 14	65.1	66.5		
Serotype 18C	95.2	86.7		
Serotype 19A	36.9	24.1		
Serotype 19F	86.9	63.5		
Serotype 23F	90.2	93.3		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody titers ≥ 0.15 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with Antibody titers ≥ 0.15 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[4]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	169		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1; Pre-dose	39.3	31.1		

Serotype 1; Post-dose	99.4	44.2		
Serotype 3; Pre-dose	88.1	83.7		
Serotype 3; Post-dose	98.7	90.2		
Serotype 4; Pre-dose	96.4	95.9		
Serotype 4; Post-dose	100	100		
Serotype 5; Pre-dose	87.6	83.3		
Serotype 5; Post-dose	99.4	89.1		
Serotype 6B; Pre-dose	94.4	94.5		
Serotype 6B; Post-dose	100	100		
Serotype 7F; Pre-dose	33.3	29.8		
Serotype 7F; Post-dose	99.4	42.2		
Serotype 9V; Pre-dose	94.7	94.7		
Serotype 9V; Post-dose	100	100		
Serotype 14; Pre-dose	98.8	98.8		
Serotype 14; Post-dose	100	100		
Serotype 18C; Pre-dose	84.5	88.7		
Serotype 18C; Post-dose	100	100		
Serotype 19A; Pre-dose	97.6	94.1		
Serotype 19A; Post-dose	100	100		
Serotype 19F; Pre-dose	100	98.8		
Serotype 19F; Post-dose	100	100		
Serotype 23F; Pre-dose	92.7	92.2		
Serotype 23F; Post-dose	100	98.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody titers ≥ 0.35 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with Antibody titers ≥ 0.35 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[5]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	169		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1; Pre-dose	12.3	9.8		
Serotype 1; Post-dose	99.4	12.3		
Serotype 3; Pre-dose	44.8	39.5		
Serotype 3; Post-dose	98.7	70.7		
Serotype 4; Pre-dose	75.7	74.6		
Serotype 4; Post-dose	100	100		
Serotype 5; Pre-dose	56.8	50.6		
Serotype 5; Post-dose	97.6	57.6		
Serotype 6B; Pre-dose	66	67.5		
Serotype 6B; Post-dose	99.4	99.4		
Serotype 7F; Pre-dose	6	11.9		
Serotype 7F; Post-dose	95.9	10.2		
Serotype 9V; Pre-dose	70.4	70.4		
Serotype 9V; Post-dose	100	99.4		
Serotype 14; Pre-dose	96.4	94.7		
Serotype 14; Post-dose	100	100		
Serotype 18C; Pre-dose	46.4	48.2		
Serotype 18C; Post-dose	100	99.4		
Serotype 19A; Pre-dose	73.2	71.6		
Serotype 19A; Post-dose	94.1	96.4		
Serotype 19F; Pre-dose	94.6	94.1		
Serotype 19F; Post-dose	100	100		
Serotype 23F; Pre-dose	71.5	70.1		
Serotype 23F; Post-dose	99.4	98.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody titers ≥ 0.5 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with Antibody titers ≥ 0.5 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[6]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	169		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1; Pre-dose	7.4	3		
Serotype 1; Post-dose	98.8	6.7		
Serotype 3; Pre-dose	27.3	16.3		
Serotype 3; Post-dose	97.5	51.2		
Serotype 4; Pre-dose	58	57.4		
Serotype 4; Post-dose	99.4	100		
Serotype 5; Pre-dose	42.6	38.1		
Serotype 5; Post-dose	95.3	43		
Serotype 6B; Pre-dose	48.8	51.5		
Serotype 6B; Post-dose	98.8	99.4		
Serotype 7F; Pre-dose	5.4	5.4		
Serotype 7F; Post-dose	92.3	6.6		
Serotype 9V; Pre-dose	50.9	55.6		
Serotype 9V; Post-dose	100	98.8		
Serotype 14; Pre-dose	92.3	92.3		
Serotype 14; Post-dose	100	100		
Serotype 18C; Pre-dose	28.6	26.8		
Serotype 18C; Post-dose	100	98.8		
Serotype 19A; Pre-dose	52.4	54.4		
Serotype 19A; Post-dose	92.3	88		
Serotype 19F; Pre-dose	87.5	84.6		
Serotype 19F; Post-dose	100	100		
Serotype 23F; Pre-dose	61.2	58.7		
Serotype 23F; Post-dose	98.2	98.2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody titers ≥ 1.0 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Percentage of Subjects with Antibody titers ≥ 1.0 µg/mL Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[7]

End point description:

Individual antibody titers for all serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) were measured by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) to Day 30 post-vaccination

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	169		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1; Pre-dose	2.5	1.2		
Serotype 1; Post-dose	97	1.8		
Serotype 3; Pre-dose	10.5	3.4		
Serotype 3; Post-dose	96.2	24.4		
Serotype 4; Pre-dose	21.3	21.3		
Serotype 4; Post-dose	99.4	98.2		
Serotype 5; Pre-dose	17.2	14.9		
Serotype 5; Post-dose	76.9	17.6		
Serotype 6B; Pre-dose	26.5	22.1		
Serotype 6B; Post-dose	98.2	96.3		
Serotype 7F; Pre-dose	1.2	1.8		
Serotype 7F; Post-dose	82.8	3		
Serotype 9V; Pre-dose	20.1	22.5		
Serotype 9V; Post-dose	98.2	96.4		
Serotype 14; Pre-dose	84	82.8		
Serotype 14; Post-dose	98.8	99.4		
Serotype 18C; Pre-dose	8.3	7.1		
Serotype 18C; Post-dose	97.6	88.6		
Serotype 19A; Pre-dose	23.8	24.3		
Serotype 19A; Post-dose	73.4	65.1		
Serotype 19F; Pre-dose	47.6	47.9		
Serotype 19F; Post-dose	98.8	98.2		
Serotype 23F; Pre-dose	29.7	26.3		
Serotype 23F; Post-dose	94.6	97		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine

End point title	Number of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following a Booster Dose of Either Pneumo23® or Prevnar® Vaccine[8]

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever (Temperature), Vomiting, Crying abnormal, Drowsiness, Appetite lost, Irritability.

Grade 3 injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 sytemic reactions: Fever (Temperature), > 39.5°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds/meals or refuses most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-vaccination

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Pneumo23	Prevnar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	168		
Units: Number of subjects				
number (not applicable)				
Injection site Tenderness	99	88		
Grade 3 Injection site Tenderness	2	2		
Injection site Erythema	60	53		
Grade 3 Injection site Erythema	0	1		
Injection site Swelling	35	33		
Grade 3 Injection site Swelling	0	0		
Fever	29	20		
Grade 3 Fever	0	1		
Vomiting	28	16		
Grade 3 Vomiting	1	1		
Crying abnormal	51	46		
Grade 3 Crying abnormal	0	3		
Drowsiness	20	24		
Grade 3 Drowsiness	0	1		
Appetite lost	41	41		
Grade 3 Appetite lost	1	0		
Irritability	54	64		
Grade Irritability	2	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event data were collected from Day 0 up to Day 30 post-vaccination.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	9
Reporting groups	
Reporting group title	Pneumo23
Reporting group description:	
Children 12 to 18 months of age received Pneumo23® vaccine as a booster dose.	
Reporting group title	Prevnar
Reporting group description:	
Children 12 to 18 months of age received Prevnar® vaccine as a booster dose.	

Serious adverse events	Pneumo23	Prevnar	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 169 (3.55%)	1 / 169 (0.59%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Near drowning			
subjects affected / exposed	1 / 169 (0.59%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Croup infectious			
subjects affected / exposed	1 / 169 (0.59%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 169 (1.18%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			

subjects affected / exposed	1 / 169 (0.59%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 169 (0.59%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pneumo23	Prevnar	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 169 (58.58%)	88 / 169 (52.07%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	20 / 169 (11.83%)	24 / 167 (14.37%)	
occurrences (all)	20	24	
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	99 / 169 (58.58%)	88 / 168 (52.38%)	
occurrences (all)	99	88	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	60 / 169 (35.50%)	53 / 167 (31.74%)	
occurrences (all)	60	53	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	35 / 169 (20.71%)	33 / 167 (19.76%)	
occurrences (all)	35	33	
Fever			
alternative assessment type: Systematic			

subjects affected / exposed[5]	29 / 168 (17.26%)	20 / 165 (12.12%)	
occurrences (all)	29	20	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[6]	28 / 169 (16.57%)	16 / 167 (9.58%)	
occurrences (all)	28	16	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed[7]	51 / 169 (30.18%)	46 / 167 (27.54%)	
occurrences (all)	51	46	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[8]	54 / 169 (31.95%)	64 / 167 (38.32%)	
occurrences (all)	54	64	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 169 (10.06%)	18 / 169 (10.65%)	
occurrences (all)	17	19	
Upper respiratory tract infection			
subjects affected / exposed	27 / 169 (15.98%)	23 / 169 (13.61%)	
occurrences (all)	28	25	
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed[9]	41 / 169 (24.26%)	41 / 167 (24.55%)	
occurrences (all)	41	41	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination;

the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2008	Serotype 19A was included in the analysis of individual Opsonophagocytosis (OPA) titers in addition to serotypes 1, 6B, 14, and 23F.
08 March 2008	Additional analysis of individual Opsonophagocytosis (OPA) titers against the serotypes 1, 6B, 14, and 23F was included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported