Clinical trial results:
A Phase III, Multi-Center, Open-Label, Controlled, Randomized Study to Evaluate the Immunogenicity, Safety, Tolerability and the Ability to Prime for Memory of Chiron Meningococcal C Conjugate Vaccine Menjugate® When Administered to Healthy Infants as One Dose Given at 2 or 6 Months of Age with a Booster at 12-16 Months of Age, in Comparison to Two Doses in the First Year of Life, Given Two Months Apart, With a Booster at 12-16 Months of Age.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2005-000924-18
Trial protocol	DE
Global end of trial date	17 April 2008

Results information

Result version number	v2 (current)
This version publication date	03 June 2016
First version publication date	19 March 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	M14P6

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00311415
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l.
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.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	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 April 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferiority, 10 days after the booster vaccination, of the memory antibody response (in terms of percent responders) to Neisseria meningitidis serogroup C after 1 dose of Menjugate® at 2 months of age plus a booster in the second year of life (study group 2) in comparison with the memory antibody response after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (study group 1), as measured by bactericidal assay using rabbit complement (rBCA).

Protection of trial subjects:

The procedures established in this study protocol were designed to ensure that the Sponsor and Investigator abide by the principles of Good Clinical Practice (GCP) established by the International Conference on Harmonisation (ICH), the current version of the Declaration of Helsinki, and the Standard Operating Procedures of the Sponsor.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	28 October 2005
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	Germany: 111
Country: Number of subjects enrolled	Poland: 146
Worldwide total number of subjects	257
EEA total number of subjects	257

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)	257
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:

Subjects were enrolled at 5 sites in Germany and 4 sites in Poland.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The trial was designed as an open-label study; after the randomization both the study personnel and the subject knew which vaccine was being administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (2+4 Months)

Arm description:

Subjects received 2 doses of Menjugate®, at 2 and 4 months of age, together with the 1st and 3rd (Germany) or 1st and 2nd (Poland) dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal C conjugated vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of 0.5 mL reconstituted vaccine.

Arm title	Group 2 (2 Months)

Arm description:

Subjects received 1 dose of Menjugate®, at 2 months of age, together with the 1st dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal C conjugated vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses of 0.5 mL reconstituted vaccine.

Arm title	Group 3 (6 Months)

Arm description:

Subjects received 1 dose of Menjugate®, at 6 months of age, together with the 3rd dose (in Poland), but respectively 2 months after the 3rd dose (in Germany), of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Arm type	Experimental

Investigational medicinal product name	Meningococcal C conjugated vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses of 0.5 mL reconstituted vaccine.

Arm title	Group 4 (12-16 Months)

Arm description:

Subjects received 1 dose of Menjugate® at 12-16 months of age (together with the 4th dose of routine hexavalent infant immunization)

Arm type	Experimental
Investigational medicinal product name	Meningococcal C conjugated vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of 0.5 mL reconstituted vaccine.

Number of subjects in period 1	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)
Started	64	64	63
Completed	64	62	57
Not completed	0	2	6
Consent withdrawn by subject	-	1	3
Unable to classify	-	-	2
Lost to follow-up	-	1	1
Protocol deviation	-	-	-

Number of subjects in period 1	Group 4 (12-16 Months)
Started	66
Completed	61
Not completed	5
Consent withdrawn by subject	3
Unable to classify	-
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 (2+4 Months)
Reporting group description:	
Subjects received 2 doses of Menjugate®, at 2 and 4 months of age, together with the 1st and 3rd (Germany) or 1st and 2nd (Poland) dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 2 (2 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate®, at 2 months of age, together with the 1st dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 3 (6 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate®, at 6 months of age, together with the 3rd dose (in Poland), but respectively 2 months after the 3rd dose (in Germany), of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 4 (12-16 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate® at 12-16 months of age (together with the 4th dose of routine hexavalent infant immunization)	

Reporting group values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)
Number of subjects	64	64	63
Age categorical			
Units: Subjects			
Age continuous			
Units: days			
arithmetic mean	62.1	63	61.6
standard deviation	± 10.3	± 10.4	± 10.1
Gender categorical			
Units: Subjects			
Female	32	30	27
Male	32	34	36

Reporting group values	Group 4 (12-16 Months)	Total	
Number of subjects	66	257	
Age categorical			
Units: Subjects			
Age continuous			
Units: days			
arithmetic mean	63.1		
standard deviation	± 9.9	-	
Gender categorical			
Units: Subjects			
Female	27	116	
Male	39	141	

End points

End points reporting groups

Reporting group title	Group 1 (2+4 Months)
Reporting group description:	
Subjects received 2 doses of Menjugate®, at 2 and 4 months of age, together with the 1st and 3rd (Germany) or 1st and 2nd (Poland) dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 2 (2 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate®, at 2 months of age, together with the 1st dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 3 (6 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate®, at 6 months of age, together with the 3rd dose (in Poland), but respectively 2 months after the 3rd dose (in Germany), of routine hexavalent infant immunization, and a booster at 12-16 months of age.	
Reporting group title	Group 4 (12-16 Months)
Reporting group description:	
Subjects received 1 dose of Menjugate® at 12-16 months of age (together with the 4th dose of routine hexavalent infant immunization)	
Subject analysis set title	All enrolled population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects enrolled in the study.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects with at least one vaccination and with some post-baseline safety data.	
Subject analysis set title	Per protocol (PP) population, Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description:	
All randomized subjects who received all the relevant doses of vaccine correctly, provided evaluable serum samples at the relevant time points, and had no major protocol violation as defined prior to analysis.	

Primary: 1. Percentages of subjects with rBCA ≥ 1:128 at 10 days after booster dose

End point title	1. Percentages of subjects with rBCA ≥ 1:128 at 10 days after booster dose[1]
End point description:	
The percentages of subject showing a rabbit bactericidal complement assay (rBCA) titer of at least 1:128 after vaccination, i.e. rBCA ≥ 1:128, 10 days after the booster vaccination, were measured to demonstrate non-inferiority of the memory antibody response to Neisseria meningitidis serogroup C after 1 dose of Menjugate® at 2 months of age plus a booster in the second year of life (2 Months group) in comparison with the memory antibody response after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group). The analysis was done on the PP population, Immunogenicity.	
End point type	Primary
End point timeframe:	
10 days after the booster vaccination	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: statistical analyses not applicable for this endpoint.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	36		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Pre-Booster	10 (3 to 23)	3 (0.07 to 15)		
10 Days After Booster (N=36,29)	100 (90 to 100)	90 (73 to 98)		

Statistical analyses

Statistical analysis title	Statistical Analysis for outcome measure 1

Statistical analysis description:

The null hypothesis associated with the primary immunogenicity objective was that the proportion of responders, defined as subjects showing a rBCA ≥ 1:128, after 1 dose of Menjugate® at 2 months of age plus a booster in the second year of life (2 Months group) is inferior to the proportion of responders after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group), by more than 10%.

Comparison groups	Group 1 (2+4 Months) v Group 2 (2 Months)
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Clopper-Pearson method
Parameter estimate	Percentage group difference
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26
upper limit	0

Secondary: 2. Percentages of subjects with rBCA ≥ 1:128 after 1 (at 6 months) or 2 (at 2 and 4 months) doses and booster

End point title	2. Percentages of subjects with rBCA ≥ 1:128 after 1 (at 6 months) or 2 (at 2 and 4 months) doses and booster[2]

End point description:

The percentages of subject showing a rabbit bactericidal complement assay (rBCA) titer of at least 1:128 after 1 dose of Menjugate at 6 months of age plus a booster in the second year of life (6 Months group) as well as after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group) were measured to compare memory antibody response to Neisseria meningitidis serogroup C.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

10 days after the booster vaccination

Notes:

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

End point values	Group 1 (2+4 Months)	Group 3 (6 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	36		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Pre-Booster at 12-16 mo	10 (3 to 23)	3 (0.07 to 15)		
10 Days After Booster (N=36,32)	100 (90 to 100)	100 (89 to 100)		

Statistical analyses

Statistical analysis title	Statistical Analysis for outcome measure 2

Statistical analysis description:

Proportion of subjects achieving protective titers (rBCA ≥ 128) against Neisseria meningitidis serogroup C at 10 days after booster in 2+4 Months and 6 Months groups and associated 95% Clopper-Pearson CIs was computed by vaccine group. Vaccine group differences and 95% CIs were computed using the normal approximation where appropriate.
6 Months group was considered non-inferior to 2+4 Months group if the lower limit of 95% CI of the difference in percentages was greater than –10%.

Comparison groups	Group 1 (2+4 Months) v Group 3 (6 Months)
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Clopper-Pearson method
Parameter estimate	Percentage group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	10

Secondary: 3. Percentages of subjects with rBCA ≥ 1:128 after 2 (at 2 and 4 months) doses and booster or after a single dose (12-16 months)

End point title	3. Percentages of subjects with rBCA ≥ 1:128 after 2 (at 2 and 4 months) doses and booster or after a single dose (12-16 months)[3]

End point description:

The percentages of subject showing a rabbit bactericidal complement assay (rBCA) titer of at least 1:128 after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group) as well as one month after a single dose of Menjugate given in the second year of life (12-16 Months group) were measured to compare memory antibody response to Neisseria meningitidis serogroup C.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

10 or 28 days after the booster vaccination.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: statistical analyses not applicable for this endpoint.

End point values	Group 1 (2+4 Months)	Group 4 (12-16 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	37		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Pre-Booster at 12-16 mo	10 (3 to 23)	0 (0 to 9)		
10 or 28 Days After Vacc at 12-16 mo (N=36,31)	100 (90 to 100)	52 (33 to 70)		

Statistical analyses

Statistical analysis title	Statistical Analysis for outcome measure 3

Statistical analysis description:

Proportion of subjects achieving protective titers (rBCA ≥ 128) against Neisseria meningitidis serogroup C at 10 days after the booster dose in 2+4 Months and one months after primary vaccination at 12-16 Months groups and associated 95% Clopper-Pearson CIs was computed by vaccine group. The 12-16 Months group was considered non-inferior to the 2+4 Months group if the lower limit of 95% CI of the difference in percentages was greater than –10%.

Comparison groups	Group 1 (2+4 Months) v Group 4 (12-16 Months)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Clopper-Pearson method
Parameter estimate	Percentage group difference
Point estimate	-48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65
upper limit	-32

Secondary: 4. Geometric mean antibody titers (GMTs) as measured by rBCA at 10 days after booster dose

End point title	4. Geometric mean antibody titers (GMTs) as measured by rBCA at 10 days after booster dose[4]

End point description:

Geometric mean antibody titers (GMTs) as measured by rabbit bactericidal complement assay (rBCA) were measured after 1 dose of Menjugate® at 2 or 6 months of age plus a booster in the second year of life (2 and 6 Months group) in comparison with the memory antibody response after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group).
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

10 days after the booster vaccination.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: statistical analyses not applicable for this endpoint.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	36	36	
Units: Titers				
geometric mean (confidence interval 95%)				
Pre-Booster	6.64 (4.05 to 11)	4 (2.56 to 6.24)	6.6 (4 to 11)	
10 Days After Booster (N=36,29,32)	2953 (2023 to 4309)	2664 (1411 to 5031)	3922 (2653 to 5799)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Geometric mean antibody titers (GMTs) as measured by rBCA at 10 days after booster dose for the 2+4 Months group and at one month after one dose given at 12-16 months of age

End point title	5. Geometric mean antibody titers (GMTs) as measured by rBCA at 10 days after booster dose for the 2+4 Months group and at one month after one dose given at 12-16 months of age[5]

End point description:

Geometric mean antibody titers (GMTs) as measured by rabbit bactericidal complement assay (rBCA) were measured after 2 doses of Menjugate at 2 and 4 months of age plus a booster in the second year of life (2+4 Months group) in comparison with that measured after 1 dose of Menjugate® given at 12-16 months of age for the 12-16 Months group.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

10 or 28 days after the booster vaccination.

Notes:

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

End point values	Group 1 (2+4 Months)	Group 4 (12-16 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	37		
Units: Titers				
geometric mean (confidence interval 95%)				
Pre-Booster at 12-16 mo	6.64 (4.05 to 11)	2.2 (1.82 to 2.66)		
10 or 28 Days After Vacc at 12-16 mo (N=36,31)	2953 (2023 to 4309)	60 (29 to 123)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Percentages of subjects with rBCA ≥ 1:128 at 1 Month After Infant Vaccination

End point title	6. Percentages of subjects with rBCA ≥ 1:128 at 1 Month After Infant Vaccination

End point description:

The percentages of subjects achieving protective titers (i.e., rBCA ≥ 128) against Neisseria meningitidis serogroup C and the rBCA GMTs at 1 month after two doses of Menjugate given at 2 and 4 months of age were evaluated.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

1 Month After Infant Vaccination.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	35	36	36
Units: Percentages of Subjects				
number (confidence interval 95%)				
Day 0 N=(0,0,0,36)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	3 (0.07 to 15)
1 Mo after Primary Infant Vacc (N=40,35,36,0)	93 (80 to 98)	51 (34 to 69)	64 (46 to 79)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Geometric Mean rBCA Titers (95% CI) Against N.meningitidis serogroup C at 1 Month After Infant Vaccination

End point title	7. Geometric Mean rBCA Titers (95% CI) Against N.meningitidis serogroup C at 1 Month After Infant Vaccination

End point description:

The rBCA GMTs 1 month after primary immunization in subjects receiving one dose of Menjugate at either 2 or 6 months of age (2 Months group and 6 Months group) were compared to those in subjects receiving two doses of Menjugate at 2 and 4 months of age (2+4 Months group).
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

1 Month After Infant Vaccination.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	35	36	36
Units: Titers				
geometric mean (confidence interval 95%)				
Day 0 N=(0,0,0,36)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.33 (1.71 to 3.19)
1 Mo after Primary Infant Vacc (N=40,35,36,0)	653 (436 to 977)	57 (32 to 100)	108 (78 to 149)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Percentages of subjects with rBCA titers ≥ 1:128 (95% CI) against N.meningitidis serogroup C - Persistence of antibody after infant vaccination or vaccination at 12-16 months of age

End point title	8. Percentages of subjects with rBCA titers ≥ 1:128 (95% CI) against N.meningitidis serogroup C - Persistence of antibody after infant vaccination or vaccination at 12-16 months of age

End point description:

To evaluate the persistence of the antibody response (in terms of percent responders) to Neisseria meningitidis serogroup C after one dose of Menjugate® at either 2 or 6 months of age (2 Months and 6 Months groups, respectively) and the persistence of antibody response after 2 doses of Menjugate at 2 and 4 months of age (2+4 Months group), before the administration of the booster at 12-16 months of age as measured by rBCA.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

at ≥8 to ≤10 months of age after the primary vaccination, at 12 to 16 months of age before the booster vaccination, and at 24 months of age after booster vaccination (2+4 Months, 2 Months and 6 Months groups) or primary vaccination (12-16 Months group)

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	36	36	31
Units: Percentages of Subjects				
number (confidence interval 95%)				
1 Mo after Primary Infant Vacc (N=40,35,36,0)	93 (80 to 98)	51 (34 to 69)	64 (46 to 79)	0 (0 to 0)
Persistence at 8-10 mo of age (N=37,35,35,0)	46 (29 to 63)	0 (0 to 10)	14 (5 to 30)	0 (0 to 0)
Persistence at 12-16 mo of age (N=41,36,36,0)	10 (3 to 23)	3 (0.07 to 15)	3 (0.07 to 15)	0 (0 to 0)

10 days after booster (N=36,29,32,0)	100 (90 to 100)	90 (73 to 98)	100 (89 to 100)	0 (0 to 0)
28 days after 1st dose at 12-16 mo age (N=0,0,0,31	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	52 (33 to 70)
Persistence at 24 mo of age (N=31,25,23,22)	26 (12 to 45)	44 (24 to 65)	43 (23 to 66)	0 (0 to 15)

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Geometric Mean rBCA Titers - Persistence of antibody after infant vaccination or vaccination at 12-16 months of age

End point title	9. Geometric Mean rBCA Titers - Persistence of antibody after infant vaccination or vaccination at 12-16 months of age

End point description:

To evaluate the persistence of the antibody response (in terms of rBCA GMTs) to Neisseria meningitidis serogroup C after one dose of Menjugate® at either 2 or 6 months of age (2 Months and 6 Months groups, respectively) and the persistence of antibody response after 2 doses of Menjugate at 2 and 4 months of age (2+4 Months group), before the administration of the booster at 12-16 months of age as measured by rBCA.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

at ≥8 to ≤10 months of age after the primary vaccination, at 12 to 16 months of age before the booster vaccination, and at 24 months of age after booster vaccination (2+4 Months, 2 Months and 6 Months groups) or primary vaccination (12-16 Months group)

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	36	36	31
Units: Titers				
geometric mean (confidence interval 95%)				
1 Mo after Primary Infant Vacc (N=40,35,36,0)	653 (436 to 977)	57 (32 to 100)	108 (78 to 149)	0 (0 to 0)
Persistence at 8-10 mo of age (N=37,35,35,0)	61 (35 to 106)	5.07 (3.23 to 7.96)	37 (26 to 52)	0 (0 to 0)
Persistence at 12-16 mo of age (N=41,36,36,0)	6.64 (4.05 to 11)	4 (2.56 to 6.24)	6.6 (4 to 11)	0 (0 to 0)
10 days after booster (N=36,29,32,0)	2953 (2023 to 4309)	2664 (1411 to 5031)	3922 (2653 to 5799)	0 (0 to 0)
28 days after 1st dose at 12-16 mo age N=0,0,0,31	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	60 (29 to 123)
Persistence at 24 mo of age (N=31,25,23,22)	28 (14 to 57)	36 (14 to 93)	47 (21 to 105)	2.83 (2.17 to 3.68)

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentages of subjects with anti-Diphtheria antibody titer ≥0.1 IU/mL

End point title	10. Percentages of subjects with anti-Diphtheria antibody titer ≥0.1 IU/mL

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	45 (23 to 68)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	18 (4 to 43)
Germany 1 mo after Primary vacc (N=20,0,0,0)	100 (83 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	93 (68 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	100 (82 to 100)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	79 (54 to 94)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	82 (57 to 96)
Germany 10 days after booster (N=19,15,14,0)	100 (82 to 100)	100 (78 to 100)	100 (77 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Percentages of subjects with anti-Tetanus antibody titer ≥0.1 IU/mL

End point title	11. Percentages of subjects with anti-Tetanus antibody titer ≥0.1 IU/mL

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	85 (62 to 97)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)
Germany 1 mo after Primary vacc (N=20,0,0,0)	100 (83 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	100 (78 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	100 (82 to 100)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	95 (74 to 100)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)
Germany 10 days after booster (N=19,15,14,0)	100 (82 to 100)	100 (78 to 100)	100 (77 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Percentages of subjects with anti-Polyribosylribitol phosphate (PRP) antibody titer ≥0.15 ug/mL

End point title	12. Percentages of subjects with anti-Polyribosylribitol phosphate (PRP) antibody titer ≥0.15 ug/mL

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life-

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	95 (75 to 100)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	88 (64 to 99)
Germany 1 mo after Primary vacc (N=20,0,0,0)	100 (83 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	100 (78 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	95 (74 to 100)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	95 (74 to 100)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)
Germany 10 days after booster (N=19,15,14,0)	100 (82 to 100)	100 (78 to 100)	100 (77 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	94 (73 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	94 (73 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 13. Percentages of subjects with anti-Polio I antibody titer ≥1:8

End point title	13. Percentages of subjects with anti-Polio I antibody titer ≥1:8

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children. The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	75 (51 to 91)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	71 (44 to 90)
Germany 1 mo after Primary vacc (N=20,0,0,0)	100 (83 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,13,0)	0 (0 to 0)	0 (0 to 0)	92 (64 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	95 (74 to 100)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	82 (57 to 96)
Germany 10 days after booster (N=18,15,13,0)	100 (81 to 100)	100 (78 to 100)	100 (75 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 14. Percentages of subjects with anti-Polio II antibody titer ≥1:8

End point title	14. Percentages of subjects with anti-Polio II antibody titer ≥1:8

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects

as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	40 (19 to 64)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	65 (38 to 86)
Germany 1 mo after Primary vacc (N=20,0,0,0)	95 (75 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,13,0)	0 (0 to 0)	0 (0 to 0)	92 (64 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	74 (49 to 91)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	89 (65 to 99)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	88 (64 to 99)
Germany 10 days after booster (N=18,15,13,0)	100 (81 to 100)	100 (78 to 100)	100 (75 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Percentages of subjects with anti-Polio III antibody titer ≥1:8

End point title	15. Percentages of subjects with anti-Polio III antibody titer ≥1:8

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children. The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	65 (41 to 85)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	6 (0 to 29)
Germany 1 mo after Primary vacc (N=20,0,0,0)	100 (83 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	100 (79 to 100)	100 (78 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,13,0)	0 (0 to 0)	0 (0 to 0)	100 (75 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	89 (67 to 99)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	82 (57 to 96)
Germany 10 days after booster (N=18,15,13,0)	100 (81 to 100)	100 (78 to 100)	100 (75 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (77 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Percentages of subjects with Anti-HbsAg (Hepatitis B) Antibody Titer ≥ 10 mIU/mL

End point title	16. Percentages of subjects with Anti-HbsAg (Hepatitis B) Antibody Titer ≥ 10 mIU/mL

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	16	19	18
Units: Percentages of Subjects				
number (confidence interval 95%)				
Germany Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	24 (7 to 50)
Poland Day 0 (N=0,0,0,16)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	25 (7 to 52)
Germany 1 mo after Primary vacc (N=21,0,0,0)	95 (76 to 100)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,19,0)	0 (0 to 0)	0 (0 to 0)	100 (82 to 100)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=18,14,0,0)	100 (81 to 100)	100 (77 to 100)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,11,0)	0 (0 to 0)	0 (0 to 0)	100 (72 to 100)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,16,0,0)	0 (0 to 0)	94 (70 to 100)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (80 to 100)
Germany 10 days after booster (N=15,14,10,0)	100 (78 to 100)	100 (77 to 100)	90 (55 to 100)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	100 (81 to 100)	100 (78 to 100)	100 (82 to 100)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,13)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (75 to 100)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (81 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Geometric mean anti-Pertussis Toxin (PT) antibody titers

End point title	17. Geometric mean anti-Pertussis Toxin (PT) antibody titers

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Titers				
geometric mean (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.91 (2.34 to 3.62)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.92 (2.29 to 3.73)
Germany 1 mo after Primary vacc (N=20,0,0,0)	34 (24 to 47)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	41 (27 to 63)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	29 (21 to 41)	17 (12 to 24)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	27 (19 to 38)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	14 (9.68 to 21)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	5.83 (4 to 8.48)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	6.14 (3.99 to 9.47)
Germany 10 days after booster (N=19,15,14,0)	68 (43 to 106)	52 (29 to 92)	59 (31 to 109)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	72 (46 to 113)	33 (20 to 56)	42 (27 to 68)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	70 (45 to 109)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	75 (50 to 112)

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Geometric mean anti-Filamentous Hemagglutinin (FHA) antibody titers

End point title	18. Geometric mean anti-Filamentous Hemagglutinin (FHA) antibody titers

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	19
Units: Titers				
geometric mean (confidence interval 95%)				
Germany Day 0 (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	8.36 (5.01 to 14)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	9.91 (7.09 to 14)
Germany 1 mo after Primary vacc (N=20,0,0,0)	138 (101 to 189)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	167 (133 to 209)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	98 (77 to 123)	77 (52 to 115)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	101 (69 to 147)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	71 (53 to 95)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	53 (33 to 83)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	52 (31 to 87)
Germany 10 days after booster (N=19,15,14,0)	606 (356 to 1032)	294 (181 to 477)	278 (172 to 450)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	220 (156 to 309)	223 (136 to 367)	226 (162 to 317)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	348 (241 to 502)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	355 (257 to 490)

Statistical analyses

No statistical analyses for this end point

Secondary: 19. Geometric mean anti-Pertactin (PRN) antibody titers

End point title	19. Geometric mean anti-Pertactin (PRN) antibody titers

End point description:

To evaluate the immunological response to the components of the hexavalent vaccine (diphtheria, tetanus, acellular Pertussis, polio, Haemophilus influenza type b and hepatitis B), with a priority on Haemophilus influenzae type b, when administered concomitantly to Menjugate®, in as many subjects as possible, depending on the availability of serum in those young children.
The analysis was done on the PP population, Immunogenicity.

End point type	Secondary

End point timeframe:

After completion of the primary hexavalent schedule and after the concomitantly received hexavalent booster vaccination in the second year of life.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	20
Units: Titers				
geometric mean (confidence interval 95%)				
Germany Day 0 (N=0,0,0,20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	8.53 (5.08 to 14)
Poland Day 0 (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	7.76 (5.53 to 11)
Germany 1 mo after Primary vacc (N=20,0,0,0)	94 (65 to 136)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Poland1 mo after Primary vacc (N=0,0,17,0)	0 (0 to 0)	0 (0 to 0)	119 (82 to 171)	0 (0 to 0)
Poland 2-4 mo after Primary vacc (N=16,15,0,0)	66 (41 to 106)	46 (23 to 91)	0 (0 to 0)	0 (0 to 0)
Germany 3 mo after Primary vacc (N=0,0,15,0)	0 (0 to 0)	0 (0 to 0)	86 (49 to 151)	0 (0 to 0)
Germany 4-6 mo after Primary vacc (N=0,19,0,0)	0 (0 to 0)	49 (33 to 73)	0 (0 to 0)	0 (0 to 0)
Poland 6-10 mo after Primary vacc (N=0,0,0,19)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	37 (24 to 56)
Germany 8-12 mo after Primary vacc (N=0,0,0,17)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	35 (18 to 69)
Germany 10 days after booster (N=19,15,14,0)	464 (289 to 745)	524 (343 to 799)	394 (192 to 810)	0 (0 to 0)
Poland 10 days after booster (N=18,15,19,0)	380 (236 to 614)	276 (155 to 490)	398 (250 to 633)	0 (0 to 0)
Germany 28 days after booster (N=0,0,0,14)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	465 (314 to 689)
Poland 28 days after booster (N=0,0,0,18)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	509 (347 to 747)

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Number of Subjects Reporting Local and Systemic Reactions by Vaccination

End point title	20. Number of Subjects Reporting Local and Systemic Reactions by Vaccination

End point description:

To evaluate the safety and tolerability of the administration of Menjugate® administered to healthy infants at 2 to 6 months of age, and as first, second or third dose in the second year of life, the number of subjects experiencing local and systemic reactions were summarized, according to severity and relatedness.
The analysis was done on the safety population.

End point type	Secondary

End point timeframe:

For 30 min after each immunization and on the following seven days, including the day of vaccination.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	58	62
Units: Subjects				
Tenderness 1st vacc N=(64,64,58,61)	6	17	8	26
Tenderness 2nd vacc (N=64,62,57,0)	8	28	18	0
Tenderness 3rd vacc (N=63,0,0,0)	21	0	0	0
Swelling 1st vacc N=(64,64,58,61)	1	5	5	10
Swelling 2nd vacc (N=64,62,57,0)	7	16	13	0
Swelling 3rd vacc (N=63,0,0,0)	10	0	0	0
Erythema 1st vacc N=(64,64,58,61)	13	7	20	24
Erythema 2nd vacc (N=64,62,57,0)	15	24	22	0
Erythema 3rd vacc (N=63,0,0,0)	25	0	0	0
Induration 1st vacc N=(64,64,58,61)	7	9	22	15
Induration 2nd vacc (N=64,62,57,0)	15	21	16	0
Induration 3rd vacc (63,0,0,0)	17	0	0	0
Diarrhea 1st vacc N=(64,64,58,61)	8	6	11	9
Diarrhea 2nd vacc (N=64,62,57,0)	6	8	10	0
Diarrhea 3rd vacc (N=63,0,0,0)	6	0	0	0
Change Eat. Habits 1st vacc N=(64,64,58,61)	17	13	8	15
Change Eat. Habits 2nd vacc (N=64,62,57,0)	12	16	14	0
Change Eat. Habits 3rd vacc (N=63,0,0,0)	14	0	0	0
Sleepiness 1st vacc N=(64,64,58,61)	29	29	9	29
Sleepiness 2nd vacc (N=64,62,57,0)	21	15	9	0
Sleepiness 3rd vacc (N=63,0,0,0)	20	0	0	0
Unusual Crying 1st vacc N=(64,64,58,61)	15	19	8	9
Unusual Crying 2nd vacc (N=64,62,57,0)	19	12	7	0
Unusual Crying 3rd vacc (N=63,0,0,0)	10	0	0	0
Irritability 1st vacc N=(64,64,58,61)	14	16	11	10
Irritability 2nd vacc (N=64,62,57,0)	14	11	11	0
Irritability 3rd vacc (N=63,0,0,0)	15	0	0	0
Vomiting 1st vacc N=(64,64,58,61)	6	2	3	7
Vomiting 2nd vacc (N=64,62,57,0)	4	4	3	0
Vomiting 3rd vacc (N=63,0,0,0)	2	0	0	0
Fever (≥ 38.5C) 1st vacc (N=64,64,57,60)	5	7	8	9
Fever (≥ 38.5C) 2nd vacc (N=64,61,57,0)	8	9	7	0
Fever (≥ 38.5C) 3rd vacc (N=61,0,0,0)	12	0	0	0
Analg. Antipyr. Med.Used 1st vacc (N=64,64,58,62)	7	7	8	13
Analg. Antipyr. Med.Used 2nd vacc (N=64,63,57,0)	8	15	6	0
Analg. Antipyr. Med.Used 3rd vacc (N=64,0,0,0)	11	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: 21. Number of Subjects Reporting Unsolicited Adverse Events After Vaccination

End point title	21. Number of Subjects Reporting Unsolicited Adverse Events After Vaccination

End point description:

To evaluate the safety and tolerability of the Menjugate® administered to healthy infants at 2 to 6 months of age, and as first, second or third dose in the second year of life, the number of subjects experiencing serious adverse events (SAEs), adverse events (AEs) necessitating a physician's visit and resulting in premature withdrawal from the study were summarized, according to severity and relatedness.
The analysis was done on the safety population.

End point type	Secondary

End point timeframe:

SAEs and AEs medically significant and/or resulting in premature withdrawal from the study were collected throughout the study and recorded by study personnel during each of the study visits.

End point values	Group 1 (2+4 Months)	Group 2 (2 Months)	Group 3 (6 Months)	Group 4 (12-16 Months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	63	66
Units: Subjects				
Serious AEs	6	8	8	5
Any AEs	56	56	52	55
At least possibly related AEs	3	11	1	4
AEs leading to premature withdrawal	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All solicited adverse events (AEs) were collected up to Day 7 after each vaccination.
All SAEs and unsolicited AEs were collected throughout the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Group 1 2+4 Months

Reporting group description:

Subjects received 2 doses of Menjugate®, at 2 and 4 months of age, together with the 1st and 3rd (Germany) or 1st and 2nd (Poland) dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Reporting group title	Group 2 2 Months

Reporting group description:

Subjects received 1 dose of Menjugate®, at 2 months of age, together with the 1st dose of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Reporting group title	Group 3 6 Months

Reporting group description:

Subjects received 1 dose of Menjugate®, at 6 months of age, together with the 3rd dose (in Poland), but respectively 2 months after the 3rd dose (in Germany), of routine hexavalent infant immunization, and a booster at 12-16 months of age.

Reporting group title	Group 4 12-16 Months

Reporting group description:

Subjects received 1 dose of Menjugate® at 12-16 months of age (together with the 4th dose of routine hexavalent infant immunization)

Serious adverse events	Group 1 2+4 Months	Group 2 2 Months	Group 3 6 Months
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 64 (9.38%)	8 / 64 (12.50%)	8 / 63 (12.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Craniocerebral injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Near drowning			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (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
Skull fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (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
Thermal burn			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Kawasaki's disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Nervous system disorders			
Convulsion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (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			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
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			
Hypothermia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (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			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 64 (3.13%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Intussusception			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular disorder			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (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
Skin and subcutaneous tissue disorders			
Purpura			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Seborrhoeic dermatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Infections and infestations			
Bronchiolitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Eczema herpeticum			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	2 / 64 (3.13%)	2 / 63 (3.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	2 / 63 (3.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (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
Varicella			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchopneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4 12-16 Months		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 66 (7.58%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Craniocerebral injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Near drowning			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skull fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thermal burn			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Kawasaki's disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hypothermia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intussusception			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular disorder			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Purpura			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seborrhoeic dermatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			

alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 66 (1.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	0 / 66 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	0 / 66 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eczema herpeticum				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	0 / 66 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	0 / 66 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 66 (1.52%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1 2+4 Months	Group 2 2 Months	Group 3 6 Months
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 64 (100.00%)	64 / 64 (100.00%)	59 / 63 (93.65%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	46 / 64 (71.88%)	38 / 64 (59.38%)	14 / 63 (22.22%)
occurrences (all)	154	102	42
Blood and lymphatic system disorders			
Anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	4 / 64 (6.25%)	2 / 63 (3.17%)
occurrences (all)	1	5	3
General disorders and administration site conditions			
Crying			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	29 / 64 (45.31%)	28 / 64 (43.75%)	12 / 63 (19.05%)
occurrences (all)	92	73	36
Injection site erythema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	28 / 64 (43.75%)	29 / 64 (45.31%)	31 / 63 (49.21%)
occurrences (all)	378	208	329
Injection site induration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	27 / 64 (42.19%)	26 / 64 (40.63%)	27 / 63 (42.86%)
occurrences (all)	363	275	334
Injection site pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 64 (40.63%)	32 / 64 (50.00%)	21 / 63 (33.33%)
occurrences (all)	72	90	52
Pyrexia			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	19 / 64 (29.69%)	17 / 64 (26.56%)	18 / 63 (28.57%)
occurrences (all)	30	24	21
Injection site swelling			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	14 / 64 (21.88%)	21 / 64 (32.81%)	14 / 63 (22.22%)
occurrences (all)	134	169	131
Gastrointestinal disorders			
Diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	18 / 64 (28.13%)	16 / 64 (25.00%)	18 / 63 (28.57%)
occurrences (all)	49	34	47
Dyspepsia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 64 (10.94%)	3 / 64 (4.69%)	5 / 63 (7.94%)
occurrences (all)	7	3	8
Infantile colic			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	2 / 63 (3.17%)
occurrences (all)	1	1	3
Teething			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 64 (3.13%)	2 / 64 (3.13%)	7 / 63 (11.11%)
occurrences (all)	3	2	8
Vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 64 (17.19%)	8 / 64 (12.50%)	6 / 63 (9.52%)
occurrences (all)	24	14	16
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 64 (3.13%)	4 / 64 (6.25%)	1 / 63 (1.59%)
occurrences (all)	2	4	1
Skin and subcutaneous tissue disorders			

Dermatitis diaper			
subjects affected / exposed	5 / 64 (7.81%)	4 / 64 (6.25%)	6 / 63 (9.52%)
occurrences (all)	6	6	10
Eczema infantile			
subjects affected / exposed	3 / 64 (4.69%)	1 / 64 (1.56%)	4 / 63 (6.35%)
occurrences (all)	3	2	5
Rash			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 64 (7.81%)	3 / 64 (4.69%)	3 / 63 (4.76%)
occurrences (all)	5	3	3
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	31 / 64 (48.44%)	25 / 64 (39.06%)	18 / 63 (28.57%)
occurrences (all)	96	59	52
Irritability			
subjects affected / exposed	33 / 64 (51.56%)	19 / 64 (29.69%)	19 / 63 (30.16%)
occurrences (all)	96	61	50
Restlessness			
subjects affected / exposed	1 / 64 (1.56%)	4 / 64 (6.25%)	1 / 63 (1.59%)
occurrences (all)	1	6	1
Infections and infestations			
Bronchitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	18 / 64 (28.13%)	20 / 64 (31.25%)	14 / 63 (22.22%)
occurrences (all)	29	31	24
Conjunctivitis			
subjects affected / exposed	6 / 64 (9.38%)	9 / 64 (14.06%)	8 / 63 (12.70%)
occurrences (all)	7	9	10
Ear infection			
subjects affected / exposed	6 / 64 (9.38%)	5 / 64 (7.81%)	2 / 63 (3.17%)
occurrences (all)	7	5	3
Exanthema subitum			
subjects affected / exposed	6 / 64 (9.38%)	5 / 64 (7.81%)	2 / 63 (3.17%)
occurrences (all)	6	5	2
Febrile infection			

subjects affected / exposed	2 / 64 (3.13%)	7 / 64 (10.94%)	2 / 63 (3.17%)
occurrences (all)	2	10	3
Gastroenteritis			
subjects affected / exposed	8 / 64 (12.50%)	4 / 64 (6.25%)	4 / 63 (6.35%)
occurrences (all)	10	4	5
Laryngitis			
subjects affected / exposed	3 / 64 (4.69%)	2 / 64 (3.13%)	4 / 63 (6.35%)
occurrences (all)	3	2	4
Nasopharyngitis			
subjects affected / exposed	4 / 64 (6.25%)	2 / 64 (3.13%)	6 / 63 (9.52%)
occurrences (all)	5	2	8
Oral candidiasis			
subjects affected / exposed	3 / 64 (4.69%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	3	0	1
Otitis media			
subjects affected / exposed	18 / 64 (28.13%)	11 / 64 (17.19%)	11 / 63 (17.46%)
occurrences (all)	18	17	13
Pharyngitis			
subjects affected / exposed	13 / 64 (20.31%)	14 / 64 (21.88%)	16 / 63 (25.40%)
occurrences (all)	22	24	28
Rhinitis			
subjects affected / exposed	17 / 64 (26.56%)	18 / 64 (28.13%)	21 / 63 (33.33%)
occurrences (all)	27	28	32
Tonsillitis			
subjects affected / exposed	3 / 64 (4.69%)	6 / 64 (9.38%)	5 / 63 (7.94%)
occurrences (all)	3	10	7
Viral infection			
subjects affected / exposed	5 / 64 (7.81%)	5 / 64 (7.81%)	4 / 63 (6.35%)
occurrences (all)	10	10	8
Upper respiratory tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	25 / 64 (39.06%)	27 / 64 (42.19%)	22 / 63 (34.92%)
occurrences (all)	48	63	34
Vulvitis			

subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Group 4 12-16 Months		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 66 (93.94%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	29 / 66 (43.94%)		
occurrences (all)	72		
Blood and lymphatic system disorders			
Anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 66 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Crying			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	9 / 66 (13.64%)		
occurrences (all)	18		
Injection site erythema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 66 (36.36%)		
occurrences (all)	198		
Injection site induration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 66 (22.73%)		
occurrences (all)	146		
Injection site pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 66 (39.39%)		
occurrences (all)	52		
Pyrexia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	12 / 66 (18.18%)		
occurrences (all)	14		
Injection site swelling			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	10 / 66 (15.15%)		
occurrences (all)	84		
Gastrointestinal disorders			
Diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	13 / 66 (19.70%)		
occurrences (all)	29		
Dyspepsia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 66 (9.09%)		
occurrences (all)	6		
Infantile colic			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	5		
Teething			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	1		
Vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 66 (12.12%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	6 / 66 (9.09%)		
occurrences (all)	11		

Eczema infantile			
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Rash			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	15 / 66 (22.73%)		
occurrences (all)	32		
Irritability			
subjects affected / exposed	11 / 66 (16.67%)		
occurrences (all)	25		
Restlessness			
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	5		
Infections and infestations			
Bronchitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	25 / 66 (37.88%)		
occurrences (all)	46		
Conjunctivitis			
subjects affected / exposed	7 / 66 (10.61%)		
occurrences (all)	8		
Ear infection			
subjects affected / exposed	5 / 66 (7.58%)		
occurrences (all)	11		
Exanthema subitum			
subjects affected / exposed	6 / 66 (9.09%)		
occurrences (all)	6		
Febrile infection			
subjects affected / exposed	2 / 66 (3.03%)		
occurrences (all)	2		
Gastroenteritis			

subjects affected / exposed	10 / 66 (15.15%)		
occurrences (all)	13		
Laryngitis			
subjects affected / exposed	2 / 66 (3.03%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	9 / 66 (13.64%)		
occurrences (all)	10		
Oral candidiasis			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		
Otitis media			
subjects affected / exposed	9 / 66 (13.64%)		
occurrences (all)	18		
Pharyngitis			
subjects affected / exposed	14 / 66 (21.21%)		
occurrences (all)	26		
Rhinitis			
subjects affected / exposed	8 / 66 (12.12%)		
occurrences (all)	16		
Tonsillitis			
subjects affected / exposed	5 / 66 (7.58%)		
occurrences (all)	8		
Viral infection			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	8		
Upper respiratory tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	22 / 66 (33.33%)		
occurrences (all)	54		
Vulvitis			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2005	Two site addresses have changed.
27 June 2005	One exclusion criteria was added due to German EC request; serology of hexavalent components was to be performed and Infanrix Hexa was therefore defined as study vaccine; biostatistician was changed.
22 July 2005	Valid for Germany only - prepared on request of German EC, as amendment no 2 was not accepted due to formal reasons (infanrix hexa becoming a study vaccine was judged as such essential, that is need to be described in a separate amendment. Therefore all changes regarding Infanrix hexa have been removed with amendment no 3).
13 September 2005	Valid for Germany only - Infanrix hexa was defined as study vaccine.
04 October 2005	Valid for Germany only - due to liability concerns raised by the German EC and only supportive data collection on hexavalent antibody titer Infanrix was defined as concomitant vaccine instead of study vaccine.

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.

N/A

Notes: