SAP Core Body

Title: A parallel-group, prevention, Phase III, modified double-blind, 2-arm, study to investigate the immunogenicity and describe the safety of a quadrivalent meningococcal conjugate vaccine (MenACYW conjugate vaccine) compared with Nimenrix® when administered in a 1+1 schedule in healthy infants and toddlers at 6 and 12 months of age

Study Code: MEQ00089

Study Phase: Phase III

SAP Core Body Version: 2.0

SAP Core Body Date: 04 March 2026

Protocol Version Number: 7.0

The SAP Code Body should be used in conjunction of the study protocol and the SAP TLF (if applicable).

Version History

Previous Version(s)	Date	Comments (optional)
1.0	13 February 2026	-
2.0	04 March 2026	Typographical errors (spacing, temperature notation) and formatting alignment corrected. No changes to statistical methodology, endpoints, or analysis features.

Table of Contents

Version History **2**

Table of Contents **3**

List of Tables **5**

List of Figures **6**

1 Overall Design **7**

2 Objectives and Endpoints **11**

3 Statistical Considerations **17**

3.1 Statistical Hypotheses 17

3.2 Sample Size Determination 20

3.3 Populations for Analyses 21

3.3.1 Safety Analysis Set 22

3.3.1.1 Overall Safety Analysis Set for Any Dose 22

3.3.1.2 Safety Analysis Set for Vaccination at 6 Months of Age 22

3.3.1.3 Safety Analysis Set for Vaccination at 12 Months of Age 22

3.3.2 Full Analysis Set 23

3.3.2.1 FAS based on hSBA measurements: 23

3.3.2.2 FAS based on rSBA measurements: 23

3.3.3 Per-Protocol Analysis Set (PPAS) 23

3.3.3.1 hSBA PPAS for Dose 1 (priming dose) 23

3.3.3.2 hSBA PPAS2 for Dose 2 (booster dose) 24

3.3.3.3 rSBA PPAS1 for Dose 1 (priming dose) 24

3.3.3.4 rSBA PPAS2 for Dose 2 (booster dose) 24

3.4 Statistical Analyses 25

3.4.1 General Considerations 25

3.4.2 Coprimary Endpoint(s) 26

3.4.3 Secondary Endpoints 27

3.4.3.1 Secondary immunogenicity endpoints: 27

3.4.3.2 Secondary safety endpoints: 28

3.4.4 Exploratory Endpoints 28

3.4.5 Other Safety Analyse[s] 30

3.4.6 Subgroup analysis 30

3.4.7 Handling of Missing Data and Outliers 30

3.4.7.1 Safety 30

3.4.7.2 Immunogenicity 31
3.4.7.3 Efficacy 31
3.5 Interim Analyse(s) 31
3.6 Data Monitoring Committee (DMC) 31

4 Complementary Information on Assessment Methods 32
4.1 Complementary Information for Endpoint(s) Assessment Method(s) 32
4.2 Complementary Information on Derived Endpoints: Calculation Methods 32
4.2.1 Safety 32
4.2.1.1 Solicited Reactions 32
4.2.1.2 Unsolicited AEs 36
4.2.2 Other Safety Endpoints 39
4.2.2.1 Action Taken 39
4.2.2.2 Seriousness 39
4.2.2.3 Outcome 39
4.2.2.4 Causal Relationship 39
4.2.2.5 Adverse Events Leading to Study Discontinuation 39
4.2.3 Immunogenicity 40
4.2.3.1 Computed Values for Analysis 40
4.2.3.2 Seroprotection 40
4.2.3.3 Fold-rise 40
4.2.3.4 Seroresponse 40
4.2.4 Efficacy 41
4.2.5 Derived Other Variables 41
4.2.5.1 Age for Demographics 41
4.2.5.2 Duration of a Participant in the Trial 41
4.2.5.3 Duration of the Study 41

5 Changes in the Conduct of the Trial or Planned Analyses 42

6 Supporting Documentation 43
6.1 Appendix 1 List of Abbreviations 43

7 References 44

List of Tables

Table 1.1: Schedule of activities 9
Table 2.1: Objectives and endpoints 11
Table 3.1: Descriptive statistics produced.....25
Table 4.1: Solicited injection site reactions: terminology, definitions, and intensity scales – Infants and toddlers aged < 24 months 33
Table 4.2: Solicited systemic reactions: terminology, definitions, and intensity scales – Infants and toddlers aged < 24 months.....34

List of Figures

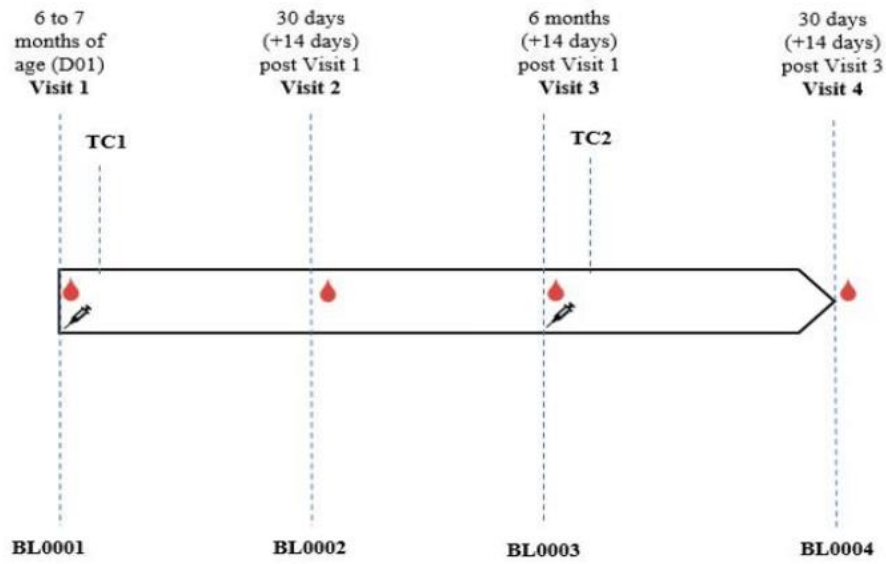
Figure 1.1: Graphical study design.....8
Figure 3.1: Sequential statistical testing for superiority exploratory objectives 20

1 Overall Design

Detailed design is provided in Sections 1.1 and 4.1 of the protocol.

Type of design	Parallel group, 2-arm, multi-center
Phase	III
Control method	Active-controlled (control = EU licensed quadrivalent meningococcal polysaccharide conjugate vaccine Nimenrix®)
Study population	Healthy infants and toddlers aged 6 to 7 months of age at inclusion (at dose 1) to 12-13 months of age (at dose 2)
Level and method of blinding	Modified double-blind
Study intervention assignment method	Randomization
Number of participants	Approximately 840 participants (420 per group) 6 to 7 months of age at enrollment.
Intervention groups	Eligible participants will be randomized to two groups in a 1:1 ratio to receive 2 doses of the assigned vaccine. The first dose (priming) will be administrated at 6 to 7 months of age and the second (booster) dose at 12 to 13 months of age. Group 1: MenACYW conjugate vaccine (n=420) Group 2: Nimenrix (n=420)
Total duration of study participation	Approximately 7 to 8.5 months (at least 7 months per participant)
Countries	Several countries in the European Union
Use of an Independent Data Monitoring Committee, Dose Escalation Committee, or similar review group	No

Figure 1.1: Graphical study design



BL: blood sample; D: day

TC1: safety follow-up call – 8 days post Visit 1 priming vaccination
TC2: safety follow-up call – 8 days post Visit 3 booster vaccination

: Blood Draw

: Vaccination

The Schedule of Activities of the study is summarized in Table 1.1.

Table 1.1: Schedule of activities

Phase III Study, 4 Visits, 2 Vaccinations, 4 Blood Samples, 2 Telephone calls, ~7 to 8.5 Months' Duration Per Participant

Visit	***Collection of information in the CRF***	**Visit 1***	**TC 1†††**	**Visit 2**	**Visit 3§§**	**TC 2†††**	**Visit 4**
Approximate age of participants		**6 - 7 months of age**			**12 - 13 months of age**		
Study timelines (days)		**D01**	**D09 Visit 1+8 days**	**D31 Visit 1+30 days**	**Visit 1+6 months**	**Visit 3+8 days**	**Visit 3+30 days**
Time windows (days)			**+2 days**	**+14 days**	**+14 days**	**+2 days**	**+14 days**
Visit procedures:							
Informed consent	X	X					
Inclusion/exclusion criteria	X	X					
Collection of demographics	X	X					
Collection of significant medical history	X	X					
Physical examination		X			X		
Pre-vaccination temperature†		X			X		
Randomization/allocation of participant number	X	X					
Review of warnings and precautions for vaccination		X			X		
Review of contraindications to subsequent vaccination	X				X‡‡		
Review of temporary contraindications for blood sampling§		X		X	X		X
Blood sampling (BL) [3 mL]	X	BL0001 Pre-vac**		BL0002	BL0003 Pre-vac**		BL0004
Vaccination (vac):							
Group 1: MenACYW conjugate vaccine (IMP)	X	X			X		
Group 2: Nimenrix® (IMP)	X	X			X		
Immediate surveillance (30 min)	X	X			X		
Diary card provided		DC1		DC2	DC3		
Diary card collected				DC1	DC2		DC3
Collection of solicited injectio site and systemic reactions‡	X	X	X		X	X	

Visit	***Collection of information in the CRF***	**Visit 1***	**TC 1††**	**Visit 2**	**Visit 3§§**	**TC 2††**	**Visit 4**
Approximate age of participants		**6 - 7 months of age**			**12 - 13 months of age**		
Study timelines (days)		**D01**	**D09 Visit 1+8 days**	**D31 Visit 1+30 days**	**Visit 1+6 months**	**Visit 3+8 days**	**Visit 3+30 days**
Time windows (days)			**+2 days**	**+14 days**	**+14 days**	**+2 days**	**+14 days**
Collection of unsolicited adverse events (AEs)	X	Up to 30 days after priming vaccination			Up to 30 days after booster vaccination		
Collection of adverse events of special interest	X	To be reported throughout the study					
Collection of reportable concomitant medications	X	X		X	X		X
Collection of serious adverse events (SAEs)	X	To be reported throughout the study					
Collection of End of Study status***	X						X

CRF: case report form; DC: diary card; IRT: interactive response technology; IMP: investigational medicinal product; TC: telephone call

*At Visit 1, participants must be at least 6 months of age. “6 to 7 months” means from the day of the 6th month after birth to the day before the 8th month after birth

†Temperature to be measured by oral, rectal, or axillary route (axillary preferred) using a standard digital thermometer and recorded in the source document

§Should a participant receive oral or injectable antibiotic therapy within 3 days prior to any blood draw, the investigator will postpone that blood draw until it has been 3 days since the participant last received oral or injectable antibiotic therapy. Postponement must still be within the timeframe for blood draw. If postponement would result in the sample collection falling outside of this timeframe, the blood sample should be collected without postponement, and it should be documented appropriately that the sample was taken less than 3 days after stopping antibiotic treatment.

‡ Solicited injection site and systemic reactions will be recorded for 8 days from the day of each vaccination at Visit 1 and Visit 3

**Blood samples at Visit 1 and Visit 3 will be drawn before administration of the vaccine

††This call is to be made 8 to 10 days after the vaccination visit. If the contact date (+2 days) falls on a weekend or holiday, the TC may be made on the following business day. During this TC, the Investigator or an authorized designee will interview the parents, guardians, or legally acceptable representatives to collect the information recorded in the DC and will attempt to clarify anything that is incomplete or unclear. They will also find out whether the participant experienced any SAEs, including AESIs, not yet reported, and are to remind the participant’s parent/legally acceptable representative to continue using the diary card (DC) up to the next visit, to bring the DC to the study center at the next visit, and to confirm the date and time of the next visit.

§§ Visit 3 is Visit 1 + 6 months meaning V1 + 180 days (+14 days). “12 to 13 months” of age at Visit 3 means from the day of the 12th month after birth to the day before the 14th month after birth

‡‡ Contraindications are included in Exclusion criteria at V01.

***In case of participant discontinuation at a visit, the entire visit will be completed.

2 Objectives and Endpoints

Table 2.1: Objectives and endpoints

Objectives	Endpoints
Coprimary	
Immunogenicity 1. To demonstrate non-inferiority of the antibody response in terms of geometric mean titers (GMTs) against meningococcal serogroups A, C, W, and Y, following the administration of a 2-dose series (1+1) of MenACYW conjugate vaccine compared to a 2 - dose series (1+1) of Nimenrix, when each vaccine is administered to infants (Dose 1) at 6-7 months of age and toddlers (Dose 2) at 12-13 months of age 2. To demonstrate non inferiority of the antibody response in terms of vaccine seroresponse against meningococcal serogroups A, C, W, and Y, following the administration of a 2-dose series (1+1) of MenACYW conjugate vaccine compared to a 2-dose series (1+1) of Nimenrix, when each vaccine is administered to infants (Dose 1) at 6-7 months of age and toddlers (Dose 2) at 12-13 months of age	Immunogenicity 1. Antibody titers (GMTs) against meningococcal serogroups A, C, W, and Y measured by serum bactericidal assays using human complement (hSBA) at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age 2. Vaccine seroresponse against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age Vaccine seroresponse is defined as follows: • For a participant with a pre-vaccination (pre-Dose 1) titer < 1:8, a post-vaccination (post-Dose 2) titer ≥ 1:16 • For a participant with a pre-vaccination (pre-Dose 1) titer ≥ 1:8, a post-vaccination (post-Dose 2) titer at least 4-fold greater than the pre-vaccination (pre-Dose 1) titer
Secondary	
Immunogenicity 1. To compare the antibody response in terms of seroprotection as measured by hSBA against meningococcal serogroups A, C, W and Y, 30 days following the administration of Dose 1 (priming dose) of MenACYW conjugate vaccine versus Dose 1 (priming dose) of Nimenrix in infants 6-7 months of age	*Immunogenicity* 1. Antibody titers ≥ 1:8, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix

Objectives	Endpoints
2. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, at Day (D)01 (baseline) before vaccination and 30 days following the administration of Dose 1 (priming dose) of MenACYW conjugate vaccine or Nimenrix in infants 6-7 months of age	2. At Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed for meningococcal serogroups A, C, W and Y as measured by hSBA: • Antibody titers against meningococcal serogroups A, C, W, and Y • Antibody titers ≥ 1:4 and ≥ 1:8 • ≥ 4-fold rise in antibody titer from pre-vaccination to post-vaccination •Vaccine seroresponse, defined as follows: • For a participant with a pre-vaccination (pre-Dose 1) titer < 1:8, a post-vaccination (post-Dose 1) titer ≥ 1:16 • For a participant with a pre-vaccination (pre-Dose 1) titer ≥ 1:8, a post-vaccination (post-Dose 1) titer at least 4-fold greater than the pre-vaccination (pre-Dose 1) titer
3. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, before and 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix in toddlers 12-13 months of age	3. Same endpoints as described in secondary endpoint #2 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
4. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before Dose 1 (priming dose) as infants 6 – 7 months of age and at 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix as toddlers at 12-13 months of age	4. Same endpoints (except vaccine seroresponse) as described in secondary endpoint #2 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix

Objectives	Endpoints
5. To describe the antibody response as measured by serum bactericidal assays using baby rabbit (rSBA)* against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before vaccination and 30 days following the administration of Dose 1 (priming dose) of MenACYW conjugate vaccine or Nimenrix in infants at 6-7 months of age	5. At Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed for meningococcal serogroups A, C, W and Y as measured by rSBA: • Antibody titers against meningococcal serogroups A, C, W, and Y • Antibody titers ≥ 1:8 and ≥ 1:128 • ≥ 4-fold rise in antibody titer from prevaccination to post-vaccination • Vaccine seroresponse defined as follows: • For a participant with a pre-vaccination titer < 1:8, a post-vaccination titer ≥ 1:32 • For a participant with a pre-vaccination titer ≥ 1:8, a post-vaccination titer at least 4-fold greater than the pre-vaccination titer
6. To describe the antibody response as measured by rSBA* against meningococcal serogroups A, C, W, and Y, before and 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix in toddlers at 12-13 months of age	6. Same endpoints as described in secondary endpoint #5 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
7. To describe the antibody response as measured by rSBA* against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before Dose 1 (priming dose) as infants 6 – 7 months of age and 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix as toddlers at 12-13 months of age *rSBA testing will be performed in a subset of participants, the first 100 participants enrolled into each study group.	7. Same endpoints as described in secondary endpoint #5 at Visit 1 (D0) before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix

Objectives	Endpoints
Safety 1. To describe the safety profile of MenACYW conjugate vaccine and Nimenrix after Dose 1 (priming dose) administered to infants at 6-7 months of age and after Dose 2 (booster dose) administered at 12-13 months of age	*Safety* 1. Presence of any unsolicited systemic adverse events (AEs) reported in the 30 minutes after each vaccination. 2. Presence of solicited (pre-listed in the participant's diary card [DC] and case report form [CRF]) injection site reactions up to 7 days after each vaccination. 3. Presence of solicited systemic reactions (pre-listed in the participant's DC and CRF) up to 7 days after each vaccination. 4. Presence of unsolicited AEs up to 30 days after each vaccination. 5. Presence of SAEs [including AESIs], throughout the trial. Depending on the items, the endpoints recorded or derived could include: Nature (Medical Dictionary for Regulatory Activities [MedDRA] preferred term), time of onset, duration/number of days of occurrence, intensity, relationship to the vaccine, whether the AE led to early termination from the study, outcome, and seriousness
Exploratory	
1. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before vaccination and at 30 days following the administration of Dose 1 (priming dose) of MenACYW conjugate vaccine or Nimenrix in infants aged 6-7 months of age according to MenB vaccination status (Men B vaccination naive or not)	1. Same endpoints as described secondary in endpoint #2 at Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)
2. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, before and at 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix in toddlers at 12-13 months of age according to MenB vaccination status (Men B vaccination naive or not)	2. Same endpoints as described in secondary endpoint #2 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)

Objectives	Endpoints
3. To describe the antibody response as measured by hSBA against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before Dose 1 (priming dose) as infants 6 – 7 months of age and at 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix as toddlers at 12-13 months of age according to MenB vaccination status (Men B vaccination naive or not)	3. Same endpoints as described in secondary endpoint #2 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)
4. To describe the antibody response as measured by rSBA* against meningococcal serogroups A, C, W, and Y, before and 30 days following the administration of Dose 1 (priming dose) of MenACYW conjugate vaccine or Nimenrix in infants aged 6-7 months of age according to MenB vaccination status (MenB vaccination naïve or not)	4. At Visit 1 (D0) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed according to MenB vaccination status (MenB vaccination naïve or not) for meningococcal serogroups A, C, W and Y as measured by rSBA: • Antibody titers against meningococcal serogroups A, C, W, and Y • Antibody titers ≥ 1:8 and ≥ 1:128 • ≥ 4-fold rise in antibody titer from prevaccination to post-vaccination • Vaccine seroresponse defined as follows: • For a participant with a prevaccination titer < 1:8, a post-vaccination titer ≥ 1:32 • For a participant with a prevaccination titer ≥ 1:8, a post-vaccination titer at least 4-fold greater than the pre-vaccination titer
5. To describe the antibody response as measured by rSBA* against meningococcal serogroups A, C, W, and Y, before and 1 month following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix in toddlers at 12-13 months of age according to MenB vaccination status (MenB vaccination naïve or not)	5. Same endpoints as described in exploratory endpoint #4 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix® by MenB vaccination status (MenB vaccination naive or not).

Objectives	Endpoints
6. To describe the antibody response as measured by rSBA* against meningococcal serogroups A, C, W, and Y, at D01 (baseline) before vaccination and at 30 days following the administration of Dose 2 (booster dose) of MenACYW conjugate vaccine or Nimenrix® in toddlers at 12-13 months of age according to MenB vaccination status (MenB vaccination naïve or not) *rSBA testing will be performed in a subset of participants, the first 100 participants enrolled into each study group.	6. Same endpoints as described in exploratory endpoint #4 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix® by MenB vaccination status (MenB vaccination naive or not).
7. To explore the superiority of the immune responses to meningococcal serogroups A, C, W, and Y measured by hSBA following the administration of 2-dose series (1+1) of MenACYW conjugate vaccine (Group 1) compared to 2-dose series (1+1) of Nimenrix (Group 2) in terms of vaccine seroresponse rate. 8. If the superiority based on vaccine sero responses demonstrated, then to explore the superiority of the immune responses to meningococcal serogroups A, C, W, and Y measured by hSBA following the administration of 2-dose series (1+1) of MenACYW conjugate vaccine (Group 1) compared to 2-dose series (1+1) of Nimenrix (Group 2) in terms of geometric mean titers (GMTs)	These endpoints are similar to those defined for the co-primary objectives. 7. Vaccine seroresponse against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age Vaccine seroresponse is defined as: • For a participant with a pre-vaccination (pre-Dose 1) titer < 1:8, a post-vaccination (post-Dose 2) titer ≥ 1:16, or • For a participant with a pre-vaccination (pre-Dose 1) titer ≥ 1:8, a post-vaccination (post-Dose 2) titer at least 4-fold greater than the pre-vaccination (pre-Dose 1) titer 8. Antibody titers (GMT) against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age
Note: Exploratory superiority testing (Objectives #7 and #8) will only be performed if non-inferiority is demonstrated for both co-primary objectives. A sequential gatekeeping approach will be used as detailed in Section 3.1	

3 Statistical Considerations

3.1 Statistical Hypotheses

The coprimary objectives will be met if the following coprimary null hypotheses are rejected.

Coprimary Objectives

- **Primary Hypothesis 1 (MenACYW antibody titers [geometric mean titers (GMTs)] after Dose 2)**

Non-inferiority of MenACYW conjugate vaccine (Group 1) compared to Nimenrix (Group 2) in terms of serum bactericidal assay using human complement (hSBA) antibody titers after a 2-dose series to toddlers at 12-13 months of age will be tested.

For each of the 4 serogroups (A, C, W, and Y), GMTs 30 days after a 2-dose vaccination series will be used to compare Group 1 and Group 2 with the following individual hypotheses:

H0 (Null hypothesis):

- $GMT_{MenACYW} / GMT_{Nimenrix} \leq 1/1.5$ (or $GMT_{Nimenrix} / GMT_{MenACYW} \geq 1.5$)

H1 (Alternative hypothesis):

- $GMT_{MenACYW} / GMT_{Nimenrix} > 1/1.5$ (or $GMT_{Nimenrix} / GMT_{MenACYW} < 1.5$)

Non-inferiority will be demonstrated if all 4 individual null hypotheses (4 serogroups) are rejected. For each serogroup, the 2-sided 95% confidence interval (CI) of the GMT ratio Group 1 (MenACYW) / Group 2 (Nimenrix) should lie above 1/1.5.

- **Primary Hypothesis 2 (MenACYW vaccine seroresponse after Dose 2)**

Non-inferiority of MenACYW conjugate vaccine (Group 1) compared to Nimenrix (Group 2) in terms of hSBA vaccine seroresponse after a 2-dose series to toddlers at 12 months of age will be tested.

For each of the 4 serogroups (A, C, W, and Y), vaccine seroresponse 30 days after a 2-dose vaccination series will be used to compare Group 1 and Group 2 with the following individual hypotheses:

H0 (Null hypothesis):

- $p(_{MenACYW}) - p(_{Nimenrix}) \leq -10\%$

H1 (Alternative hypothesis):

- $p(_{MenACYW}) - p(_{Nimenrix}) > -10\%$

where $p(_{MenACYW})$ and $p(_{Nimenrix})$ are the % of participants who achieve an hSBA vaccine seroresponse in the MenACYW conjugate vaccine group and the Nimenrix group, respectively.

Each of the serogroups A, C, W, and Y will be tested separately. If the lower limit of the 2-sided 95% CI of the difference between the 2 proportions is > -10%, the inferiority assumption will be rejected.

Vaccine seroresponse is defined as follows:

- For a participant with a pre-vaccination (pre-Dose 1) titer < 1:8, a post-vaccination (post-Dose 2) titer ≥ 1:16
- For a participant with a pre-vaccination (pre-Dose 1) titer ≥ 1:8, a post-vaccination (post-Dose 2) titer at least 4-fold greater than the pre-vaccination titer

Exploratory Objectives

Exploratory superiority testing will only be conducted if non-inferiority is successfully demonstrated for both co-primary objectives (vaccine seroresponse rates and GMTs for all 4 serogroups).

A formal superiority test was not specified as part of the MEQ00089 protocol. Thus, superiority of the immune response of MenACYW conjugate vaccine as compared to Nimenrix is proposed to be tested as an exploratory analysis.

If the non-inferiority testing succeeds for both GMTs and vaccine seroresponse rates (for all 4 serogroups), then a hierarchical superiority approach will be used to compare vaccine seroresponse rates and antibody titers (GMTs) of MenACYW conjugate vaccine (Group 1) to that of Nimenrix (Group 2) 30 days post-vaccination at visit 4.

The exploratory objectives are to demonstrate that 30 days after the administration of MenACYW conjugate vaccine or Nimenrix, the immune response of participants who received MenACYW conjugate vaccine (Group 1) is superior to the one of participants who received Nimenrix (Group 2) in terms of vaccine seroresponse rates and GMTs for meningococcal serogroups A, C, W, Y.

A gatekeeping approach will be applied to protect the overall type I error rate at the level of 0.05 for this study. A superiority test will be performed to compare post-vaccination (ie, 30 days after the vaccination at visit 3) vaccine seroresponse rates and GMTs among participants receiving of MenACYW conjugate vaccine (Group 1) to those among Nimenrix recipients (Group 2), with the following hypotheses:

- **Exploratory Hypothesis (MenACYW vaccine seroresponse after Dose 2)**

H0 (Null hypothesis):

$$P(_{MenACYW}) - P(_{Nimenrix}) \leq 0$$

H1 (Alternative hypothesis):

$$P(_{MenACYW}) - P(_{Nimenrix}) > 0$$

where $P(_{MenACYW})$ and $P(_{Nimenrix})$ are percentages of participants who achieve hSBA vaccine seroresponse at D30 in the MenACYW conjugate vaccine group (Group 1) and the Nimenrix vaccine group (Group 2), respectively. Group 1(MenACYW) will be considered as superior to Group 2(Nimenrix) if the hypothesis H_0 is rejected. The null hypothesis will be rejected if the

lower limit of the 2-sided 95% confidence interval for the difference in seroresponse rates (Group 1 – Group 2) is greater than 0.

- **Exploratory Hypothesis (MenACYW GMTs after Dose 2)**

H0 (Null hypothesis):

$GMT_{MenACYW} / GMT_{Nimenrix} \leq 1$

H1 (Alternative hypothesis):

$GMT_{MenACYW} / GMT_{Nimenrix} > 1$

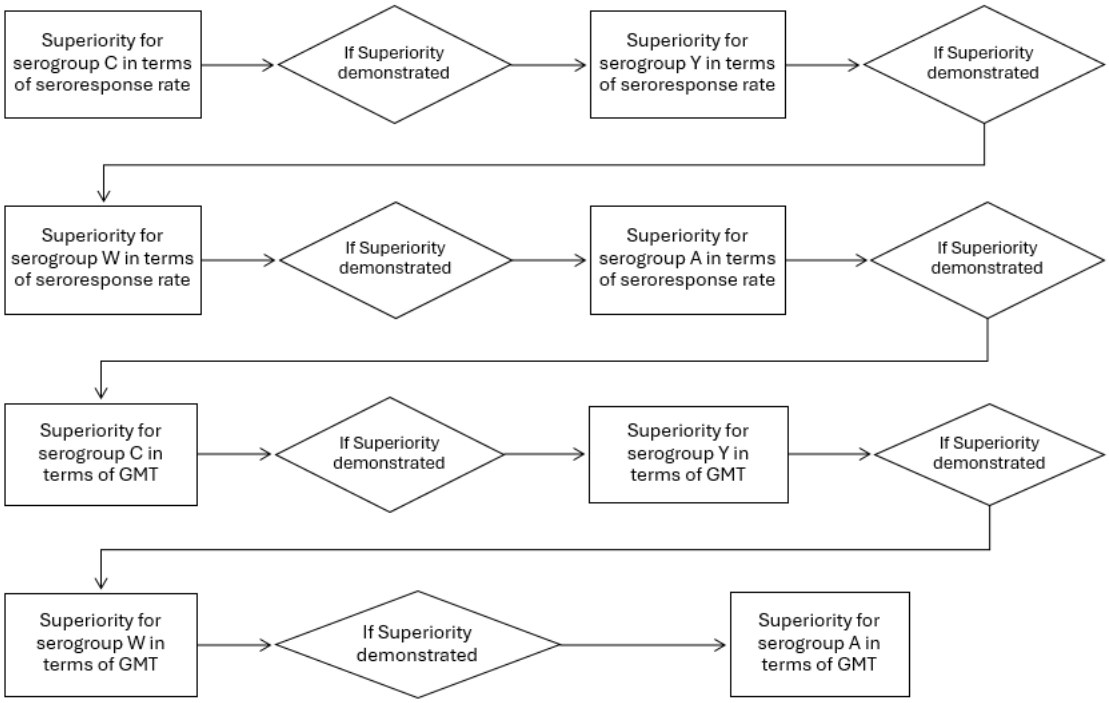
where $GMT_{MenACYW}$ and $GMT_{Nimenrix}$ are the geometric mean of hSBA antibody titers at Day 30 in the MenACYW conjugate vaccine group (Group 1) and the Nimenrix vaccine group (Group 2), respectively. Group 1(MenACYW) will be considered as superior to Group 2(Nimenrix) if the hypothesis H_0 is rejected. The null hypothesis will be rejected if the lower limit of the 2-sided 95% confidence interval for the GMT ratio (Group 1 / Group 2) is greater than 1.

The sequential gatekeeping approach will be applied for the exploratory superiority on vaccine seroresponse rate and GMT for the study, as follows:

- The endpoints will be sequentially tested in the order of vaccine seroresponse rate, and GMT.
- Serogroups will be sequentially tested in the order of C, Y, W, and A to follow the epidemiological prevalence as observed globally across various age groups
- Superiority testing of serogroups in the order of C, Y, W, and A using an alpha of 0.05 will be performed for each step until a test does not succeed (i.e., failure to reject the specified null hypothesis occurs). For example, an alpha of 0.05 will be used for testing superiority of vaccine seroresponse rate in serogroup C first. If this test succeeds, vaccine seroresponse rate of serogroup Y will be tested on an alpha of 0.05. If the test on vaccine seroresponse rate of serogroup C does not succeed, no further superiority testing will be performed.

If superiority testing on vaccine seroresponse rate succeeds for all 4 serogroups, then superiority testing will proceed to compare post-vaccination GMTs among recipients of MenACYW conjugate vaccine (Group 1) to those among recipients of Nimenrix (Group 2). The time point for each immune measure (seroresponse rate, and GMT) is 30 days post-vaccination at Visit 4.

Figure 3.1: Sequential statistical testing for superiority exploratory objectives



3.2 Sample Size Determination

A total of approximately 840 (420 per group) participants are planned to be enrolled with the aim to obtain a total of 672 (336 per group) evaluable participants.

For Coprimary Objective 1:

With 420 enrolled participants in Group 1 and in Group 2, the study will have > 90% power to declare the non-inferiority of Group 1 versus Group 2 based on A, C, W, and Y hSBA antibody titers (ratio of GMTs in the 2 groups) after a 2-dose series administered to toddlers at 12 months of age, assuming a:

- 20% dropout rate from the PPAS (336 participants evaluable by group),
- 1-sided alpha level of 2.5%,
- a non-inferiority margin of 1.5 (GMT ratio),
- standard deviation (SD) of log10-transformed titers of 0.6 for serogroups A, C and W, and 0.5 for serogroup Y

For Coprimary Objective 2:

With 420 evaluable participants in Group 1 and in Group 2, the study will have 98.37% power by using the Farrington and Manning's method to declare the non-inferiority of Group 1 vs Group 2 based on A, C, W, and Y hSBA vaccine seroresponse in the 2 groups, after a 2-dose series to toddlers at 12 months of age, assuming a:

- 20% dropout rate from the PPAS (336 participants evaluable by group),
- 1-sided alpha level of 2.5%,
- a non-inferiority margin of 10% (percentage difference)

Power of the study for the coprimary objectives:

The study will have 88.53% overall power to declare non-inferiority based on the coprimary objectives.

Coprimary Objective#	Antigen	MenACYW conjugate vaccine Estimated Standard Deviation*/Response†	Non-inferiority margin	Power (%)
Coprimary Objective 1	A	0.6	1.5	96.7
	C	0.6	1.5	96.7
	W	0.6	1.5	96.7
	Y	0.5	1.5	99.5
	Overall			≥ 90%
Coprimary Objective 2	A	89.4%	10%	98.37
	C	99.3%	10%	100
	W	98.6%	10%	100
	Y	99.3%	10%	100
	Overall			98.37%
Overall, for Coprimary Objectives				88.53%

Since the hypothesis needs to be met for all serogroups, no alpha adjustment for multiple comparisons is necessary in these calculations.

* Standards deviations are based on the MET39 study results

† Vaccine responses are based on results from Study MET61.

A non-inferiority margin of 10% has been widely used in previous studies evaluating the same antigens.

3.3 Populations for Analyses

In this study, antibody titers will be measured with 2 different assay methods: hSBA or serum bactericidal assay using baby rabbit complement (rSBA).

Coprimary, secondary, and exploratory endpoints will be analyzed according to the type of measurement and also according to the doses and timepoints of administration: Dose 1 (priming dose) / Dose 2 (booster dose). Several analysis sets will be used for the analyses as follows:

	To assess Dose 1 (BL0002)		**To assess Dose 2/ To assess the 2-dose schedule (BL0004)**	
Measurement	**hSBA**	**rSBA**	**hSBA**	**rSBA**
Analysis set to use	hSBA PPAS1	rSBA PPAS1	hSBA PPAS2	rSBA PPAS2
	hSBA FAS1	rSBA FAS1	hSBA FAS2	rSBA FAS2

Note: rSBA testing will be performed in a subset of the first 100 participants enrolled into each study group.

The safety analyses will be performed on the overall SafAS, SafAS1 and SafAS2. Participants will be analyzed according to the vaccine they actually received.

For exploratory superiority testing, the analyses will be based on the hSBA analysis population sets.

If the difference in the number of participants between hSBA/rSBA PPAS1 and FAS1 (or hSBA/rSBA PPAS2 and FAS2) is greater than 10%, a supplemental analysis based on hSBA/rSBA FAS1 (or FAS2) will be performed to evaluate consistency of the results.

3.3.1 Safety Analysis Set

The safety analysis set (SafAS) is defined as those participants who have received at least one dose of the study vaccine(s) and have any safety data available. All participants will have safety analyzed after each dose according to the vaccine they received, and after any dose according to the vaccine received at the first dose. Safety data recorded for a vaccine received outside of the protocol design will be excluded from the analysis (and listed separately).

3.3.1.1 Overall Safety Analysis Set for Any Dose

The overall SafAS is defined as those participants who have received at least one dose of the study vaccines and have any safety data available. All participants will have their safety analyzed after any dose according to the vaccine received at the first dose.

Safety data recorded for a vaccine received out of the protocol design will be excluded from the analysis (and listed separately).

3.3.1.2 Safety Analysis Set for Vaccination at 6 Months of Age

The SafAS1 for vaccination at 6-7 months of age is defined as those participants who have received the study vaccine at Visit 1 and have any safety data available. All participants will have their safety analyzed after the Visit 1 dose according to the vaccines they actually received at visit 1.

Safety data recorded for a vaccine received out of the protocol design will be excluded from the analysis (and listed separately).

3.3.1.3 Safety Analysis Set for Vaccination at 12 Months of Age

The SafAS2 for vaccination at 12-13 months of age is defined as those participants who received the study vaccine at Visit 3 and have any safety data available. All participants will have their safety analyzed after the Visit 3 dose according to the vaccines they actually received at Visit 3.

Safety data recorded for a vaccine received out of the protocol design will be excluded from the analysis.

3.3.2 Full Analysis Set

There will be 4 FASs, 2 FASs for the priming vaccination (hSBA FAS1 and rSBA FAS1) and 2 FASs for the booster vaccination (hSBA FAS2 and rSBA FAS2).

3.3.2.1 FAS based on hSBA measurements:

- hSBA FAS1 (for Dose 1 [priming dose]) is defined as the subset of randomized participants who received a dose of the study vaccine at V1 and had a valid post-vaccination hSBA result at V2.
- hSBA FAS2 (for Dose 2 [booster dose]) is defined as the subset of randomized participants who received a dose of the study vaccine at V3 and had a valid post-booster vaccination hSBA result at V4.

3.3.2.2 FAS based on rSBA measurements:

- rSBA FAS1 (for Dose 1 [priming dose]) is defined as the subset of randomized participants who received a dose of the study vaccine at V1 and had a valid post-vaccination rSBA result at V2.
- rSBA FAS2 (for Dose 2 [booster dose]) is defined as the subset of randomized participants who received a dose of the study vaccine at V3 and had a valid post-booster vaccination rSBA result at V4.

3.3.3 Per-Protocol Analysis Set (PPAS)

The PPAS is a subset of the FAS. There will be 4 PPASs: 2 PPASs for the priming vaccination (hSBA PPAS1 and rSBA PPAS1) and 2 PPASs for the booster vaccination (hSBA PPAS2 and rSBA PPAS2). PPAS based on hSBA measurements:

- hSBA PPAS1 (for Dose 1 [priming dose]; BL0002)
- hSBA PPAS2 (for Dose 2 [booster dose]; BL0004)

PPAS based on rSBA measurements:

- rSBA PPAS1 (for Dose 1 [priming dose]; BL0002)
- rSBA PPAS2 (for Dose 2 [booster dose]; BL0004)

The definitions of all PPASs are detailed as below:

3.3.3.1 hSBA PPAS for Dose 1 (priming dose)

The participants presenting with at least one of the following relevant protocol deviations will be excluded from the hSBA PPAS1 for the priming dose:

- Participant did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria
- Participant did not receive Dose 1 (priming dose)
- Participant received a vaccine other than the one that he / she was randomized to receive

- Preparation and / or administration of vaccine was not done as per-protocol
- Participant did not receive vaccine in the proper time window
- Participant did not provide serology samples in the proper time window post-Dose 1 vaccination
- Post-Dose 1 vaccination serology samples were not drawn
- Participant received a protocol-prohibited therapy / medication / vaccine
- Serology samples did not produce a valid hSBA result (ie, results for all antigens are missing)
- Participant had other protocol violations that may have affected the participant's immune response, as determined by the clinical team before locking the database

3.3.3.2 hSBA PPAS2 for Dose 2 (booster dose)

The participants presenting with at least one of the following relevant protocol deviations will be excluded from the hSBA PPAS2 for the booster dose:

- Participant did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria
- Participant did not receive Dose 2 (booster dose)
- Participant received a vaccine other than the one that he / she was randomized to receive
- Preparation and / or administration of vaccine was not done as per-protocol
- Participant did not receive vaccine at 12 to 13 months of age and at least 180 days after Visit 1
- Participant did not provide serology samples in the proper time window post-Dose 2 vaccination
- Post-Dose 2 vaccination serology samples were not drawn
- Participant received a protocol-prohibited therapy / medication / vaccine
- Serology samples did not produce a valid hSBA result (ie, results for all antigens are missing)
- Participant had other protocol violations that may have affected the participant's immune response, as determined by the clinical team before locking the database

3.3.3.3 rSBA PPAS1 for Dose 1 (priming dose)

The definition of the rSBA PPAS1 is the same as for the hSBA PPAS1 except for the following criterion:
Serology samples did not produce a valid rSBA result (ie, results for all antigens are missing)

3.3.3.4 rSBA PPAS2 for Dose 2 (booster dose)

The definition of the rSBA PPAS2 is the same as for the hSBA PPAS2 except for the following criterion:
Serology samples did not produce a valid rSBA result (ie, results for all antigens are missing)

3.4 Statistical Analyses

3.4.1 General Considerations

The statistical analyses will be performed under the responsibility of the Sponsor's Biostatistics platform using SAS® Version 9.4 or later.

For descriptive purposes, the following statistics will be presented:

Table 3.1: Descriptive statistics produced

Disposition and follow-up description	**Categorical data**	Number of participants Percentage of participants.
	Continuous data	Mean, standard deviation, quartiles, minimum and maximum.
Baseline characteristics	**Categorical data**	Number of participants. Percentage of participants.
	Continuous data	Mean, standard deviation, quartiles, minimum and maximum.
Clinical safety results	**Categorical data**	Solicited: Number and percentage (95% CIs for main endpoints) of participants. Unsolicited: Number and percentage (95% CIs for main endpoints) of participants and number of events.
Immunogenicity results	**Categorical data (seroprotection, vaccine seroresponse, cutoff)**	Number and percentage (95% CIs) of participants.
	Continuous data (titer / data†)	Log10: Mean and standard deviation. Anti-Log10 (work on Log10 distribution, and anti-Log10 applied): Geometric mean, 95% CI of the geometric mean, quartiles, minimum, and maximum. Graphical representation by reverse cumulative distribution curve (RCDC).

The confidence interval (CI) for a single proportion will be calculated using the exact binomial method (Clopper-Pearson method, quoted by Newcombe (1), i.e., using the inverse of the beta integral with SAS®.

For immunogenicity results, assuming that Log10 transformation of the titers / data follows a normal distribution, at first, the mean and the 95% CI will be calculated on Log10 (titers / data) using the usual calculation for normal distribution (using Student's t distribution with n-1 degree of freedom), then antilog transformations will be applied to the results of calculations, to provide geometric means (GMs) and their 95% CI.

3.4.2 Coprimary Endpoint(s)

The coprimary endpoints for the evaluation of immunogenicity are:

1. Antibody titers (GMTs) against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age

   Assuming that Log10 transformation of the data follows a normal distribution, the Log10 (data) will be used for the statistical analysis and antilog transformations will be applied to the results of calculations, in order to provide the results in terms of GMT.

   The statistical methodology will be based on the use of the 2-sided 95% CI of the ratio of post-vaccination GMTs between Group 1 and Group 2. The CI will be calculated using a normal approximation of log-transformed titers.

   Non-inferiority will be demonstrated if all 4 individual null hypotheses (4 serogroups) are rejected. For each serogroup, the 2-sided 95% CI of the GMT ratio, Group 1 (MenACYW) / Group 2 (Nimenrix), should lie above 1/1.5.

2. Vaccine seroresponse against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age

   If the lower limit of the 2-sided 95% CI of the difference between the 2 proportions is > -10%, the inferiority assumption will be rejected.

   For the non-inferiority hypotheses using seroresponse rates, the CI of the difference in proportions is computed using the Wilson Score method without continuity correction.

   There are no primary safety endpoints.

See protocol Section 9.4.2. Depending on the study, several aspects have to be considered. Therefore, subsections could be created to better present the analysis, or add cross reference to other SAP sections. The following items could be considered (not exhaustive):

- Estimand
- Sensitivity analyses
- Supportive/supplementary analyses
- Subgroups of analyses, co-factors (including of stratification in the randomization) and eventually pool of data
- Multiplicity issues
- Reference to population of analysis

3.4.3 Secondary Endpoints

No hypotheses will be tested. The analyses will be descriptive.

3.4.3.1 Secondary immunogenicity endpoints:

1. Antibody titers ≥ 1:8, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
2. At Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed for meningococcal serogroups A, C, W and Y as measured by hSBA:
   - Antibody titers against meningococcal serogroups A, C, W, and Y
   - Antibody titers ≥ 1:4 and ≥ 1:8
   - ≥ 4-fold rise in antibody titer from pre-vaccination to post-vaccination
   - Vaccine seroresponse, defined as follows:
     - For a participant with a pre-vaccination titer < 1:8, a post-vaccination titer ≥ 1:16
     - For a participant with a pre-vaccination titer ≥ 1:8, a post-vaccination titer at least 4-fold greater than the pre-vaccination titer
3. Same endpoints as described in secondary endpoint #2 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
4. Same endpoints as described in secondary endpoint #2 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
5. At Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed for meningococcal serogroups A, C, W and Y as measured by rSBA:
   - Antibody titers against meningococcal serogroups A, C, W, and Y
   - Antibody titers ≥ 1:8 and ≥ 1:128
   - ≥ 4-fold rise in antibody titer from pre-vaccination to post-vaccination
   - Vaccine seroresponse defined as follows:
     - For a participant with a pre-vaccination titer < 1:8, a post-vaccination titer ≥ 1:32
     - For a participant with a pre-vaccination titer ≥ 1:8, a post-vaccination titer at least 4-fold greater than the pre-vaccination titer
6. Same endpoints as described in secondary endpoint #5 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix
7. Same endpoints as described in secondary endpoint #5 at Visit 1 (D0) before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix

In general, categorical variables will be summarized and presented by frequency counts, percentages, and CIs. The 95% CIs of point estimates will be calculated using the normal approximation for quantitative data and the exact binomial distribution (Clopper-Pearson method) for proportions. For GMTs 95% CIs of point estimates will be calculated using a normal approximation assuming they are log-normally distributed.

For secondary objective 1, the difference of titers between Group 1 and Group 2 in terms of seroprotection after Dose 1 will be calculated. The 95% CI of the difference of rates will be computed using the Wilson Score method without continuity correction (Newcombe method).

3.4.3.2 Secondary safety endpoints:

1. Presence of any unsolicited systemic adverse events (AEs) reported in the 30 minutes after vaccination.
2. Presence of solicited (pre-listed in the participant's diary card (DC) and case report form (CRF) injection site reactions up to 7 days after vaccination.
3. Presence of solicited systemic reactions (pre-listed in the participant's DC and CRF) up to 7 days after vaccination.
4. Presence of unsolicited AEs up to 30 days after vaccination.
5. Presence of SAEs [including AESIs], throughout the trial.

Safety results will be described for participants in all study groups. The main parameters for the safety endpoints will be described by 95% CI using the exact binomial method (Clopper-Person method).

See protocol Section 9.4.3. See section 3.4.2 as instructions, when applicable.

3.4.4 Exploratory Endpoints

1. Same endpoints as described secondary in endpoint #2 at Visit 1 (D01) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)
2. Same endpoints as described in secondary endpoint #2 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)
3. Same endpoints as described in secondary endpoint #2 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not)
4. At Visit 1 (D0) before Dose 1 (priming dose) and at Visit 2, 30 days after Dose 1 (priming dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix the following will be assessed according to MenB vaccination status (MenB vaccination naïve or not) for meningococcal serogroups A, C, W and Y as measured by rSBA:
    - Antibody titers against meningococcal serogroups A, C, W, and Y
    - Antibody titers ≥ 1:8 and ≥ 1:128

- ≥ 4-fold rise in antibody titer from pre-vaccination to post-vaccination
- Vaccine seroresponse defined as follows:
  - For a participant with a pre-vaccination titer < 1:8, a post-vaccination titer ≥ 1:32
  - For a participant with a pre-vaccination titer ≥ 1:8, a post-vaccination titer at least 4-fold greater than the pre-vaccination titer

5. Same endpoints as described in exploratory endpoint #4 at Visit 3 before Dose 2 (booster dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not).
6. Same endpoints as described in exploratory endpoint #4 at Visit 1 before Dose 1 (priming dose) and at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] of MenACYW conjugate vaccine or Nimenrix by MenB vaccination status (MenB vaccination naive or not).

7. Vaccine seroresponse against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age

   Vaccine seroresponse is defined as:

   - For a participant with a pre-vaccination (pre-Dose 1) titer < 1:8, a post-vaccination (post-Dose 2) titer ≥ 1:16, or
   - For a participant with a pre-vaccination (pre-Dose 1) titer ≥ 1:8, a post-vaccination (post-Dose 2) titer at least 4-fold greater than the pre-vaccination (pre-Dose 1) titer

   Superiority in terms of vaccine seroresponse will be demonstrated if the lower limit of 2-sided 95% CI of the difference between MenACYW conjugate vaccine group (Group 1) and Nimenrix vaccine group (Group 2) is > 0%. The CI of the difference in percentages will be computed using the Wilson score method without continuity correction (2).

8. Antibody titers (GMT) against meningococcal serogroups A, C, W, and Y measured by hSBA at Visit 4, 30 days after Dose 2 (booster dose) [+14 days] with MenACYW conjugate vaccine or Nimenrix, at 12-13 months of age

   For each serogroup, superiority in terms of GMTs will be demonstrated if the lower limit of 2-sided 95% CI of the GMT ratio (MenACWY conjugate vaccine group [Group 1] / Nimenrix vaccine [Group 2]) is > 1. The CI of the GMT ratio will be computed using normal approximation method following log transformation (log_{10} scale)

In general, categorical variables will be summarized and presented by frequency counts, percentages, and CIs. The 95% CIs of point estimates will be calculated using the normal approximation for quantitative data and the exact binomial distribution (Clopper-Pearson method) for proportions. For GMTs, 95% CIs of point estimates will be calculated using a normal approximation assuming they are log-normally distributed.

For exploratory endpoints 7 and 8, superiority testing will only be performed if non-inferiority is successfully demonstrated for both co-primary endpoints (GMTs and vaccine seroresponse rates for all 4 serogroups A, C, W, and Y). The detailed statistical hypotheses, sequential gatekeeping

approach, and testing procedures are described in Section 3.1 (Statistical Hypotheses). The hierarchical testing strategy follows the sequence shown in Figure 3.1.

See protocol Section 9.4.4. See section 3.4.2 as instructions, when applicable.

3.4.5 Other Safety Analyse[s]

Not applicable.

3.4.6 Subgroup analysis

Additional subgroup analyses by gender and race group, based on primary and main secondary hSBA immunogenicity endpoints and using the applicable PPAS, will be provided in Appendix 15 of the CSR.

The gender subgroup analyses will have two categories (Female and Male), and the race subgroup analyses will have four categories (White, Black or African American, Asian, and Other).

The following immunogenicity parameters will be assessed:

- GMTs with 95% CIs, with a comparison between Group 1 and Group 2 (ratio) at 30 days after dose 2
- Percentages of participants with vaccine seroresponse and 95% CIs, with a comparison between Group 1 and Group 2 (difference) at 30 days after dose 2 compared to pre-dose 1
- Percentages of participants with titer ≥ 1:8 and 95% CIs, with a comparison between Group 1 and Group 2 (difference) at 30 days after dose 1
- GMTs with 95% CIs at pre-dose 1 and 30 days after dose 2
- Percentages of participants with titer ≥ 1:8 and 95% CIs at pre-dose 1and 30 days after dose 2

The safety overview after any vaccine injections will be also described.

3.4.7 Handling of Missing Data and Outliers

3.4.7.1 Safety

No replacement will be done in all participant listings; partial and missing data will be clearly indicated as missing.

3.4.7.1.1 Immediate

For unsolicited systemic AEs, a missing response to the “Immediate” field is assumed to have occurred after the 30-minute surveillance period and will not be imputed.

3.4.7.1.2 Causal Relationship

By convention, all events reported at the injection site (either solicited or unsolicited) will be considered as related to the administered product and then referred to as reactions. In a same way,

all solicited systemic events pre-listed in the CRF are also considered as related to vaccination and will be considered as reactions.

- For unsolicited systemic AE, missing relationship will be considered as related to study vaccine at the time of analysis.
- The missing relationships to study procedures for SAEs will not be imputed.

3.4.7.1.3 Intensity

For solicited reactions, missing intensities will be handled as described in Section 4.2.1.1.1. For unsolicited AEs, missing intensities will remain missing and will not be imputed.

3.4.7.1.4 Start Date and End Date

Missing or partially missing start dates or end dates for unsolicited AEs (including SAEs) will remain missing and not be imputed. If the start date is missing or partially missing, the time of onset will be considered to be missing. Nevertheless, unsolicited AEs with missing time of onset will be included in analyses within or not within the defined time window (according to the Section 4.2.1.2.4), according to the last vaccination (computed according to the Section 4.2.1.2.3). If either the start date or end date is missing or partially missing, the duration will be considered missing.

Missing or partially missing end dates for ongoing solicited AEs will remain missing and not be imputed.

3.4.7.1.5 Action Taken

Missing actions taken will remain missing and not be imputed.

3.4.7.2 Immunogenicity

No imputation of missing values and no search for outliers will be performed. LLOQ and ULOQ management will be performed as described in Section 4.2.3.

3.4.7.3 Efficacy

No clinical efficacy data will be obtained in the study.

3.5 Interim Analyse(s)

No analyses are planned to be performed prior to the formal completion of the study.

3.6 Data Monitoring Committee (DMC)

Not applicable.

4 Complementary Information on Assessment Methods

Study assessments and procedures are detailed in Section 8 of the protocol. This section focusses on complementary/additional information not detailed in the protocol.

4.1 Complementary Information for Endpoint(s) Assessment Method(s)

Not applicable.

4.2 Complementary Information on Derived Endpoints: Calculation Methods

4.2.1 Safety

4.2.1.1 Solicited Reactions

4.2.1.1.1 Daily Intensity

All daily records for solicited reactions will be derived into daily intensity according to the following classification: None, Grade 1, Grade 2, Grade 3, or Missing (Unknown).

For the derivation of daily intensities, the following sequential steps will be applied:

1) Solicited reactions (except Fever/Pyrexia) with CRF presence recorded as “No” and with all daily records missing (Unknown), then all daily intensities will be derived as None.

2) For non-measurable solicited reactions, daily intensities will correspond to daily records reported in the clinical database. For measurable solicited reactions, the daily measurements reported in the clinical database will be converted based upon the intensity scales defined in the protocol; this assumes a reaction that is too large to measure (non-measurable, “NM”) is Grade 3.

Note: The maximum intensity on the ongoing period is derived from the record of the maximum intensity/measurement after the end of the solicited period following the rule described above.

In instances where the investigator’s assessment is available, it should be used for analysis for the corresponding days. In the absence of an investigator’s assessment for any given day, the participant’s assessment will be utilized.

Table 4.1: Solicited injection site reactions: terminology, definitions, and intensity scales – Infants and toddlers aged < 24 months

CRF term (MedDRA lowest level term [LLT])	**Injection site tenderness**	**Injection site erythema**	**Injection site swelling**
Diary card term	Tenderness	Redness	Swelling
Definition	Pain when the injection site is touched or injected limb mobilized	Presence of a redness including the approximate point of needle entry	Swelling at or near the injection site Swelling or edema is caused by a fluid infiltration in tissue or cavity and, depending on the space available for the fluid to disperse, swelling may be either soft (typically) or firm (less typical) to touch and thus can be best described by looking at the size of the swelling
CRF and DC intensity scale*	**Grade 1:** Minor reaction when injection site is touched **Grade 2:** Cries or protests when injection site is touched **Grade 3**: Cries when injected limb is moved or the movement of the injected limb is reduced	**Grade 1:** > 0 to < 25 mm **Grade 2:** ≥ 25 to < 50 mm **Grade 3:** ≥ 50 mm	**Grade 1:** > 0 to < 25 mm **Grade 2:** ≥ 25 to < 50 mm **Grade 3:** ≥ 50 mm

* For tenderness, the scale will be provided in the DC and the intensity will be transcribed in the CRF. For other injection site reactions (erythema and swelling), the classification as Grade 1, 2, or 3 will be applied at the time of statistical analysis; the scale is provided for informational purposes only. The actual size of the reaction will be reported in the CRF.
MedDRA: Medical Dictionary for Regulatory Activities

Table 4.2: Solicited systemic reactions: terminology, definitions, and intensity scales – Infants and toddlers aged < 24 months

CRF term (MedDRA lowest level term [LLT])	Fever	Vomiting	Crying abnormal	Drowsiness	Appetite lost	Irritability
Diary card term	Body temperature	Vomiting	Abnormal crying	Drowsiness	Loss of appetite	Irritability
Definition	Elevation of body temperature to ≥ 38.0°C (≥ 100.4°F)	Vomiting (emesis): forceful expulsion of the stomach contents through the mouth, associated with coordinated contraction of the abdominal and chest wall musculature. Vomiting does not include spitting up.	Inconsolable crying without a determined reason	Reduced interest in surroundings, or increased sleeping	Eating less than normal	An excessive response to stimuli: increased fussiness, whining, and fretfulness despite attempts to comfort the infant and despite caregiver responses that would normally be soothing
CRF and DC intensity scale*	**Grade 1:** ≥ 38.0°C to ≤ 38.5°C **or** ≥ 100.4°F to ≤ 101.3°F	**Grade 1:** 1 episode per 24 hours	**Grade 1:** Less than 1 hour	**Grade 1:** Sleepier than usual or less interested in surroundings	**Grade 1:** Eating less than normal	**Grade 1:** Easily consolable
	Grade 2: > 38.5°C to ≤ 39.5°C **or** > 101.3°F to ≤ 103.1°F	**Grade 2:** From 2 to 5 episodes per 24 hours	**Grade 2:** From 1 to 3 hours	**Grade 2:** Not interested in surroundings or did not wake up for a feed / meal	**Grade 2:** Missed 1 or 2 feeds / meals completely	**Grade 2:** Requiring increased attention
	Grade 3: > 39.5°C **or** > 103.1°F	**Grade 3:** At least 6 episodes per 24 hours or requiring intravenous hydration (fluids administered in the arm or leg)	**Grade 3:** More than 3 hours	**Grade 3:** Sleeping most of the time or difficult to wake up	**Grade 3:** Refuses at least 3 feeds / meals or refuses most feeds / meals	**Grade 3:** Inconsolable (cannot be comforted)

* For all reactions (except fever), the scale will be provided in the DC and the intensity will be transcribed in the CRF. For fever, the body temperature will be recorded, and the classification as Grade 1, 2, or 3 will be assigned at the time of the statistical analysis based on the unit used to measure the body temperature and the intensity scale.

4.2.1.1.2 Maximum Intensity

Maximum overall intensity is derived from the daily intensities computed as described in Section 4.2.1.1.1 and is calculated as the maximum of the daily intensities over the period considered.

4.2.1.1.3 Presence

Presence is derived from the maximum overall intensity over the time period considered:

- None: No presence
- Grade 1, Grade 2, or Grade 3: Presence
- Missing or Unknown: Missing presence

Participants with at least one non-missing presence for a specific endpoint will be included in the analysis. Conversely, those without a non-missing presence will not be included in the analysis of the endpoint.

The time period is displayed as D1-D4, D5-D8, D9 and later.

4.2.1.1.4 Time of Onset

Time of onset is derived from the daily intensities computed as described in Section 4.2.1.1.1. It corresponds to the first day with intensity of Grade 1, Grade 2, or Grade 3.

Note: If a reaction is not continuous (i.e., reaction occurs over two separate periods of time intervened by at least one daily intensity Missing or None) then the time of onset is the first day of the first occurrence.

Time of onset period is displayed as, D1-D4, D5-D8.

4.2.1.1.5 Number of Days of Occurrence During the Solicited Period

Number of days of occurrence over the solicited period (D0 to D7) considered is derived from the daily intensities as described in 4.2.1.1.1. It corresponds to the number of days with one of daily intensities of Grade 1, Grade 2, or Grade 3. Number of days of occurrence on the solicited period with a specified intensity (e.g, Grade 3) may also be derived.

4.2.1.1.6 Overall Number of Days of Occurrence

If a reaction is ongoing at the end of the solicited period, then the overall number of days of occurrence after each vaccination is derived from the daily intensities and the stop date of the reaction after the end of the solicited period. The overall number of days of occurrence is:

(The stop date of the solicited event – last vaccination date) + (number of days of occurrence within the solicited period) – length of the solicited period + 1

If stop date of the solicited reaction is missing or incomplete (contains missing data), the overall number of days of occurrence will be considered as Missing.

4.2.1.1.7 Ongoing

Ongoing is derived from the last daily intensity of the solicited period computed as described in Section 4.2.1.1.1 and the maximum intensity on the ongoing period. The investigator's ongoing flag is not used because the measurement would determine the ongoing status of the reaction.

- Ongoing: if the last daily intensity of the solicited period is at least Grade 1 and the maximum intensity on the ongoing period is at least Grade 1
- Not ongoing: if the last daily intensity of the solicited period is None or the maximum intensity of the ongoing period is None.
- Missing: all other conditions (in this case, it is not included in the denominator of the ongoing analysis in the safety tables)

4.2.1.2 Unsolicited AEs

4.2.1.2.1 Presence

An observation will be considered an event if it has at least a verbatim term and is not a Grade 0 intensity event.

Grade 0 events are not included in safety analysis but are included in separate listings.

4.2.1.2.2 Intensity

Intensity will be derived according to the following classification: None, Grade 1, Grade 2, Grade 3, or Missing.

If the unsolicited AE is measurable and its preferred term is part of the list of solicited reactions, then the measurement is derived based upon and following the same rule of the intensity scales defined in the protocol for that measurable injection site or systemic reaction.

Intensity for the other unsolicited AEs will correspond to the value reported in the CRF.

The maximum intensity corresponds to the highest intensity for a unique term.

4.2.1.2.3 Last Vaccination

Last vaccination before an unsolicited AE is derived from the start date of the unsolicited AE provided in the CRF and is calculated as follows:

- If an unsolicited AE has a complete start date and different to any of the vaccination dates, the start date is used to determine the last vaccination before the unsolicited AE
- If an unsolicited AE has a partially missing start date and there is clear evidence about the last vaccination from the partially missing start date, then the start date is used to determine the last vaccination before the unsolicited AE. Situations may happen as:
  - If the start date of AE has missing Day and non-missing Month and Year:
    - If the "Month/Year of vaccination (i) date" < "Month/Year of AE start date" < "Month/Year of vaccination (i+1) date", then it is clear that the last vaccination before this unsolicited AE is the vaccination i.

- If the "Month/Year of vaccination (i) date" < "Month/Year of AE start date" and there is no injection (i+1), then it is clear that the last vaccination before this unsolicited AE is the vaccination i.

- If the start date of AE has missing Day and Month and non-missing Year:
  - If the "Year of vaccination (i) date" < "Year of AE start date" < "Year of vaccination (i+1) date", then it is clear that the last vaccination before this unsolicited AE is the vaccination i.
  - If the "Year of vaccination (i) date" < "Year of AE start date" and there is no injection (i+1), then it is clear that the last vaccination before this unsolicited AE is the vaccination i.

- If the start date is missing or partially missing (with no clear evidence about the last vaccination), or equal to any vaccination date, then the visit number in the "Appeared after Visit" or similar field, is used to determine the last vaccination before the unsolicited AE.

4.2.1.2.4 Time of Onset

Time of onset is derived from the start date of the unsolicited AE and the date of last vaccination as described in Section 4.2.1.2.3:

Time of Onset = start date of the unsolicited AE - date of last vaccination before the unsolicited AE + 1

The time of onset is considered as missing only if one or both dates are missing or partially missing.

The unsolicited AEs will be analyzed "Within 30 days" after each vaccination, which corresponds to AEs with a time of onset between 1 and 31 days.

Unsolicited AEs that occurred before vaccination (negative time of onset) will not be included in analysis but will be listed separately.

Unsolicited AE which is non-serious, non-AESI that occurred with a time of onset higher than defined above (i.e., >30 days after vaccination) will not be included in analysis but will be listed separately.

- For unsolicited AE with missing day, month and year, the unsolicited AE will be classified as "Within 30 days"
- For unsolicited AE with partially missing start date, the partial available information will be used to determine if this AE is classified "Within 30 days" or "Not within 30 days". An AE will be categorized as "Not within 30 days" only if there is clear evidence from the partially missing start date that this AE happens before the first vaccination or after the last vaccination + 30 days. In all other situations, this AE is considered as "Within 30 days". Situations may happen as:
  - If the start date of AE has missing Day and non-missing Month and Year:
    - If the "Month/Year of AE start date" < "Month/Year of first vaccination date", then it is clear that this unsolicited AE happened before the first vaccination and this unsolicited AE will not be included in the analysis but will be listed separately.

- Else if the "Month/Year of last vaccination date" <= "Month/Year of AE start date" <= "Month/Year of (last vaccination date + 30 days)", then this unsolicited AE will be categorized as "Within 30 days".
- Else if the "Month/Year of AE start date" > "Month/Year of (last vaccination date + 30 days),", then this unsolicited AE will be categorized as "not within 30 days". If the AE is non-serious, non-AESI, then it will not be included in the analysis but will be listed separately.

- If the start date of AE has missing Day and Month and non-missing Year:
  - If the "Year of AE start date" < "Year of first vaccination date", then it is clear that this unsolicited AE happens before the first vaccination and this unsolicited AE will not be included in the analysis but will be listed separately.
  - Else if the "Year of last vaccination date" <= "Year of AE start date" <= "Year of (last vaccination date + 30 days),", then this unsolicited AE will be categorized as "Within 30 days".
  - Else if the "Year of AE start date" > "Year of (last vaccination date + 30 days),", then this unsolicited AE will be categorized as "not within 30 days." If the AE is non-serious, non-AESI, then it will not be included in the analysis but will be listed separately.

Time of onset period is displayed as D1-D4, D5-D8, D9-D15, D16 or later, and Missing.

4.2.1.2.5 Duration

Duration is derived from the start and stop dates of the unsolicited AE:

Stop date of unsolicited AE - start date of unsolicited AE + 1.

The duration should be considered as missing only if one or both of the start and stop dates of the unsolicited non-serious AE is missing or partially missing.

4.2.1.2.6 Serious Adverse Events

An event will be considered as a serious event if "Yes" is checked for "Serious" in the CRF.

SAEs will be analyzed throughout the study using the following periods:

- Within 7 days after vaccination
- Within 30 days after vaccination
- During the study (i.e., all SAEs occurred during the study)

4.2.1.2.7 Adverse Events of Special Interest

An event will be considered as an AESI if "Yes" is checked for "Is the event an AESI?" in the CRF.

AESI will be analyzed throughout the study using the following periods:

- Within 7 days after vaccination
- Within 30 days after vaccination
- During the study (i.e., all AESIs occurred during the study)

4.2.2 Other Safety Endpoints

4.2.2.1 Action Taken

This information will be summarized as collected, including missing observations. No derivation or imputation will be done.

4.2.2.2 Seriousness

This information will be summarized as collected. No derivation or imputation will be done.

4.2.2.3 Outcome

This information will be summarized as collected. No derivation or imputation will be done.

4.2.2.4 Causal Relationship

This information will be summarized as collected in the field "Relationship to IMP".

4.2.2.5 Adverse Events Leading to Study Discontinuation

This information will be summarized as collected. A flag is available in the clinical database for all AEs in order to identify AEs leading to discontinuation before the end of active phase.
In general, the items that are counted are:

- Disposition table: A participant who, on the "End of Study" form question "What was the participant's status?" has "Adverse Event" checked.
- Safety overview table: A participant who has either on the "End of Study" form, question" What was the participant's status?" has "Adverse Event" checked or lists a solicited AE that has "Caused Study Termination" checked that is at least Grade 1 or an unsolicited AE that has "Caused Study Discontinuation" checked that is at least Grade 1 or missing and is within the time period indicated.
- System Organ Class (SOC)/Preferred Term (PT) table: A solicited AE that has "Caused Study Termination" checked that is at least Grade 1 or an unsolicited AE that has "Caused Study Discontinuation" checked that is at least Grade 1 or missing and is within the time period indicated.

4.2.3 Immunogenicity

4.2.3.1 Computed Values for Analysis

To appropriately manage extreme values (undetectable responses < the lower limit of quantitation [LLOQ] and ≥ the upper limit of quantitation [ULOQ]) for analysis purposes, the following computational rule is applied to the values provided in the clinical database for each blood sample drawn:

- If a value is < LLOQ, then use the computed value LLOQ/2
- If a value is between ≥ LLOQ and < ULOQ, then use the value
- If a value is ≥ ULOQ, then use the computed value ULOQ

4.2.3.2 Seroprotection

For each meningococcal serogroup (A, C, W, and Y) measured by hSBA:

- If the computed value is ≥ 1:8, then the derived seroprotection indicator will be “Yes” for that test; otherwise, seroprotection will be "No.” Note: If the computed value is missing, seroprotection will be missing.

4.2.3.3 Fold-rise

The derived endpoint fold-rise is driven by both baseline and post-baseline computed values and is computed as follows:

- Calculate the fold-rise of values as the ratio of the post-baseline computed value divided by the baseline computed value

Note: If the baseline or post-baseline value is missing, then fold-rise is missing.

4.2.3.4 Seroresponse

4.2.3.4.1 hSBA Vaccine Seroresponse

The derived hSBA vaccine seroresponse indicator for serogroups A, C, W, and Y will be taken as “Yes” if:

When evaluating the immunogenicity of MenACYW conjugate vaccine compared with Nimenrix (Group 1 and Group 2, respectively).

- For a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:16
- For a participant with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer

4.2.3.4.2 rSBA Vaccine Seroresponse

The derived rSBA vaccine seroresponse indicator for serogroups A, C, W, and Y will be taken as "Yes" if:

When evaluating the immunogenicity of MenACYW conjugate vaccine compared with Nimenrix (Group 1 and Group 2, respectively).

- For a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:32
- For a participant with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer

4.2.4 Efficacy

Not applicable.

4.2.5 Derived Other Variables

4.2.5.1 Age for Demographics

The age of a participant in the study is the calendar age in months at the time of inclusion. The age collected in the CRF is displayed as an integer.

4.2.5.2 Duration of a Participant in the Trial

The duration of a study participant participation in the study is computed as follows: Maximum (Termination date, Follow-up date) - V01 date + 1.

4.2.5.3 Duration of the Study

The durations are computed in days as follows: Latest period date - Earliest period date + 1.

5 Changes in the Conduct of the Trial or Planned Analyses

The PPAS criterion for booster dose "*Participant did not receive vaccine in the proper time window*" is clarified as "*Participant did not receive vaccine at 12 to 13 months of age and at least 180 days after Visit 1*" to specify both an age-based window and a minimum interval requirement for receipt of the booster dose. This clarification was implemented to align with clinical practice for pediatric vaccine schedules, in which minimum interval requirements are emphasized, and maximum intervals are generally not defined, except in rare circumstances (e.g., oral typhoid vaccine).

Additionally, to further characterize the immunogenicity profile of MenQuadfi, an exploratory analysis of superiority based on hierarchical testing strategy will be implemented. This strategy aims to explore the potential superiority of MenQuadfi over Nimenrix across the same four serogroups, using a gatekeeping approach to control for Type I error inflation.

6 Supporting Documentation

6.1 Appendix 1 List of Abbreviations

AE	Adverse event
AESI	Adverse event of special interest
AR	Adverse reaction
CRF	Case report form
DMC	Data Monitoring Committee
FAS	Full analysis set
GM	Geometric mean
GMT	Geometric mean of titer
hSBA	serum bactericidal assay using human complement
IMP	Investigational Medicinal Product
LLOQ	Lower level of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
NA	Not applicable
NC	Not computed
PPAS	Per-protocol analysis set
RCDC	Reverse cumulative distribution curve
rSBA	serum bactericidal assay using baby rabbit complement
SAE	Serious adverse events
SafAS	Safety analysis set
SAP	Statistical analysis plan
SOC	(Primary) System organ class
PT	Preferred term
TLF	Tables, listings and figures
ULOQ	Upper level of quantitation

7 References

1. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med. 1998;17(8):857-72.

2. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Stat Med. 1998;17(8):873-90.

3. General Best Practices for Immunization | Vaccines & Immunizations | CDC