Clinical trial results:
A Phase 3, Partially Blinded, Randomized, Multi-Center, Controlled Study to Evaluate Immunogenicity, Safety and Lot to Lot Consistency of Novartis Meningococcal B Recombinant Vaccine When Administered with Routine Infant Vaccinations to Healthy Infants

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

Summary

EudraCT number	2007-007781-38
Trial protocol	CZ FI DE IT AT
Global end of trial date	22 January 2010

Results information

Result version number	v2 (current)
This version publication date	03 June 2016
First version publication date	19 December 2014
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V72P13

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00657709
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 S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000139-PIP01-07
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	17 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 January 2010
Global end of trial reached?	Yes
Global end of trial date	22 January 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the immunogenicity of 3 doses of rMenB+OMV NZ (3 lots combined) given to healthy infants at 2, 4 and 6 months of age concomitantly with routine infant vaccines, by evaluation of the serum bactericidal activity (SBA), at 1 month after the third vaccination.
- To show the consistency of immune response from 3 lots of rMenB+OMV NZ, by serum bactericidal activity geometric mean titer response (SBA GMTs), when administered to healthy infants at 2, 4 and 6 months of age, at 1 month after the third vaccination.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for GCP, with applicable local regulations, including the European Directive 2001/20/EC, the US CFR Title 21, and the Japanese Ministry of Health, Labor, and Welfare, Novartis codes on the protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 68
Country: Number of subjects enrolled	Czech Republic: 1020
Country: Number of subjects enrolled	Finland: 1717
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	Italy: 774
Worldwide total number of subjects	3630
EEA total number of subjects	3630

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)	3630
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:

16 sites in Finland, 28 sites in the Czech Republic, 13 sites in Germany,6 sites in Austria, 7 sites in Italy.

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	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

The trial was designed as partially open label, and partially observer-blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB Lot1

Arm description:

Subjects received one injection of rMenB+OMV NZ (Lot 1) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Arm title	rMenB Lot2

Arm description:

Subjects received one injection of rMenB+OMV NZ (Lot 2) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Arm title	rMenB Lot3

Arm description:

Subjects received one injection of rMenB+OMV NZ (Lot 3) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Arm title	Routine

Arm description:

Subjects received the routinely administered infant vaccines at 2, 4, 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

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

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Arm title	MenC + Routine

Arm description:

Subjects received the routinely administered infant vaccines and Men C vaccine at 2, 4 and 6 months of age.

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

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Investigational medicinal product name	Infanrix Hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age.

Investigational medicinal product name	Meningococcal (group C) oligosaccharide diphtheria CRM-197 conjugate 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:

Vaccination consisted of one 0.5 mL dose administered IM into the antero-lateral area of the thigh at 2, 4, and 6 months of age. The MenC vaccine was administered into right thigh, and both routine vaccines were administered into the left thigh.

Number of subjects in period 1	rMenB Lot1	rMenB Lot2	rMenB Lot3
Started	833	828	820
Completed	810	795	792
Not completed	23	33	28
Consent withdrawn by subject	7	15	15
Lost to follow-up	9	9	7
Adverse events or death	7	7	6
Protocol deviation	-	2	-

Number of subjects in period 1	Routine	MenC + Routine
Started	659	490
Completed	645	457
Not completed	14	33
Consent withdrawn by subject	5	9
Lost to follow-up	1	21
Adverse events or death	7	1
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	rMenB Lot1
Reporting group description:	
Subjects received one injection of rMenB+OMV NZ (Lot 1) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.	
Reporting group title	rMenB Lot2
Reporting group description:	
Subjects received one injection of rMenB+OMV NZ (Lot 2) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.	
Reporting group title	rMenB Lot3
Reporting group description:	
Subjects received one injection of rMenB+OMV NZ (Lot 3) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.	
Reporting group title	Routine
Reporting group description:	
Subjects received the routinely administered infant vaccines at 2, 4, 6 months of age.	
Reporting group title	MenC + Routine
Reporting group description:	
Subjects received the routinely administered infant vaccines and Men C vaccine at 2, 4 and 6 months of age.	

Reporting group values	rMenB Lot1	rMenB Lot2	rMenB Lot3
Number of subjects	833	828	820
Age categorical Units: Subjects			
Age continuous Units: days			
arithmetic mean	73.8	74.1	73.3
standard deviation	± 9.5	± 9.6	± 9.4
Gender categorical Units: Subjects			
Female	403	400	416
Male	430	428	404

Reporting group values	Routine	MenC + Routine	Total
Number of subjects	659	490	3630
Age categorical Units: Subjects			
Age continuous Units: days			
arithmetic mean	74.7	70.6	
standard deviation	± 9.3	± 9.7	-
Gender categorical Units: Subjects			
Female	318	234	1771
Male	341	256	1859

End points

End points reporting groups

Reporting group title	rMenB Lot1

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 1) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	rMenB Lot2

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 2) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	rMenB Lot3

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 3) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	Routine

Reporting group description:

Subjects received the routinely administered infant vaccines at 2, 4, 6 months of age.

Reporting group title	MenC + Routine

Reporting group description:

Subjects received the routinely administered infant vaccines and Men C vaccine at 2, 4 and 6 months of age.

Subject analysis set title	All enrolled population
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who were enrolled in this study irrespective of whether they have been randomized or not.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects enrolled who:
- have received study vaccination
- provided post-baseline safety data

Subject analysis set title	rMenB All - hSBA per protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the Full Analysis Set/MITT population who:
- received one injection of rMenB+OMV NZ (Lot 1, 2 and 3) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines, and
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at the relevant time points, and
- had no major protocol violation as defined prior to analysis

Subject analysis set title	Immunogenicity hSBA MITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects in the enrolled population who:
- actually received a study vaccination, and
- provided at least one evaluable serum sample after baseline

Subject analysis set title	rMenB All Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects enrolled who received one injection of rMenB+OMV NZ (Lot 1, 2 and 3).
- have received study vaccination
- provided post-baseline safety data

Subject analysis set title	Immunogenicity hSBA PP
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the Full Analysis Set/MITT population who:
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at the relevant time points, and
- had no major protocol violation as defined prior to analysis

Subject analysis set title	Immunogenicity Routine MITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects in the enrolled population who:
- actually received a study vaccination, and
- provided at least one evaluable serum sample after baseline

Subject analysis set title	Immunogenicity Polio MITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects in the enrolled population who:
- actually received a study vaccination, and
- provided at least one evaluable serum sample after baseline

Subject analysis set title	Immunogenicity Polio PP
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the Full Analysis Set/MITT population who:
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at the relevant time points, and
- had no major protocol violation as defined prior to analysis

Subject analysis set title	Immunogenicity Routine PP
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the Full Analysis Set/MITT population who:
- received all the relevant doses of vaccine correctly, and
- provided evaluable serum samples at the relevant time points, and
- had no major protocol violation as defined prior to analysis

Primary: 1. The Geometric Mean Human Serum Antibatericidal Activity Titers After Three Doses of rMenB+OMV NZ Vaccination

End point title	1. The Geometric Mean Human Serum Antibatericidal Activity Titers After Three Doses of rMenB+OMV NZ Vaccination[1]

End point description:

The hSBA antibody titer responses, one month after receiving the third vaccination of rMenB+OMV NZ vaccination, are reported as geometric mean titers (GMTs).

End point type	Primary

End point timeframe:

From baseline to one month after the third 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	rMenB Lot1	rMenB Lot2	rMenB Lot3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	386	380	394	
Units: Titers				
geometric mean (confidence interval 95%)				
44/76-SL strain (Baseline) (N=383,379,394)	1.21 (1.14 to 1.29)	1.19 (1.12 to 1.27)	1.19 (1.12 to 1.27)	
44/76-SL 1 Month after 3rd vacc (N=384,377,388)	87 (80 to 95)	98 (90 to 106)	85 (78 to 93)	
5/99 strain (Baseline) (N=385,379,390)	1.21 (1.14 to 1.3)	1.2 (1.12 to 1.28)	1.21 (1.13 to 1.29)	
5/99 1 Month after 3rd vacc (N=384,380,388)	598 (550 to 651)	681 (626 to 741)	607 (558 to 661)	
NZ98/254 strain (Baseline)	1.03 (1 to 1.06)	1.06 (1.03 to 1.1)	1.04 (1 to 1.07)	
NZ98/254 1 Month after 3rd vacc (N=385,378,389)	15 (13 to 17)	14 (12 to 16)	15 (14 to 17)	

Statistical analyses

Statistical analysis title	1. Equivalence rMenB Lot1 and rMenB Lot2 for 44/76

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot2 for 44/76-SL strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot2 v rMenB Lot1
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	0.99

Notes:

[2] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for 44/76-SL strain with respect to the immune response to the vaccine lot.

Statistical analysis title	2. Equivalence rMenB Lot1 and rMenB Lot3 for 44/76

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot3 for 44/76-SL strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot1 v rMenB Lot3

Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.13

Notes:

[3] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for 44/76-SL strain with respect to the immune response to the vaccine lot.

Statistical analysis title	3. Equivalence rMenB Lot2 and rMenB Lot3 for 44/76

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot2 to rMenB Lot3 for 44/76-SL strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot2 v rMenB Lot3
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.27

Notes:

[4] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for 44/76-SL strain with respect to the immune response to the vaccine lot.

Statistical analysis title	4. Equivalence rMenB Lot1 and rMenB Lot2 for 5/99

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot2 for 5/99 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot1 v rMenB Lot2
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.98

Notes:

[5] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for 5/99 strain with respect to the immune response to the vaccine lot.

Statistical analysis title	5. Equivalence rMenB Lot1 and rMenB Lot3 for 5/99

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot3 for 5/99 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot1 v rMenB Lot3
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.1

Notes:

[6] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for 5/99 strain with respect to the immune response to the vaccine lot.

Statistical analysis title	6. Equivalence rMenB Lot2 and rMenB Lot3 for 5/99

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot2 to rMenB Lot3 for 5/99 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot2 v rMenB Lot3
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.26

Notes:

[7] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for 5/99 strain with respect to the immune response to the vaccine lot.

Statistical analysis title	7. Equivalence rMenB Lot1 and Lot2 for NZ98/254

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot2 for NZ98/254 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot1 v rMenB Lot2
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.23

Notes:

[8] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for NZ98/254 with respect to the immune response to the vaccine lot.

Statistical analysis title	8. Equivalence rMenB Lot1 and Lot3 for NZ98/254

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing rMenB Lot1 to rMenB Lot3 for NZ98/254 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot1 v rMenB Lot3
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[9]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.13

Notes:

[9] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for NZ98/254 with respect to the immune response to the vaccine lot.

Statistical analysis title	9. Equivalence rMenB Lot2 and Lot3 for NZ98/254

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA

GMT ratios comparing rMenB Lot2 to rMenB Lot3 for NZ98/254 strain at one month after the third vaccination was contained within the equivalence interval (0.5, 2.0).

Comparison groups	rMenB Lot2 v rMenB Lot3
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[10]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.08

Notes:

[10] - The equivalence margin was (0.5, 2.0). If the two sided 95% CIs for the ratio of the hSBA GMT at one month following third vaccination was within this equivalence interval for each of the two co-primary comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for NZ98/254 with respect to the immune response to the vaccine lot.

Primary: 2. The Percentages of Subjects With hSBA Titer ≥1:5 After Receiving Three Doses of rMenB+OMV Vaccination (3 Lots Combined)

End point title	2. The Percentages of Subjects With hSBA Titer ≥1:5 After Receiving Three Doses of rMenB+OMV Vaccination (3 Lots Combined)[11][12]

End point description:

The immunogenicity was assessed in terms of the percentages of subjects who had received the three doses of rMenB+OMV NZ (3 lots combined) given concomitantly with routine infant vaccinations and percentages of subjects who received only the routine infant vaccinations as measured by hSBA titer ≥1:5 following rMenB+OMV NZ vaccinations one month after the third vaccination is reported.

End point type	Primary

End point timeframe:

From baseline to one month after the third vaccination

Notes:

[11] - 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: statistical analyses not applicable for this endpoint.

[12] - 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	Routine	rMenB All - hSBA per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	121	1160		
Units: Percentages of subjects				
number (confidence interval 95%)				
44/76-SL strain (Baseline) (N=119, 1156)	3 (1 to 8)	3 (2 to 4)		
1 Month after 3rd vacc (N=117, 1149)	3 (1 to 7)	100 (99 to 100)		
5/99 strain (Baseline) (N=120, 1154)	7 (3 to 13)	4 (3 to 5)		
1 Month after 3rd vacc (N=116, 1152)	2 (0 to 6)	100 (99 to 100)		

NZ98/254 strain (Baseline) (N=120, 1160)	1 (0.021 to 5)	1 (1 to 2)		
1 Month after 3rd vacc (N=121, 1152)	2 (0 to 6)	84 (82 to 86)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. The Percentages of Subjects With hSBA Titer ≥1:5 After Receiving Three Doses of rMenB+OMV Vaccination (From 3 Lots)

End point title	3. The Percentages of Subjects With hSBA Titer ≥1:5 After Receiving Three Doses of rMenB+OMV Vaccination (From 3 Lots)[13]

End point description:

The immmunogenicity was evaluated to assess the consistency of the immune response from three lots of rMenB+OMV NZ in terms of percentage of subjects as measured by hSBA titer ≥1:5 when given to healthy infants at 2, 4, and 6 months of age, at 1 month after the third vaccination.

End point type	Secondary

End point timeframe:

From baseline to one month after the third vaccination

Notes:

[13] - 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	rMenB Lot1	rMenB Lot2	rMenB Lot3	Routine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	386	380	394	121
Units: Percentages of subjects				
number (confidence interval 95%)				
44/76-SL (Baseline) (N=383,379,394,119)	4 (2 to 6)	2 (1 to 4)	3 (2 to 6)	3 (1 to 8)
1 Month after 3rd vacc (N=384,377,388,117)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	3 (1 to 7)
5/99 strain (Baseline) (N=385,379,390,120)	3 (2 to 5)	4 (3 to 7)	4 (2 to 7)	7 (3 to 13)
1 Month after 3rd vacc (N=384,380,388,121)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	2 (0 to 6)
NZ 98/254 Baseline (N =386,380,394,120)	1 (0 to 2)	2 (1 to 4)	1 (0 to 2)	1 (0.021 to 5)
1 Month after 3rd vacc (N=385,378,389,121)	84 (80 to 88)	81 (77 to 85)	85 (81 to 89)	2 (0 to 6)

Statistical analyses

Statistical analysis title	1. Vaccine group difference rMenB Lot1/rMenB Lot2

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot1 v rMenB Lot2
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[14]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Notes:

[14] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for 44/76-SL strain.

Statistical analysis title	2. Vaccine group difference rMenB Lot1/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%]

Comparison groups	rMenB Lot1 v rMenB Lot3
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[15]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Notes:

[15] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for 44/76-SL strain.

Statistical analysis title	3. Vaccine group difference rMenB Lot2/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%]

Comparison groups	rMenB Lot3 v rMenB Lot2
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[16]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Notes:

[16] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for 44/76-SL strain.

Statistical analysis title	4. Vaccine group difference rMenB Lot1/ rMenB Lot2

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%]

Comparison groups	rMenB Lot1 v rMenB Lot2
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[17]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Notes:

[17] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for 5/99 strain.

Statistical analysis title	5. Vaccine group difference rMenB Lot1/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot1 v rMenB Lot3
Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[18]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Notes:

[18] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for 5/99 strain.

Statistical analysis title	6. Vaccine group difference rMenB Lot2/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot2 v rMenB Lot3
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[19]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Notes:

[19] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for 5/99 strain.

Statistical analysis title	7. Vaccine group difference rMenB Lot1/ rMenB Lot2

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot1 v rMenB Lot2
Number of subjects included in analysis	766
Analysis specification	Pre-specified
Analysis type	equivalence[20]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	8

Notes:

[20] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot2 would be equivalent for NZ98/254 strain.

Statistical analysis title	8. Vaccine group difference rMenB Lot1/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot1 v rMenB Lot3

Number of subjects included in analysis	780
Analysis specification	Pre-specified
Analysis type	equivalence[21]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	4

Notes:

[21] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot1 and rMenB Lot3 would be equivalent for NZ98/254 strain.

Statistical analysis title	9. Vaccine group difference rMenB Lot2/ rMenB Lot3

Statistical analysis description:

The three vaccine lots were considered equivalent if, for each of the three strains and each pair of vaccine lots, the 95% CIs of the differences in the percentages of subjects with hSBA titers ≥ 1:5 at 1 month after the third dose, was contained within the interval [-10%, 10%].

Comparison groups	rMenB Lot2 v rMenB Lot3
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	equivalence[22]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	-1

Notes:

[22] - The equivalence margin was (-10%, 10%). If the two sided 95% CIs of the differences in the percentages of subjects at one month following third vaccination was within this equivalence interval for each of the two comparisons, rMenB Lot2 and rMenB Lot3 would be equivalent for NZ98/254 strain.

Secondary: 4. Geometric Mean Human Serum Bactericidal Activity Titers After the Routine Vaccination Without rMenB OMV NZ

End point title	4. Geometric Mean Human Serum Bactericidal Activity Titers After the Routine Vaccination Without rMenB OMV NZ[23]

End point description:

The immunogenicity was assessed in terms of prevalence of meningococcal B antibodies as measured by the hSBA, at baseline and at one month after the third vaccination, in the subjects that received routine infant vaccines without rMenB+OMV NZ.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[23] - 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	Routine	rMenB All - hSBA per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	121	1160		
Units: Titers				
geometric mean (confidence interval 95%)				
44/76-SL strain (Baseline) (N=119, 1156)	1.12 (1.04 to 1.22)	1.15 (1.12 to 1.19)		
1 Month after 3rd vacc (N=117, 1149)	1.2 (1.1 to 1.31)	91 (87 to 95)		
5/99 strain (Baseline) (N=120, 1154)	1.21 (1.1 to 1.33)	1.18 (1.14 to 1.22)		
1 Month after 3rd vacc (N=116, 1152)	1.06 (0.97 to 1.17)	635 (606 to 665)		
NZ98/254 strain (Baseline) (N=120, 1160)	1.01 (0.99 to 1.04)	1.05 (1.03 to 1.07)		
1 Month after 3rd vacc (N=121, 1152)	1.04 (0.98 to 1.11)	14 (13 to 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Geometric Mean Concentrations After Three Doses of rMenB+OMV NZ Vaccination (Against the 287-953 Antigen)

End point title	5. Geometric Mean Concentrations After Three Doses of rMenB+OMV NZ Vaccination (Against the 287-953 Antigen)[24]

End point description:

The immunogenicity was evaluated to characterize the immune response against vaccine antigen 287-953, as measured by ELISA at one month after third vaccination.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[24] - 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	rMenB Lot1	rMenB Lot2	rMenB Lot3	Routine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	615	600	611	113
Units: Concentration (IU/mL)				
geometric mean (confidence interval 95%)				
Baseline (N=611,596,611,113)	22 (21 to 23)	22 (21 to 22)	22 (21 to 23)	21 (20 to 21)
1 Month after 3rd vacc (N=615,600,608,113)	3149 (2960 to 3352)	3484 (3270 to 3712)	3103 (2915 to 3304)	22 (21 to 23)

End point values	rMenB All - hSBA per protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	1823			
Units: Concentration (IU/mL)				
geometric mean (confidence interval 95%)				
Baseline (N=611,596,611,113)	22 (21 to 22)			
1 Month after 3rd vacc (N=615,600,608,113)	3370 (3270 to 3472)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Geometric Mean Concentrations for Antigens (Pertussis Components) for the Routine Vaccinations

End point title	6. Geometric Mean Concentrations for Antigens (Pertussis Components) for the Routine Vaccinations[25]

End point description:

Immunogenicity of the pertussis components (PT, FHA, pertactin) of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 would be considered non-inferior to that of the routine vaccines given alone if the lower limit of the two-sided CI for the ratio of GMCs one month after third vaccination.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[25] - 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	Routine	rMenB All - hSBA per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	246	241		
Units: Titers				
geometric mean (confidence interval 95%)				
FHA (Baseline)	9.28 (8.17 to 11)	9.98 (8.78 to 11)		
FHA 1 Month after 3rd vaccination (N=244, 239)	147 (136 to 158)	123 (114 to 133)		
Pertactin (Baseline)	5.36 (4.71 to 6.11)	6.3 (5.52 to 7.17)		
Pertactin 1Month after 3rdvaccination (N=244, 239)	139 (126 to 155)	107 (97 to 119)		
PT (Baseline)	2.82 (2.68 to 2.96)	2.82 (2.68 to 2.96)		
PT 1 Month after 3rd vaccination (N=244, 239)	51 (46 to 55)	41 (37 to 44)		

Statistical analyses

Statistical analysis title	1. Vaccine group difference -FHA

Statistical analysis description:

Immunogenicity of the pertussis components (FHA) of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 would be considered non-inferior to that of routine vaccines given alone if the lower limit of the two-sided CI for the ratio of GMCs one month after the third vaccination is ≥0.67.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Method	ANOVA
Parameter estimate	Vaccine group difference
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.94

Notes:

[26] - GMCs (GMCrMenB+OMV NZlot1+lot2+lot3+InfanrixHexa / GMCInfanrixHexa)

Statistical analysis title	2. Vaccine group difference - Pertactin

Statistical analysis description:

Immunogenicity of the pertussis components (Pertactin) of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 would be considered non-inferior to that of routine vaccines given alone if the lower limit of the two-sided CI for the ratio of GMCs one month after the third vaccination is ≥0.67.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Method	ANOVA
Parameter estimate	Vaccine group difference
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.89

Notes:

[27] - GMCs (GMCrMenB+OMV NZlot1+lot2+lot3+InfanrixHexa / GMCInfanrixHexa)

Statistical analysis title	3. Vaccine group difference - PT

Statistical analysis description:

Immunogenicity of the pertussis components (PT) of DTPa-HBV-IPV when given concomitantly with

rMenB and PCV7 would be considered non-inferior to that of routine vaccines given alone if the lower limit of the two-sided CI for the ratio of GMCs one month after the third vaccination is ≥0.67.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Method	ANOVA
Parameter estimate	vaccine group difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.91

Notes:

[28] - GMCs (GMCrMenB+OMV NZlot1+lot2+lot3+InfanrixHexa / GMCInfanrixHexa)

Secondary: 7. Percentages of Subjects With Antibody Response Against the Routine Antigens

End point title	7. Percentages of Subjects With Antibody Response Against the Routine Antigens[29]

End point description:

The immunogenicity of routine infant vaccines when given concomitantly with rMenB+OMV NZ at 2, 4, and 6 months of age, was non-inferior to that of routine infant vaccines given without rMenB+OMV NZ at 1 month after third vaccination with B pertussis, diptheria and tetanus toxoid, H influenza type b, Hepatitis B antigens as measured by ELISA (Enzyme-linked immunosorbent assay) and for polio type 1, type 2 and type 3 by neutralization test (NT)(>=1:8). Diptheria and Tetanus: primary endpoint ELISA >=0.1 (international unit -IU) IU/mL and the secondary endpoint is ELISA>=1.0 IU/mL. HepB (HBV):primary endpoint ELISA >=10mU/mL. PRP-T: primary endpoint ≥ 0.15 mcg/mL and ≥ 1.00

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[29] - 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	Routine	rMenB All - hSBA per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	246	243		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Anti-DiphtheriaToxin ≥0.1IU/mL(Baseline) N=246,241	38 (32 to 45)	38 (32 to 44)		
Anti-DiphtheriaToxin ≥0.1IU/mL(post vacc)N=244,239	100 (98 to 100)	100 (98 to 100)		
Anti-DiphtheriaToxin ≥1.0 IU/mL(Baseline)N=246,241	2 (1 to 5)	2 (1 to 5)		
Anti-DiphtheriaToxin ≥1.0IU/mL(post vacc)N=244,239	86 (81 to 90)	80 (75 to 85)		
Anti-TetanusToxin ≥0.1IU/mL(Baseline) N=246,241	95 (91 to 97)	93 (88 to 96)		

Anti-TetanusToxin ≥0.1IU/mL (post vacc)N=244,239	100 (98 to 100)	100 (98 to 100)		
Anti-Tetanus Toxin ≥1.0IU/mL(Baseline)N=246,241	27 (22 to 33)	24 (18 to 30)		
Anti-Tetanus Toxin ≥1.0IU/mL(post vacc) N=244,239	95 (91 to 97)	91 (86 to 94)		
Polio 1 ≥1:8 (Baseline) N=246,245	72 (66 to 77)	75 (69 to 80)		
Polio 1 ≥1:8 (post vacc) N=248,243	97 (94 to 99)	95 (92 to 98)		
Polio 2 (Baseline) N=246,245	69 (63 to 74)	68 (62 to 74)		
Polio 2 (Post vacc) N=248,243	94 (90 to 97)	88 (84 to 92)		
Polio 3 (Baseline) N=246,245	49 (42 to 55)	48 (41 to 54)		
Polio 3 (Post vacc) N=248,243	98 (95 to 99)	97 (94 to 99)		
HBV ≥10 mIU/mL (Baseline) N=248,241	15 (10 to 20)	22 (17 to 28)		
HBV ≥10 mIU/mL (Post vacc) N=252,245	100 (99 to 100)	98 (95 to 99)		
Anti-PRP (HIB) ≥ 0.15µg/mL(Baseline) N=246,241	55 (49 to 62)	54 (47 to 60)		
Anti-PRP (HIB) ≥ 0.15µg/mL(Post vacc) N=244,239	100 (98 to 100)	99 (97 to 100)		
Anti-PRP (HIB) ≥ 1.0µg/mL(Baseline) N=246,241	10 (7 to 15)	12 (9 to 17)		
Anti-PRP (HIB) ≥ 1.0µg/mL(Post vacc) N=244,239	79 (73 to 84)	79 (73 to 84)		
PnC4 ≥0.35µg/mL (Baseline) N=245,243	2 (1 to 5)	2 (0 to 4)		
PnC4 ≥0.35µg/mL (Post vacc) N=243,242	100 (98 to 100)	98 (95 to 99)		
PnC 6B ≥0.35µg/mL (Baseline) N=245,243	16 (12 to 22)	14 (10 to 19)		
PnC 6B ≥0.35µg/mL (Post vacc) N=243,242	88 (83 to 92)	90 (85 to 93)		
PnC 9V ≥0.35µg/mL (Baseline) N=245,243	3 (1 to 6)	4 (2 to 7)		
PnC 9V ≥0.35µg/mL (Post vacc) N=243,242	100 (98 to 100)	100 (98 to 100)		
PnC 14 ≥0.35µg/mL (Baseline) N=245,243	38 (31 to 44)	33 (27 to 39)		
PnC 14 ≥0.35µg/mL (Post vacc) N=243,242	97 (94 to 99)	96 (93 to 98)		
PnC 18C ≥0.35µg/mL(Baseline) N=245,243	17 (12 to 22)	10 (7 to 15)		
PnC 18C ≥0.35µg/mL(Post vacc) N=243,242	99 (97 to 100)	98 (96 to 100)		
PnC 19F ≥0.35µg/mL(Baseline) N=245,243	21 (16 to 27)	20 (15 to 26)		
PnC 19F ≥0.35µg/mL(Post vacc) N=243,242	96 (93 to 98)	96 (93 to 98)		
PnC 23F ≥0.35µg/mL(Baseline) N=245,243	22 (17 to 28)	16 (12 to 21)		
PnC 23F ≥0.35µg/mL(Post vacc) N= 243,242	95 (92 to 97)	92 (88 to 95)		

Statistical analyses

Statistical analysis title	1. Group difference for diphtheria toxoids antigen

Statistical analysis description:

Immunogenicity of the routine infant vaccines, when given concomitantly with rMenB+OMV NZ at 2, 4, and 6 months of age, was considered non-inferior to that of routine infant vaccines given alone, for diphtheria toxoids antigen, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than or equal to the cut-offlevel ≥0.1 IU/mL for that antigen.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Notes:

[30] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	2. Group difference for diphtheria toxoids antigen

Statistical analysis description:

Immunogenicity of the routine infant vaccines, when given concomitantly with rMenB+OMV NZ at 2, 4, and 6 months of age, was considered non-inferior to that of routine infant vaccines given alone, for diphtheria toxoids antigen, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than or equal to the cut-offlevel ≥1.0 IU/mL for that antigen.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	1

Notes:

[31] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	3. Group difference for Tetanus toxoids antigen

Statistical analysis description:

Immunogenicity of the routine infant vaccines, when given concomitantly with rMenB+OMV NZ at 2, 4, and 6 months of age, was considered non-inferior to that of routine infant vaccines given alone, for Tetanus toxoids antigen, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than or equal to the cut-offlevel ≥0.1 IU/mL for that antigen.

Comparison groups	Routine v rMenB All - hSBA per protocol population

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Notes:

[32] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	4. Group difference for Tetanus toxoids antigen

Statistical analysis description:

Immunogenicity of the routine infant vaccines, when given concomitantly with rMenB+OMV NZ at 2, 4, and 6 months of age, was considered non-inferior to that of routine infant vaccines given alone, for Tetanus toxoids antigen, if the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than or equal to the cut-offlevel ≥1.0 IU/mL for that antigen.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	1

Notes:

[33] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	5. Group difference for polio type 1

Statistical analysis description:

Immunogenicity of the polio type 1 of Diphtheria-Tetanus-Acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-HBVIPV) when given concomitantly with rMenB and Pneumococcal 7-valent conjugate vaccine (PCV7) at 2, 4, and 6 months of age was considered non-inferior to that of the confidence interval for the difference in the percentage of subjects with NT titers ≥1:8 was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	2

Notes:

[34] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	6. Group difference for polio type 2

Statistical analysis description:

Immunogenicity of the polio type 2 of Diphtheria-Tetanus-Acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-HBVIPV) when given concomitantly with rMenB and Pneumococcal 7-valent conjugate vaccine (PCV7) at 2, 4, and 6 months of age was considered non-inferior to that of the confidence interval for the difference in the percentage of subjects with NT titers ≥1:8 was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	-1

Notes:

[35] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	7. Group difference for polio type 3

Statistical analysis description:

Immunogenicity of the polio type 3 of Diphtheria-Tetanus-Acellular Pertussis, Hepatitis B, Inactivated Poliovirus and Haemophilus influenzae type b (DTPa-HBVIPV) when given concomitantly with rMenB and Pneumococcal 7-valent conjugate vaccine (PCV7) at 2, 4, and 6 months of age was considered non-inferior to that of the confidence interval for the difference in the percentage of subjects with NT titers ≥10.0 mIU/m was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	2

Notes:

[36] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	8. Group difference for the hepatitis B surface Ag

Statistical analysis description:

Immunogenicity of the hepatitis B surface antigen component of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4, and 6 months of age would be considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two sided 95% confidence interval for the difference in the percentage of subjects with NT titers ≥1:8 was greater than -10%

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	-1

Notes:

[37] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	9. Group difference for Anti-PRP (Hib)

Statistical analysis description:

Immunogenicity of the PRP-Hib component of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4, and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two sided 95% confidence interval for the difference in the percentage of subjects with Hib capsular polysaccharide (PRP) antibody response greater than the protective cutoff of ≥0.15 µg/mL was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	1

Notes:

[38] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	10. Group difference for Anti-PRP (Hib)

Statistical analysis description:

Immunogenicity of the PRP-Hib component of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4, and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two sided 95% confidence interval for the difference in the percentage of subjects with Hib capsular polysaccharide (PRP) antibody response greater than the protective cutoff of ≥1.0 µg/mL was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	7

Notes:

[39] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	11. Group difference for pneumococcal antigen PnC4

Statistical analysis description:

Immunogenicity of the 7 components of PCV7 when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4 and 6 months of age would be considered non-inferior to that of the routine vaccinations given alone, becaus the lower limit of the two-sided 95% confidence interval for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL was, for the pneumococcal antigen PnC4.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	0

Notes:

[40] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	12. Group difference for pneumococcal Ag PnC 6B

Statistical analysis description:

Immunogenicity of the 7 components of PCV7 when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4, and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC 6B antigen greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	8

Notes:

[41] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	13. Group difference for pneumococcal Ag PnC 9V

Statistical analysis description:

Immunogenicity of the 7 components of PCV7 when given concomitantly with rMenB and DTPa_HBV-IPV vaccine at 2, 4, and 6 months of age was considered noninferior to that of the routine vaccinations given alone, because the lower limit of the two sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC 9V, greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1

Notes:

[42] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	14. Group difference for pneumococcal antigenPnC14

Statistical analysis description:

Immunogencity of the 7 components of PCV7 vaccine when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4, and 6 months of age would be considered noninferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC14 antigen, greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3

Notes:

[43] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	15. Group difference for pneumococcal Ag PnC18C

Statistical analysis description:

Immunogencity of the 7 components of PCV7 vaccine when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4, and 6 months of age would be considered noninferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC 18C antigen, greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	1

Notes:

[44] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	16. Group difference for pneumococcal Ag PnC19F

Statistical analysis description:

Immunogencity of the 7 components of PCV7 vaccine when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4, and 6 months of age would be considered noninferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC19F antigen, greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	4

Notes:

[45] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	17. Group difference for pneumococcal Ag PnC 23F

Statistical analysis description:

Immunogencity of the 7 components of PCV7 vaccine when given concomitantly with rMenB and DTPa-HBV-IPV at 2, 4, and 6 months of age would be considered noninferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects with antibody response greater than the cutoff of ≥0.35 µg/mL, was, for PnC 23F antigen, greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Method	Miettinen and Nurminen
Parameter estimate	vaccine group difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	2

Notes:

[46] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Secondary: 8. Percentages of Subjects With Fourfold Increase in Antibody Concentrations Against the Routine Antigens

End point title	8. Percentages of Subjects With Fourfold Increase in Antibody Concentrations Against the Routine Antigens[47]

End point description:

Immunogenicity was assessed in terms of the percentages of subjects with fourfold increase in antibody concentrations against the routine pertussis antigens FHA, Pertactin and PT.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[47] - 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	Routine	rMenB All - hSBA per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	243	238		
Units: Percentages of Subjects				
number (confidence interval 95%)				
FHA	87 (82 to 91)	84 (79 to 88)		
Pertactin	88 (84 to 92)	79 (73 to 84)		
PT	95 (91 to 97)	92 (88 to 95)		

Statistical analyses

Statistical analysis title	1. Vaccine group difference for the FHA antigen

Statistical analysis description:

Immunogenicity of the FHA antigen of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4 and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population

Number of subjects included in analysis	481
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	4

Notes:

[48] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	2. Vaccine group difference for the Pertactin Ag

Statistical analysis description:

Immunogenicity of the Pertactin antigen of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4 and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	481
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	-3

Notes:

[49] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Statistical analysis title	3. Vaccine group difference for the PT antigen

Statistical analysis description:

Immunogenicity of the PT antigen of DTPa-HBV-IPV when given concomitantly with rMenB and PCV7 vaccine at 2, 4 and 6 months of age was considered non-inferior to that of the routine vaccinations given alone, because the lower limit of the two-sided 95% CI for the difference in the percentage of subjects was greater than -10%.

Comparison groups	Routine v rMenB All - hSBA per protocol population
Number of subjects included in analysis	481
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
Method	Miettinen and Nurminen
Parameter estimate	Vaccine group difference
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	2

Notes:

[50] - {PConcomitant Vaccine +rMenB+OMV NZlot1+lot2+lot3 minus PConcomitant Vaccine}

Secondary: 9. Percentages of Subjects With Fourfold Rise in hSBA Titers After Three Doses of rMenB+OMV NZ Vaccination

End point title	9. Percentages of Subjects With Fourfold Rise in hSBA Titers After Three Doses of rMenB+OMV NZ Vaccination[51]

End point description:

Immunogenicity was assessed in terms of the percentages of subjects with fourfold rise in hSBA titers after the three doses of rMenB+OMV NZ (lot 1 or lot 2 or lot 3) vaccination at 2, 4 and 6 months of age.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[51] - 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	rMenB Lot1	rMenB Lot2	rMenB Lot3	Routine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	370	359	376	114
Units: Percentages of Subjects				
number (confidence interval 95%)				
44/76-SL(N=369,356,373,111,1098)	99 (97 to 100)	100 (99 to 100)	98 (97 to 99)	1 (0.023 to 5)
5/99(N=370,359,369,111,1098)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	2 (0 to 6)
NZ98/254(N=369,357,376,114,1102)	70 (66 to 75)	69 (64 to 74)	75 (70 to 79)	1 (0.022 to 5)

End point values	rMenB All - hSBA per protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	1102			
Units: Percentages of Subjects				
number (confidence interval 95%)				
44/76-SL(N=369,356,373,111,1098)	99 (98 to 100)			
5/99(N=370,359,369,111,1098)	100 (99 to 100)			
NZ98/254(N=369,357,376,114,1102)	71 (69 to 74)			

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentage of Subjects With hSBA Titers ≥1:8

End point title	10. Percentage of Subjects With hSBA Titers ≥1:8[52]

End point description:

Immunogenicity was assesed in terms of the percentages of subjects achieving hSBA titers ≥1:8 at one month after third vaccination with rMenB (lot 1 or lot 2 or lot 3) against the three vaccine strains.

End point type	Secondary

End point timeframe:

One month after the third vaccination

Notes:

[52] - 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	rMenB Lot1	rMenB Lot2	rMenB Lot3	Routine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	385	379	394	119
Units: Percentages of Subjects				
number (confidence interval 95%)				
44/76-SL (Baseline)(N=283, 379,394,119,1156)	2 (1 to 4)	2 (1 to 3)	2 (1 to 4)	2 (0 to 6)
1 Month after 3rd vacc(N=384,377,388,117,1149)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	1 (0.022 to 5)
5/99 (Baseline)(N=385, 379, 390, 120, 1154)	3 (1 to 5)	3 (1 to 5)	2 (1 to 4)	2 (0 to 6)
1 Month after 3rd vacc(N=384, 380, 388, 116, 1152)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	2 (0 to 6)
NZ98/254 (Baseline)(N=386, 380, 394, 120, 1160)	1 (0.063 to 2)	1 (0 to 3)	1 (0.0064 to 1)	0 (0 to 3)
1 Month after 3rd vacc(N=385, 378, 389, 121, 1152)	70 (66 to 75)	70 (65 to 74)	75 (70 to 79)	1 (0.021 to 5)

End point values	rMenB All - hSBA per protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	1156			
Units: Percentages of Subjects				
number (confidence interval 95%)				
44/76-SL (Baseline)(N=283, 379,394,119,1156)	2 (1 to 3)			
1 Month after 3rd vacc(N=384,377,388,117,1149)	100 (99 to 100)			
5/99 (Baseline)(N=385, 379, 390, 120, 1154)	3 (2 to 4)			
1 Month after 3rd vacc(N=384, 380, 388, 116, 1152)	100 (99 to 100)			
NZ98/254 (Baseline)(N=386, 380, 394, 120, 1160)	1 (0 to 1)			

1 Month after 3rd vacc(N=385, 378, 389, 121, 1152)	72 (69 to 74)			

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Number of Subjects Reporting Solicited Adverse Events After Receiving Three Doses of rMenB+OMV NZ Vaccine

End point title	11. Number of Subjects Reporting Solicited Adverse Events After Receiving Three Doses of rMenB+OMV NZ Vaccine[53]

End point description:

The safety and tolerability of three doses of rMenB+OMV NZ when given concomitantly with routine infant vaccines at 2, 4 and 6 months of age was assessed by the number of subjects reporting solicited local and systemic adverse events.

End point type	Secondary

End point timeframe:

Up to 7 days after any vaccination

Notes:

[53] - 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	MenC + Routine	rMenB All Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	490	2479		
Units: Participants				
Any Local	443	2388		
Injection site tenderness	266	2147		
Injection site erythema	261	2049		
Injection site induration	227	1908		
Injection site swelling	84	1174		
Any Systemic	459	2450		
Change in Eating Habits	257	1787		
Sleepiness	353	2159		
Vomiting	116	662		
Diarrhea	164	1086		
Irritability	370	2296		
Unusual Crying	352	2109		
Rash	43	318		
Fever >= 38.5C	228	1912		
Others	325	2302		
Medical Attend. Fever	16	57		
Analg. Antipyr. Med.Used	325	2302		
Antipyr. Med.Used	314	2240		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All serious adverse events and medically attended adverse events are collected from Day 8 after each vaccination to next vaccination or to 30 days after the last vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	rMenB Lot2

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 2) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	rMenB Lot1

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 1) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	MenC + Routine

Reporting group description:

Subjects received the routinely administered infant vaccines and MenC vaccine at 2, 4 and 6 months of age.

Reporting group title	rMenB Lot3

Reporting group description:

Subjects received one injection of rMenB+OMV NZ (Lot 3) at 2, 4, 6 months of age concomitantly with the routinely administered infant vaccines.

Reporting group title	Routine

Reporting group description:

Subjects received the routinely administered infant vaccines at 2, 4, 6 months of age

Serious adverse events	rMenB Lot2	rMenB Lot1	MenC + Routine
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 828 (9.66%)	70 / 832 (8.41%)	28 / 490 (5.71%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Kawasaki's disease			

subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Labial frenectomy			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Tendon operation			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 828 (0.12%)	3 / 832 (0.36%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased activity			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Immune system disorders			
Hypersensitivity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Milk allergy			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Balanoposthitis			

subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	2 / 828 (0.24%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Pleural effusion			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breath holding			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Bone fissure			

subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Concussion			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Contusion			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Fall			
subjects affected / exposed	3 / 828 (0.36%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Head injury			
subjects affected / exposed	0 / 828 (0.00%)	2 / 832 (0.24%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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			

subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Vaccination complication			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cerebral palsy			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital coronary artery malformation			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Cryptorchism			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Faciodigitogenital dysplasia			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Gastroschisis			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Hydrocele			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Microcephaly			

subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Thalassaemia beta			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	2 / 828 (0.24%)	1 / 832 (0.12%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infantile spasms			

subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Nystagmus			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Presyncope			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Aplasia pure red cell			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Blindness			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enteritis			
subjects affected / exposed	2 / 828 (0.24%)	2 / 832 (0.24%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Infantile colic			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Intestinal haemorrhage			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Intussusception			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Eczema nummular			

subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Rash			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Urticaria			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vesicoureteric reflux			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Premature closure of cranial sutures			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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

Tendon disorder			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Anal abscess			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Bacterial infection			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Bronchiolitis			
subjects affected / exposed	2 / 828 (0.24%)	4 / 832 (0.48%)	2 / 490 (0.41%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	12 / 828 (1.45%)	6 / 832 (0.72%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 12	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Bronchopneumonia			
subjects affected / exposed	4 / 828 (0.48%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			

subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Exanthema subitum			
subjects affected / exposed	0 / 828 (0.00%)	2 / 832 (0.24%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
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			
subjects affected / exposed	7 / 828 (0.85%)	12 / 832 (1.44%)	2 / 490 (0.41%)
occurrences causally related to treatment / all	0 / 7	0 / 12	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Gastroenteritis rotavirus			
subjects affected / exposed	4 / 828 (0.48%)	3 / 832 (0.36%)	2 / 490 (0.41%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Influenza			
subjects affected / exposed	2 / 828 (0.24%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	4 / 828 (0.48%)	7 / 832 (0.84%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Mastitis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Mastoiditis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Nasopharyngitis			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	0 / 490 (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
Otitis media			

subjects affected / exposed	2 / 828 (0.24%)	3 / 832 (0.36%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	1 / 828 (0.12%)	2 / 832 (0.24%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			
subjects affected / exposed	1 / 828 (0.12%)	1 / 832 (0.12%)	0 / 490 (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
Pharyngitis			
subjects affected / exposed	2 / 828 (0.24%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 828 (0.48%)	3 / 832 (0.36%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocroup			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	3 / 828 (0.36%)	1 / 832 (0.12%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	3 / 828 (0.36%)	2 / 832 (0.24%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	2 / 828 (0.24%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (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
Tracheitis			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Upper respiratory tract infection			
subjects affected / exposed	2 / 828 (0.24%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 828 (0.00%)	2 / 832 (0.24%)	3 / 490 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 828 (0.00%)	1 / 832 (0.12%)	0 / 490 (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
Viral infection			

subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Viral pharyngitis			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (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
Hypercholesterolaemia			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	1 / 490 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Feeding disorder of infancy or early childhood			
subjects affected / exposed	1 / 828 (0.12%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight gain poor			
subjects affected / exposed	0 / 828 (0.00%)	0 / 832 (0.00%)	0 / 490 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	rMenB Lot3	Routine	
Total subjects affected by serious adverse events			
subjects affected / exposed	60 / 820 (7.32%)	51 / 659 (7.74%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 820 (0.12%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Labial frenectomy			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon operation			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 820 (0.37%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased activity			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Milk allergy			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 820 (0.00%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breath holding			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental exposure to product			

subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone fissure			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 820 (0.00%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			

subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaccination complication			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cerebral palsy			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital coronary artery malformation			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptorchism			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faciodigitogenital dysplasia			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroschisis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			

subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcephaly			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalassaemia beta			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	3 / 820 (0.37%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			

subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nystagmus			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplasia pure red cell			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea			
subjects affected / exposed	1 / 820 (0.12%)	3 / 659 (0.46%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 820 (0.00%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile colic			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Dermatitis allergic			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema nummular			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vesicoureteric reflux			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Premature closure of cranial sutures			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	5 / 820 (0.61%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	7 / 820 (0.85%)	11 / 659 (1.67%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	1 / 820 (0.12%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	12 / 820 (1.46%)	7 / 659 (1.06%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 820 (0.12%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			

subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	3 / 820 (0.37%)	3 / 659 (0.46%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	1 / 820 (0.12%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	6 / 820 (0.73%)	3 / 659 (0.46%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 820 (0.37%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudocroup			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	6 / 820 (0.73%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	3 / 820 (0.37%)	2 / 659 (0.30%)		
occurrences causally related to treatment / all	0 / 3	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Respiratory syncytial virus bronchiolitis				
subjects affected / exposed	0 / 820 (0.00%)	2 / 659 (0.30%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Respiratory tract infection				
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Sepsis				
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Tonsillitis				
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Tracheitis				
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Upper respiratory tract infection				
subjects affected / exposed	0 / 820 (0.00%)	1 / 659 (0.15%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Urinary tract infection				
subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Varicella				

subjects affected / exposed	1 / 820 (0.12%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding disorder of infancy or early childhood			
subjects affected / exposed	0 / 820 (0.00%)	0 / 659 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight gain poor			
subjects affected / exposed	0 / 820 (0.00%)	2 / 659 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	rMenB Lot2	rMenB Lot1	MenC + Routine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	825 / 828 (99.64%)	827 / 832 (99.40%)	482 / 490 (98.37%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	729 / 828 (88.04%)	714 / 832 (85.82%)	353 / 490 (72.04%)
occurrences (all)	1684	1657	711
General disorders and administration site conditions			
Crying			
subjects affected / exposed	711 / 828 (85.87%)	714 / 832 (85.82%)	352 / 490 (71.84%)
occurrences (all)	1750	1740	752
Injection site erythema			
subjects affected / exposed	733 / 828 (88.53%)	729 / 832 (87.62%)	385 / 490 (78.57%)
occurrences (all)	4135	4171	1788
Injection site induration			
subjects affected / exposed	680 / 828 (82.13%)	692 / 832 (83.17%)	390 / 490 (79.59%)
occurrences (all)	3915	4024	1761
Injection site pain			
subjects affected / exposed	736 / 828 (88.89%)	736 / 832 (88.46%)	358 / 490 (73.06%)
occurrences (all)	4497	4472	1615
Injection site swelling			
subjects affected / exposed	466 / 828 (56.28%)	440 / 832 (52.88%)	184 / 490 (37.55%)
occurrences (all)	1688	1683	519
Pyrexia			
subjects affected / exposed	646 / 828 (78.02%)	656 / 832 (78.85%)	248 / 490 (50.61%)
occurrences (all)	1338	1344	425
Vaccination site induration			
subjects affected / exposed	30 / 828 (3.62%)	42 / 832 (5.05%)	51 / 490 (10.41%)
occurrences (all)	60	76	105
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	380 / 828 (45.89%)	370 / 832 (44.47%)	168 / 490 (34.29%)
occurrences (all)	632	607	286
Vomiting			

subjects affected / exposed	234 / 828 (28.26%)	217 / 832 (26.08%)	120 / 490 (24.49%)
occurrences (all)	329	315	178
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	58 / 828 (7.00%)	59 / 832 (7.09%)	40 / 490 (8.16%)
occurrences (all)	66	66	51
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	119 / 828 (14.37%)	121 / 832 (14.54%)	50 / 490 (10.20%)
occurrences (all)	168	180	79
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	603 / 828 (72.83%)	588 / 832 (70.67%)	257 / 490 (52.45%)
occurrences (all)	1223	1152	492
Irritability			
subjects affected / exposed	761 / 828 (91.91%)	769 / 832 (92.43%)	370 / 490 (75.51%)
occurrences (all)	2168	2181	877
Infections and infestations			
Bronchitis			
subjects affected / exposed	98 / 828 (11.84%)	102 / 832 (12.26%)	59 / 490 (12.04%)
occurrences (all)	132	129	80
Conjunctivitis			
subjects affected / exposed	80 / 828 (9.66%)	74 / 832 (8.89%)	16 / 490 (3.27%)
occurrences (all)	100	91	19
Ear infection			
subjects affected / exposed	70 / 828 (8.45%)	86 / 832 (10.34%)	26 / 490 (5.31%)
occurrences (all)	106	119	38
Exanthema subitum			
subjects affected / exposed	47 / 828 (5.68%)	46 / 832 (5.53%)	21 / 490 (4.29%)
occurrences (all)	47	46	21
Gastroenteritis			
subjects affected / exposed	47 / 828 (5.68%)	34 / 832 (4.09%)	14 / 490 (2.86%)
occurrences (all)	51	34	15
Nasopharyngitis			
subjects affected / exposed	79 / 828 (9.54%)	78 / 832 (9.38%)	12 / 490 (2.45%)
occurrences (all)	108	97	12

Otitis media			
subjects affected / exposed	145 / 828 (17.51%)	152 / 832 (18.27%)	28 / 490 (5.71%)
occurrences (all)	267	256	38
Rhinitis			
subjects affected / exposed	99 / 828 (11.96%)	78 / 832 (9.38%)	30 / 490 (6.12%)
occurrences (all)	120	90	33
Upper respiratory tract infection			
subjects affected / exposed	126 / 828 (15.22%)	142 / 832 (17.07%)	47 / 490 (9.59%)
occurrences (all)	172	190	59

Non-serious adverse events	rMenB Lot3	Routine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	817 / 820 (99.63%)	652 / 659 (98.94%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	716 / 820 (87.32%)	476 / 659 (72.23%)	
occurrences (all)	1624	914	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	685 / 820 (83.54%)	424 / 659 (64.34%)	
occurrences (all)	1693	822	
Injection site erythema			
subjects affected / exposed	704 / 820 (85.85%)	497 / 659 (75.42%)	
occurrences (all)	4034	1792	
Injection site induration			
subjects affected / exposed	664 / 820 (80.98%)	452 / 659 (68.59%)	
occurrences (all)	3926	1741	
Injection site pain			
subjects affected / exposed	728 / 820 (88.78%)	415 / 659 (62.97%)	
occurrences (all)	4541	1364	
Injection site swelling			
subjects affected / exposed	436 / 820 (53.17%)	254 / 659 (38.54%)	
occurrences (all)	1743	653	
Pyrexia			
subjects affected / exposed	643 / 820 (78.41%)	319 / 659 (48.41%)	
occurrences (all)	1332	493	
Vaccination site induration			

subjects affected / exposed	38 / 820 (4.63%)	4 / 659 (0.61%)	
occurrences (all)	74	5	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	368 / 820 (44.88%)	225 / 659 (34.14%)	
occurrences (all)	624	358	
Vomiting			
subjects affected / exposed	216 / 820 (26.34%)	108 / 659 (16.39%)	
occurrences (all)	317	149	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	60 / 820 (7.32%)	43 / 659 (6.53%)	
occurrences (all)	69	48	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	110 / 820 (13.41%)	88 / 659 (13.35%)	
occurrences (all)	147	116	
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	596 / 820 (72.68%)	329 / 659 (49.92%)	
occurrences (all)	1211	580	
Irritability			
subjects affected / exposed	766 / 820 (93.41%)	544 / 659 (82.55%)	
occurrences (all)	2183	1339	
Infections and infestations			
Bronchitis			
subjects affected / exposed	94 / 820 (11.46%)	97 / 659 (14.72%)	
occurrences (all)	123	125	
Conjunctivitis			
subjects affected / exposed	77 / 820 (9.39%)	60 / 659 (9.10%)	
occurrences (all)	91	66	
Ear infection			
subjects affected / exposed	57 / 820 (6.95%)	59 / 659 (8.95%)	
occurrences (all)	85	91	
Exanthema subitum			

subjects affected / exposed	46 / 820 (5.61%)	38 / 659 (5.77%)	
occurrences (all)	46	38	
Gastroenteritis			
subjects affected / exposed	38 / 820 (4.63%)	25 / 659 (3.79%)	
occurrences (all)	41	25	
Nasopharyngitis			
subjects affected / exposed	81 / 820 (9.88%)	73 / 659 (11.08%)	
occurrences (all)	106	107	
Otitis media			
subjects affected / exposed	156 / 820 (19.02%)	124 / 659 (18.82%)	
occurrences (all)	284	229	
Rhinitis			
subjects affected / exposed	58 / 820 (7.07%)	63 / 659 (9.56%)	
occurrences (all)	66	84	
Upper respiratory tract infection			
subjects affected / exposed	133 / 820 (16.22%)	94 / 659 (14.26%)	
occurrences (all)	175	124	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 August 2008	Amendment 4: This substantial amendment was mainly issued to revise the safety assessment and assessment of concomitant vaccines as requested by the US FDA Center for Biologics Evaluation & Research (CBER): The collection of safety data was revised. This included the collection of medically attended fever events and all teething and colic events fever within 7 days after each vaccination. The immunogenicity assessment of pertussis antigens was revised. The interim analysis of the first 360 subjects was not planned any longer. The localization of routine injection sites was designated. Furthermore, the exclusion criteria were revised (i.e. family and household members of research staff were excluded from participation). The temperature measurement by axillary route was allowed, if rectal measurement was not possible, and the analysis of the data described in the protocol. The severity grading of fever was aligned with other rMenB+OMV NZ trial protocols. In order to increase the validity of the safety data it was decided to replace the final study phone call by a final study visit.
29 October 2008	Amendment 5: This substantial amendment addressed a request from the German competent authority (PEI): The wording of the stopping rules with respect to a fatal or life-threatening event was revised. Furthermore, this amendment addressed requests from Center for Biologics Evaluation & Research (CBER): The immunogenicity of routine vaccinations was to be assessed in the same subset of subjects evaluated for rMenB+OMV NZ hSBA responses. The analysis sequence of the co-primary immunogenicity objectives was reversed (i.e., demonstration of lot-to-lot consistency before demonstration of overall immunogenicity). Moreover, the cut-off in the analysis of hSBA results was changed and based on the new hSBA results, and sample size estimates for hSBA responses against strain 5/99 have been recalculated. This amendment also clarified how subjects from each of the immunogenicity treatment groups will be assigned to the different serological tests. A secondary immunogenicity objective (ELISA testing for antigen 287-953) was added. In addition, contraindications to further vaccinations were revised. This amendment also clarifies that subjects in the safety subset will remain blinded until the study is completed and the database is unblinded. The supply of Menjugate as a booster of the study vaccinations was clarified. The enrolment of safety subjects in Finland was allowed with this amendment. In addition, administrative changes and corrections have been implemented

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23324563