Amsterdam, 13 November 2025
EMADOC-1700519818-2390991
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

MenQuadfi

Meningococcal Group A, C, W and Y conjugate vaccine

Procedure no: EMA/PAM/0000293638

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	Start of procedure	15 September 2025	15 September 2025
☐	CHMP Rapporteur AR	20 October 2025	21 October 2025
☐	CHMP comments	3 November 2025	3 November 2025
☐	Updated CHMP Rapporteur AR	6 November 2025	6 November 2025
☒	CHMP outcome	13 November 2025	13 November 2025

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1. Introduction

On 26 August 2025, the MAH (Sanofi Winthrop Industrie) submitted a completed paediatric study for MenQuadfi, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as part of the post-authorisation measure.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The European Marketing Authorisation for MenQuadfi has been granted by the European Commission on 18 November 2020 for active immunization of individuals from the age of 12 months and older against invasive meningococcal disease caused by *Neisseria (N.) meningitidis* serogroups A, C, W, and Y.

The MAH stated that study MEQ00074 "A Phase III, open-label, single-centre study to describe the immunogenicity and safety of a single dose of MenACYW Conjugate Vaccine in participants aged 12 months and older in Vietnam" is a stand-alone study, has not been included in the MenQuadfi Paediatric Investigational Plan (PIP) and was submitted as according to Article 46 of the regulation, the Marketing Authorisation Holders (MAHs) are requested to submit information on studies conducted in children of authorised medicines that have been completed since 26 January 2007 and are sponsored by the MAH, within 6 months of completion of each study.

Of note, study MEQ00074 was conducted in a population covered by the current license in the EU (12 months of age and older) and has not been included in the data package that has been submitted for the currently ongoing type II variation intended to extend the indication to individuals aged 6 weeks to below 12 months.

No amendments to the Product Information have been submitted as part of the current procedure.

2.2. Information on the pharmaceutical formulation used in the study

The formulation of the MenACYW conjugate vaccine (MenQuadfi) as solution for injection is approved for the active immunization of individuals from the age of 12 months and older against invasive meningococcal disease caused by *Neisseria (N.) meningitidis* serogroups A, C, W, and Y (as 10µg polysaccharides each and with 55µg conjugated tetanus toxoid carrier protein).

Name of the medicinal product: MenQuadfi

Pharmaceutical form: Solution for injection

INN/active substances:

Neisseria meningitidis group A polysaccharide	10 micrograms
Neisseria meningitidis group C polysaccharide	10 micrograms
Neisseria meningitidis group Y polysaccharide	10 micrograms
Neisseria meningitidis group W-135 polysaccharide	10 micrograms
Conjugated to tetanus toxoid carrier protein	55 micrograms

ATC Code: J07AH08

Agency Product Number: EMEA/H/C/005084

EU Number: EU/1/20/1483

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study MEQ00074 – A Phase III, open-label, single-centre study to describe the immunogenicity and safety of a single dose of MenACYW Conjugate Vaccine in participants aged 12 months and older in Vietnam.

2.3.2. Clinical study

Study MEQ00074 – A Phase III, open-label, single-centre study to describe the immunogenicity and safety of a single dose of MenACYW Conjugate Vaccine in participants aged 12 months and older in Vietnam.

Description

Study MEQ00074 is a Phase III, open-label, single-centre study (1 main site [Centre 0001] with 3 satellite sites [participant enrolment took place at Centres 0003 and 0004 while sample processing was carried out at Centre 0002]), to describe the immunogenicity and safety of a single dose of MenACYW Conjugate Vaccine (MenQuadfi) in participants aged 12 months and older in Vietnam.

MEQ00074 was conducted from 18 January 2024 (first participant first visit) to 31 March 2024 (last participant last visit).

Database lock for the provided CSR (Final CSR Version 1.0, dated 8 August 2025) was 17 April 2025.

Methods

Study design

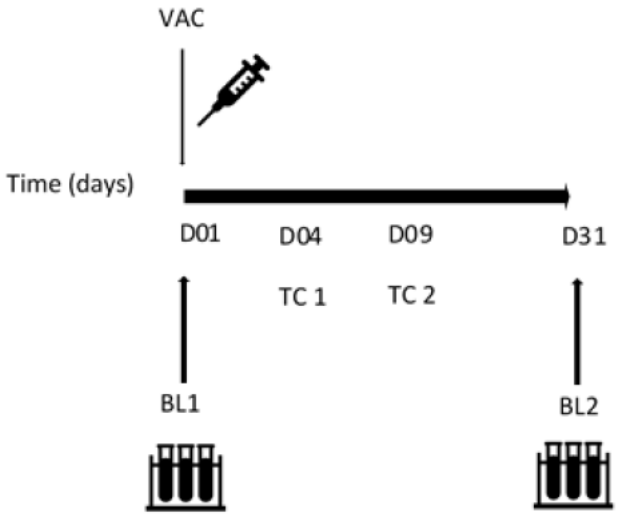
A total of 446 participants were to be enrolled with the aim to obtain a total of 400 evaluable participants:

- 223 participants were 12-23 months of age
- 223 participants were 24 months of age and above. To ensure all sub-groups were represented, within the 24 months of age and above group, a minimum of 20 participants were enrolled from each of the sub-groups mentioned below:
    - Children 2 to 9 years of age
    - Adolescents 10 to 17 years of age
    - Adults 18 to 55 years of age
    - Older adults 56 years and above

Blood sampling:

All participants were to provide blood samples for immunogenicity assessments at baseline (prevaccination, Visit 1 on D01) and 443/446 participants provided blood samples at 1-month postvaccination on Visit 2 (D31 [+14 days]).

Figure 1: Study design



BL: blood sample; TC: telephone call; VAC: vaccination

Safety collection:

Solicited adverse event (AE) information was collected for vaccination day and 7 days after vaccination (D01-D08); unsolicited AE information was collected from Visit 1 (D01) to Visit 2 (D31 [+14 days]), and serious adverse event (SAE) information (including adverse events of special interest [AESIs]) was collected throughout the study period.

Table 1: Schedule of activities (as per Protocol version 1.0 dated 29 March 2021)

Phase III Study, 2 Visits, 2 Telephone calls, 1 Vaccination, 2 Blood Samples, 30 to 44 Days' Duration Per Participant

Visit/Contact	*Collection of information in the CRF*	Visit 1	TC1	TC2	Visit 2
Study timelines (days)		D01	D04 Visit 1 + 3 days	D09 Visit 1 + 8 days	D31 Visit 1 + 30 days
Time windows (days)		-	+2 days	+2 days	+14 days
Visit procedures:					
Informed consent/assent*	X	X			
Inclusion/exclusion criteria	X	X			
Collection of demographic data	X	X			
Urine pregnancy test (if applicable)		X			
Collection of significant medical history	X	X			
Physical examination (including pre-vaccination temperature)**		X			
Review of temporary contraindications for blood sampling †	X				X
Blood sampling (BL) ‡ [3 mL]	X	BL0001			BL0002
Vaccination	X	X			
Immediate surveillance (30 min)	X	X			
Information on DC provided		X			
Telephone call (TC) §	X		X	X	
Collection of solicited injection site and systemic reactions**	X	Day 1 to Day 8			
Collection of unsolicited AEs	X	Visit 1 to Visit 2			
DC reviewed and information collected					X
Visit procedures:					
Collection of reportable concomitant medications	X	X			X
Collection of SAEs, including AESIs ††	X	To be reported at any time during the study period			
Collection of pregnancies	X	To be reported at any time during the study period			
End of study participation record ‡‡	X				X

Abbreviations: AE: adverse event; AESI: adverse events of special interest; BL: blood sampling; CRF: case report form; DC: diary card; SAE: serious adverse event; TC: telephone call

* Assent required for participants aged 12 to 15 years.

**Physical examination should be performed as per standard of care. If a routine examination had been performed within the last week by the Investigator, a sub-Investigator, or a licensed nurse practitioner, it does not need to be repeated unless there were some changes in health status, in which case it may be limited to the affected area. Temperature needs to be measured before vaccination and daily during the 7 days after vaccination and recorded in the DC.

†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 appropriately documented that the sample was taken less than 3 days after stopping antibiotic treatment.

‡Blood sample at Visit 1 to be drawn before administration of the vaccine.

§The first telephone call will be made 3 days to 5 days after the vaccination. The second telephone call will be made 8 days to 10 days after the vaccination. If Day 04 (+ 2 days) and Day 09 (+2 days) fall on a weekend or holiday, the telephone call may be made on the following business day. During this telephone call, the staff will find out whether the participant experienced any SAE (including any AESI) not yet reported, and will remind the participant/participant's parent/legally acceptable representative to continue using the DC, bring the DC to the study center at the next visit, and confirm the date and time of the next visit.

** Solicited injection site and systemic reactions will be recorded from the day of vaccination through 7 days after vaccination.

††AESI will be collected throughout the study as SAEs to ensure that the events are communicated to the Sponsor in an expedited manner and followed up until the end of the follow-up period or resolution, as per the assigned causal relationship

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

Study participants

As per Protocol version 1.0 dated 29 March 2021.

Inclusion Criteria

Participants are eligible for the study only if all of the following criteria are met:

- Aged 12 months and above on the day of inclusion.

Adults (aged 18 and above on the day of inclusion):

- A female participant is eligible to participate if she is not pregnant or breastfeeding and one of the following conditions applies:
    - Is of non-childbearing potential. To be considered of non-childbearing potential, a female must be pre-menarche (Pre-menarche females will declare by themselves that they have not yet started menstruation. If a young female participant reaches menarche during the study, then she is to be considered as a woman of childbearing potential from that time forward) or post-menopausal for at least 1 year, or surgically sterile.

      OR

    - Is of childbearing potential and agrees to use an effective contraceptive method or abstinence from at least 4 weeks prior to study intervention administration until at least 4 weeks after study intervention administration.

      A female participant of childbearing potential must have a negative highly sensitive pregnancy test (urine) within 1 week before the dose of study intervention.
- Informed consent form has been signed and dated.
- Able to attend all scheduled visits and to comply with all study procedures.

Adolescents (aged 10 to 17 years on the day of inclusion ["10 to 17 years" means from the day of the 10th birthday to the day before the 18th birthday]):

- A female participant is eligible to participate if she is not pregnant or breastfeeding and one of the following conditions applies:
    - Is of non-childbearing potential. To be considered of non-childbearing potential, a female must be pre-menarche (Pre-menarche females will declare by themselves that they have not yet started menstruation. If a young female participant reaches menarche during the study, then she is to be considered as a woman of childbearing potential from that time forward).

      OR

    - Is of childbearing potential and agrees to use an effective contraceptive method or abstinence from at least 4 weeks prior to study intervention administration until at least 4 weeks after study intervention administration.

      A female participant of childbearing potential must have a negative highly sensitive pregnancy test (urine) within 1 week before the dose of study intervention.

- Informed consent form has been signed and dated by both the participant (if aged 16 to 18 years) and the parent(s) or another legally acceptable representative and by an independent witness, if required by local regulations Assent form has been signed and dated by the participant (assent form required for participants aged 12 to 15 years) or verbal consent has been obtained (for participants aged 10 to 11 years), and informed consent form has been signed and dated by the parent(s) or another legally acceptable representative and by an independent witness, if required by local regulations.
- Participant and parent/legally acceptable representative are able to attend all scheduled visits and to comply with all study procedures.

Children (aged 2 to 9 years on the day of inclusion ["2 to 9 years" means from the day of the 2nd birthday to the day before the 10th birthday]):

- Verbal consent has been obtained (for participants aged 7 to 9 years), and informed consent form has been signed and dated by the parent(s) or another legally acceptable representative and by an independent witness, if required by local regulations.
- Participant and parent/legally acceptable representative are able to attend all scheduled visits and to comply with all study procedures.

Toddlers (aged 12 to 23 months on the day of inclusion ["12 to 23 months" means from the 12th month after birth to the day before the 25th month after birth]):

- Informed consent form has been signed and dated by the parent(s) or other legally acceptable representative and by an independent witness if required by local regulations.
- Participant and parent/legally acceptable representative are able to attend all scheduled visits and to comply with all study procedures.

Exclusion Criteria

Participants are not eligible for the study if any of the following criteria are met:

Adults (aged 18 years and above), Adolescents (aged 10 to 17 years), Children (aged 2 to 9 years) and Toddlers (aged 12 to 23 months)

- Participation at the time of study enrolment (or in the 4 weeks preceding the study intervention administration) or planned participation during the present trial period in another clinical study investigating a vaccine, drug, medical device, or medical procedure.
- Receipt of any vaccine in the 4 weeks preceding the study intervention administration or planned receipt of any vaccine in the 4 weeks following study intervention administration except for influenza vaccination, which may be received at least 2 weeks before or after study vaccine. This exception includes monovalent pandemic influenza vaccines and multivalent influenza vaccines.
- Previous vaccination against meningococcal disease with either the study vaccine or another vaccine (i.e., polysaccharide, or conjugate meningococcal vaccine containing serogroups A, C, W, or Y; or meningococcal B serogroup-containing vaccine).
- Receipt of immune globulins, blood or blood-derived products in the past 3 months.
- History of any N. meningitidis infection, confirmed either clinically, serologically, or microbiologically.

- At high risk for meningococcal disease during the study (specifically but not limited to participants with persistent complement deficiency, with anatomic or functional asplenia, or participants traveling to countries with high endemic or epidemic disease).
- Known systemic hypersensitivity to any of the study intervention components, or history of a life-threatening reaction to the study intervention used in the study or to a product containing any of the same substances.
- Personal history of Guillain-Barré syndrome.
- Bleeding disorder, or receipt of anticoagulants in the 3 weeks preceding inclusion, contraindicating intramuscular injection.
- Deprived of freedom by an administrative or court order, or in an emergency setting, or hospitalized involuntarily.
- Chronic illness that, in the opinion of the Investigator, is at a stage where it might interfere with study conduct or completion (Chronic illness may include, but is not limited to, cardiac disorders, renal disorders, auto-immune disorders, diabetes, psychiatric disorders or chronic infection).
- Moderate or severe acute illness/infection (according to Investigator judgment) on the day of vaccination or febrile illness (axillary temperature ≥ 37.5°C) or hypothermia (axillary temperature ≤ 35.5°C) on the day of vaccination. A prospective participant should not be included in the study until the condition has resolved or the febrile event has subsided.
- Receipt of oral or injectable antibiotic therapy within 72 hours prior to the first blood draw.

Adults (aged 18 years and above) and Adolescents (aged 10 to 17 years)

- Known or suspected congenital or acquired immunodeficiency; or receipt of immunosuppressive therapy, such as anti-cancer chemotherapy or radiation therapy, within the preceding 6 months; or long-term systemic corticosteroid therapy (prednisone or equivalent for more than 2 consecutive weeks within the past 3 months).
- Personal history of an Arthus-like reaction after vaccination with a tetanus toxoid-containing vaccine within at least 10 years of the proposed study vaccination.
- Self-reported thrombocytopenia, contraindicating intramuscular injection.
- Alcohol, prescription drug, or substance abuse that, in the opinion of the Investigator, might interfere with the study conduct or completion.
- Identified as an Investigator or employee of the Investigator or study centre with direct involvement in the proposed study, or identified as an immediate family member (i.e., parent, spouse, natural or adopted child) of the Investigator or employee with direct involvement in the proposed study.

Children (aged 2 to 9 years)

- Known or suspected congenital or acquired immunodeficiency; or receipt of immunosuppressive therapy, such as anti-cancer chemotherapy or radiation therapy, within the preceding 6 months; or long-term systemic corticosteroid therapy (prednisone or equivalent for more than 2 consecutive weeks within the past 3 months).

- Personal history of an Arthus-like reaction after vaccination with a tetanus toxoid-containing vaccine.
- Thrombocytopenia as reported by the parent/legally acceptable representative, or suspected thrombocytopenia contraindicating intramuscular injection.
- Identified as a natural or adopted child of the Investigator or employee with direct involvement in the proposed study.

Toddlers (aged 12 to 23 months)

- Known or suspected congenital or acquired immunodeficiency; or receipt of immunosuppressive therapy, such as anti-cancer chemotherapy or radiation therapy, within the preceding 6 months; or long-term systemic corticosteroid therapy (prednisone or equivalent for more than 2 consecutive weeks since birth).
- Personal history of an Arthus-like reaction after vaccination with a tetanus toxoid-containing vaccine.
- Thrombocytopenia as reported by the parent/legally acceptable representative, or suspected thrombocytopenia contraindicating intramuscular injection.
- Identified as a natural or adopted child of the Investigator or employee with direct involvement in the proposed study.

If the participant has a primary physician who is not the Investigator, the site is recommended to contact this physician with the participant's consent to inform him/her of the participant's participation in the study. In addition, the site may ask this primary physician to verify exclusion criteria relating to previous therapies, such as receipt of blood products or previous vaccines.

Treatments

Table 2: Study intervention administered

Intervention Name	**MenACYW conjugate vaccine**: Meningococcal Polysaccharide (Serogroups A, C, W, and Y) Tetanus Toxoid Conjugate Vaccine (Sanofi Pasteur Inc., Swiftwater, PA, USA)
Use	Investigational
IMP and NIMP	IMP
Type	Vaccine
Dose Formulation	Liquid solution
Unit Dose Strength(s)	Each dose of MenACYW conjugate vaccine contains the following components: Meningococcal capsular polysaccharides: • Serogroup A*: 10 µg • Serogroup C*: 10 µg • Serogroup Y*: 10 µg • Serogroup W*: 10 µg * Conjugated to tetanus toxoid protein carrier: 55 µg** • ***Tetanus toxoid protein quantity is approximate and dependent on the polysaccharide-to-protein ratio for the conjugates used in each formulation*
Excipients/Diluent	Sodium acetate buffered saline solution
Dosage Level	0.5 mL per dose
Number of Doses / Dosing Interval	1 dose
Route of Administration	Intramuscular injection
Site of Administration	Anterolateral area of the thigh or deltoid muscle
Sourcing	Provided by the Sponsor
Packaging and Labeling	MenACYW conjugate vaccine (single-dose vial) was supplied with investigational labeling and packaging according to national regulations. Each single dose of study interventions was identified by a unique number on the detachable label and on the outer carton label. The detachable label was for the sites to attach to the source documents. See the Operating Guidelines for additional label detail.
Current/Former Name or Alias	MenQuadfi™
Batch Number	VA032792
Storage Conditions	Study interventions were stored in a refrigerator at a temperature ranging from +2°C to +8°C. The study interventions were not to be frozen.

Abbreviations, IMP: investigational medicinal product; NIMP: non-investigational medicinal product

Objectives

Immunogenicity

To describe the antibody responses to meningococcal serogroups A, C, W, and Y before and 30 days after the administration of a single dose of MenACYW conjugate vaccine.

Safety

To describe the safety profile of a single dose of MenACYW conjugate vaccine.

Outcomes/endpoints

Immunogenicity

- Antibody titres against meningococcal serogroups A, C, W, and Y measured by serum bactericidal assay using human complement (hSBA) were assessed before and 30 days (+14 days) after vaccination with a single dose of MenACYW conjugate vaccine.

Safety

The safety profile was evaluated within 30 days (+14 days) after vaccination. The following endpoints were used for the evaluation of safety:

- Presence of any unsolicited systemic adverse events (AEs) reported in the 30 minutes after vaccination.
- Presence of solicited (prelisted in the participant's diary card [DC] and case report form [CRF]) injection site and systemic reactions starting any time from the day of vaccination through 7 days after vaccination.
- Presence of unsolicited (recorded in a DC) non-serious AEs up to 30 days after vaccination; unsolicited nonserious AEs occurring after Day 31 (D31) are presented in a specific listing.
- Presence of serious adverse events (SAEs) (including adverse events of special interest [AESIs]) throughout the study, i.e. from D01 (vaccination) to the last study day D31; SAEs occurring after D31 were also to be reported if they were considered related to vaccination with the investigational medicinal product (IMP).

Depending on the items, the endpoints recorded or derived included: 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 criterion.

Sample size

A total of 446 participants were to be enrolled in the study, 223 participants were to be enrolled in age category 12 months to 23 months, 223 participants were to be enrolled in age category 24 months and above. An estimated 10% non-adherence rate from enrolment resulted in approximately 400 evaluable participants in total, and 200 evaluable participants in each age category (12 months – 23 months, ≥ 24 months).

The overall evaluable study cohort (N=400) provided a probability of approximately 95% of observing any AE (at least 1 occurrence) with a true incidence of 0.75%.

For participants aged 12 to 23 months, 200 participants provided a probability of approximately 95% of observing any AE (at least 1 occurrence) with a true incidence of 1.5%.

For participants aged 24 months and above, 200 participants provided a probability of approximately 95% of observing any AE (at least 1 occurrence) with a true incidence of 1.5%.

Table 3: Study MEQ000074 sample size

	MenACYW 12-23 months of age	MenACYW 24 months of age and above	MenACYW All
Planned	223	223	446
Actual	223	224	447
FAS	220	223	443
SafAS	223	223	446
PPAS	200	221	421

Abbreviations: FAS, Full Analysis Set, PPAS, Per-Protocol Analysis Set; SafAS, Safety Analysis Set
FAS: Participants who received the study vaccine and had a valid post-vaccination serology result.
SafAS: Participants who received the study vaccine and had any safety data available.
PPAS: Subset of the FAS. Participants presenting with at least 1 of the following relevant protocol deviations were excluded from the PPAS:

- Participants did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria.
- Participant did not receive vaccine.
- Preparation and / or administration of vaccine was not done as per-protocol.
- Participants did not provide the post-vaccination serology sample at Visit 2 in the proper time window, or a post-vaccination serology sample was not drawn.
- Participants received a category 2 or 3 protocol-prohibited therapy / medication / vaccine.
- Participants had other protocol violations that affected the participant's immune response, as determined by the clinical team before locking the database.

In addition to the reasons listed above, participants were excluded from the PPAS if their Visit 2 serology sample did not produce a valid test result.

Randomisation and blinding (masking)

Participants were not randomized.

This was a single-arm study that was not blinded.

Statistical Methods

As per Protocol version 1.0 dated 29 March 2021:

The following populations are defined for immunogenicity and safety analyses:

Table 4: Analysis sets

Analysis Set	Description
Full analysis set (FAS)	Participants who received the study vaccine and had a valid post-vaccination serology result.
Per-protocol analysis set (PPAS)	Subset of the FAS. Participants presenting with at least one of the following relevant protocol deviations will be excluded from the PPAS: • Participants did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria • Participant did not receive vaccine • Preparation and / or administration of vaccine was not done as per-protocol • Participants did not provide the post-dose serology sample at Visit 2 in the proper time window or a post-dose serology sample was not drawn • Participants received a category 2 or 3 protocol-prohibited therapy / medication / vaccine • Participants had other protocol violations that affected the participant's immune response, as determined by the clinical team before locking the database. In addition to the reasons listed above, participants will also be excluded from the PPAS if their Visit 2 serology sample did not produce a valid test result. In the event of a local or national immunization program with a pandemic COVID-19 vaccine, participants who receive COVID-19 vaccine between an IMP dose and the collection of blood will not be withdrawn from the study, but will be excluded from PPAS.
Safety analysis set (SafAS)	Participants who have received the study vaccine and have any safety data available.

Immunogenicity Endpoint

No statistical hypotheses will be tested. Descriptive statistics will be provided for the antibody titres against meningococcal serogroups A, C, W, and Y by using hSBA before and 30 days after a single dose of meningococcal conjugate vaccine.

All immunogenicity analyses will be performed on the PPAS. Additional immunogenicity analyses will be performed for exploratory purposes on the FAS.

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 percentages. For GMTs, 95% CIs of point estimates will be calculated using normal approximation assuming they are log10-normally distributed.

Descriptive analyses of antibody responses to A, C, W, and Y serogroups using hSBA will include but not be limited to:

- GMTs and 95% CI.
- Titre distribution and reverse cumulative distribution curves (RCDCs).
- Percentage of participants with titres ≥ 4-fold rise from pre-vaccination to postvaccination, and 95% CI.
- Percentage of participants with hSBA titres ≥ 1:4 and ≥ 1:8, and 95% CI.
- Percentage of participants with hSBA vaccine seroresponse, and 95% CI.

Note: hSBA vaccine seroresponse for serogroups A, C, W, and Y is defined as:

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

Safety Endpoints

No statistical hypotheses will be tested.

Safety results will be described for participants in the study. The main parameters for the safety endpoints will be described by 95% CIs (based on the Clopper-Pearson method).

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 criterion.

All safety analyses will be performed on the SafAS.

Interim Analyses

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

Results

Participant flow

Participant enrolment took place at Centres 0003 and 0004 that enrolled 447 participants in Vietnam. At study centre level, the proportion of participants enrolled in each age group was not homogeneous:

- In Centre 0003, 89 participants (39.9%) in the 12-23 months of age group and 101 participants (45.1%) in the 24 months of age and above group.
- In Centre 0004, 134 participants (60.1%) in the 12-23 months of age group and 123 participants (54.9%) in the 24 months of age and above group.

Figure 2: Participant disposition flow chart

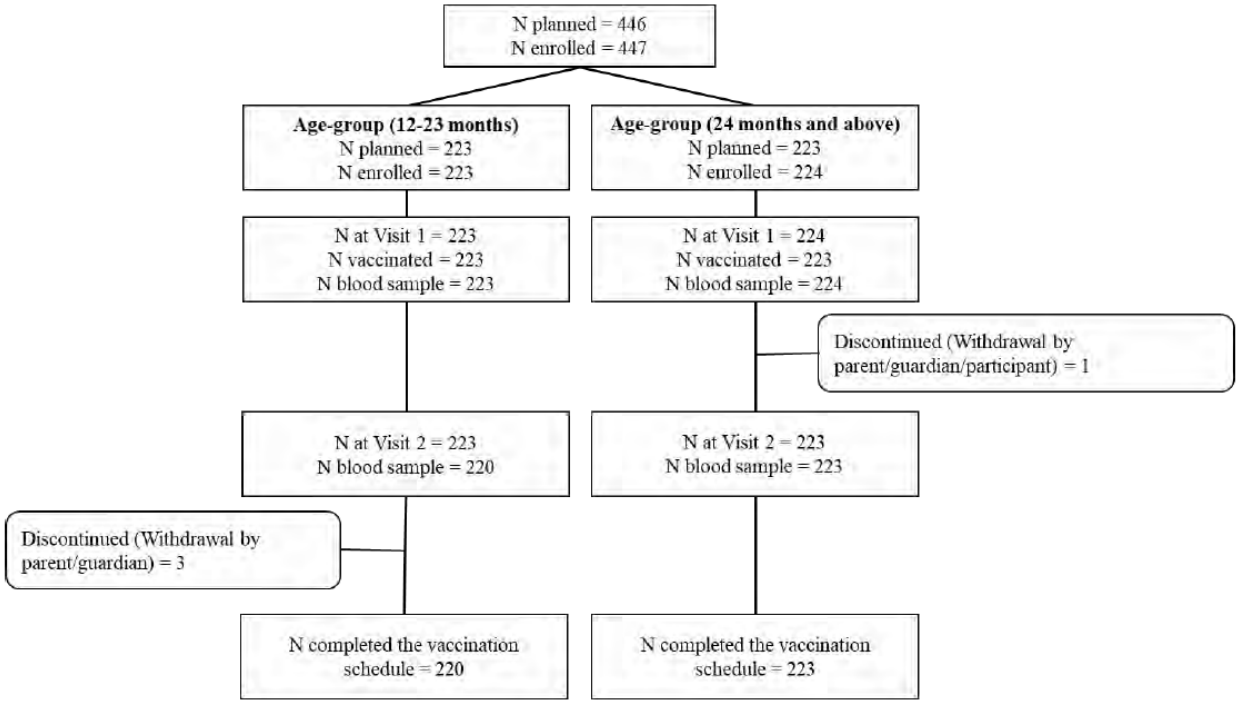


Table 5: Duration of the study - Enrolled participants

	Earliest (DDMMMYYYY)	Latest (DDMMMYYYY)	Duration (days)
Visit 01 (D01)	18JAN2024	28FEB2024	
Visit 02 (D31)	29FEB2024	31MAR2024	
Active phase termination date	20JAN2024	31MAR2024	
Active phase duration (V01 to V02)			74
Study duration			74
Mean study participant duration (SD)			41 (3.2)

Active phase duration (days) = Max (Last active visit date, Last termination date) - Min (V01 date) + 1.
Study duration (days) = Max (latest of visit dates, latest termination date) - Min (V01 date) + 1
Mean study participant duration: the mean of participant durations defined as Maximum (visit dates, termination date) - V01 date + 1

Protocol deviations

No participants presented critical deviations. A total of 25 participants (5.6%) presented at least 1 major protocol deviation: 23 participants (10.3%) in the 12-23 months of age group and 2 participants (0.9%) in the 24 months of age and above group. Most of the protocol deviations were due to administration of protocol prohibited therapy/medication/vaccine for 23 participants (5.1%), and mainly in 12-23 months of age group for 21 participants.

Table 6: Major and critical protocol deviations - Enrolled participants

	MenACYW 12-23 months of age (N=223) n (%)	MenACYW 24 months of age and above (N=224) n (%)	MenACYW All (N=447) n (%)
Study participants with at least one major or critical protocol deviation	23 (10.3)	2 (0.9)	25 (5.6)
Study participants with at least one major protocol deviation	23 (10.3)	2 (0.9)	25 (5.6)
Protocol prohibited therapy/medication/vaccine/ administered	21 (9.4)	2 (0.9)	23 (5.1)
Study physical visit, phone call or safety contact not performed within the protocol-specified time window	1 (0.4)	0	1 (0.2)
Planned sample not performed	2 (0.9)	0	2 (0.4)
Study participants with at least one critical protocol deviation	0	0	0

N: number of enrolled participants
n: number of study participants fulfilling the item listed
Percentages are based on N.

Recruitment

Study initiation date: 18 January 2024 (first participant first visit)

Study completion: 31 March 2024 (last participant last visit)

Database lock date: 17 April 2025

Baseline data

Overall, there were 248 females (55.5%) and 199 males (44.5%) included. There were more females than males in both vaccination groups. There were 118 females (52.9%) and 105 males (47.1%) in the 12-23 months of age group and 130 females (58.0%) and 94 males (42.0%) in the 24 months of age and above group. The male/female ratio was 0.89 in the 12-23 months of age group and 0.72 in the 24 months of age and above group.

The mean age (standard deviation [SD]) in the 12-23 months of age group was 17.6 (3.20) months whereas in the 24 months of age and above group was 28.9 (23.3) years.

Race and ethnicity were not collected in this study.

Table 7: Baseline demographic - Enrolled participants

	MenACYW 12-23 months of age (N=223)	MenACYW 24 months of age and above (N=224)	MenACYW All (N=447)
Sex: n (%)			
Male	105 (47.1)	94 (42.0)	199 (44.5)
Female	118 (52.9)	130 (58.0)	248 (55.5)
Missing	0	0	0
Sex ratio: Male/Female	0.89	0.72	0.80
Age (*)			
M	223	224	-
Mean (SD)	17.6 (3.20)	28.9 (23.3)	-
Min ; Max	12.0 ; 23.0	2.00 ; 73.0	-
Median	17.0	16.0	-
Q1 ; Q3	15.0 ; 20.0	8.00 ; 54.0	-

N: number of enrolled participants
n: number of study participants fulfilling the item listed
M: number of study participants with available data for the relevant endpoint
Q1 ; Q3: first quartile ; third quartile
SD: Standard Deviation
Percentages are based on N
*For 12-23 months of age, the age unit is months. For 24 months of age and above group, the age unit is years.

Number analysed

Table 8: Immunogenicity analysis sets - Enrolled participants

	MenACYW 12-23 months of age (N=223) n (%)	MenACYW 24 months of age and above (N=224) n (%)	MenACYW All (N=447) n (%)
Full Analysis Set FAS	220 (98.7)	223 (99.6)	443 (99.1)
Participants with at least one criterion for exclusion from FAS	3 (1.3)	1 (0.4)	4 (0.9)
Not injected study vaccine	0	1 (0.4)	1 (0.2)
Did not have a valid post vaccination serology result	3 (1.3)	1 (0.4)	4 (0.9)
Per Protocol Analysis Set (PPAS)	200 (89.7)	221 (98.7)	421 (94.2)
Participants with at least one criterion for exclusion from PPAS	23 (10.3)	3 (1.3)	26 (5.8)
Did not meet all protocol-specified inclusion criteria or met at least one exclusion criteria	0	0	0
Did not receive vaccine	0	1 (0.4)	1 (0.2)
Preparation and / or administration of vaccine was not done as per-protocol	0	0	0
Did not provide the post-dose serology sample at visit 2 in the proper time window	0	0	0
Post-dose serology sample was not drawn	3 (1.3)	1 (0.4)	4 (0.9)
Did not provide a valid post-dose serology result	0	0	0
Received a category 2 or 3 protocol-prohibited therapy / medication / vaccine	20 (9.0)	2 (0.9)	22 (4.9)
Other protocol deviations	0	0	0

N: number of enrolled participants
n: number of study participants fulfilling the item listed
Note: a study participant may be associated with more than one criterion

Table 9: Safety analysis set - study participants who received at least one administration

	MenACYW 12-23 months of age (N=223) n (%)	MenACYW 24 months of age and above (N=224) n (%)	MenACYW All (N=447) n (%)
Participants received vaccine	223 (100)	223 (99.6)	446 (99.8)
Safety Analysis Set after injection at V01	223 (100)	223 (99.6)	446 (99.8)

N: number of enrolled participants n: number of participants experiencing the endpoint,
"Safety analysis set" is defined as participants who received at least one dose of study vaccines and for whom any safety data are available.

Immunogenicity results

Table 10: Summary of hSBA Vaccine Seroresponse 30 days after MenACYW conjugate vaccine dose received at V01 - PPAS

	MenACYW 12-23 months of age (N=200)			MenACYW 24 months of age and above (N=221)			MenACYW All (N=421)		
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	163/200	81.5	(75.4 ; 86.6)	147/221	66.5	(59.9 ; 72.7)	310/421	73.6	(69.1 ; 77.8)
C	199/200	99.5	(97.2 ; 100)	216/221	97.7	(94.8 ; 99.3)	415/421	98.6	(96.9 ; 99.5)
Y	193/200	96.5	(92.9 ; 98.6)	211/221	95.5	(91.8 ; 97.8)	404/421	96.0	(93.6 ; 97.6)
W	189/200	94.5	(90.4 ; 97.2)	211/221	95.5	(91.8 ; 97.8)	400/421	95.0	(92.5 ; 96.9)

n: number of participants with titers that meet the hSBA vaccine seroresponse criteria
M: number of participants with valid serology results for the particular serogroup
N: number of participants in PPAS; percentages are based on M
hSBA vaccine seroresponse is defined as:
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
95% CI of the single proportion calculated using the exact binomial method

Table 11: Summary of geometric means of hSBA titres for each serogroup before and 30 days after a single dose of meningococcal conjugate vaccine - PPAS

		MenACYW 12-23 months of age (N=200)			MenACYW 24 months of age and above (N=221)			MenACYW All (N=421)		
Serogroup	**Time Point**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**
A	Pre-Dose (D01)	200	4.44	(4.00 ; 4.92)	221	7.58	(6.76 ; 8.51)	421	5.88	(5.42 ; 6.38)
	Post-Dose (D31)	200	39.0	(32.9 ; 46.2)	221	43.2	(34.6 ; 54.1)	421	41.2	(35.7 ; 47.4)
C	Pre-Dose (D01)	200	2.61	(2.34 ; 2.91)	221	5.65	(4.82 ; 6.62)	421	3.92	(3.53 ; 4.35)
	Post-Dose (D31)	200	1226	(1076 ; 1398)	221	895	(781 ; 1026)	421	1039	(945 ; 1144)
Y	Pre-Dose (D01)	200	2.86	(2.55 ; 3.20)	221	4.08	(3.47 ; 4.78)	421	3.44	(3.11 ; 3.81)
	Post-Dose (D31)	200	132	(112 ; 156)	221	288	(244 ; 340)	421	199	(176 ; 225)
W	Pre-Dose (D01)	200	2.26	(2.09 ; 2.44)	221	4.33	(3.81 ; 4.92)	421	3.18	(2.92 ; 3.45)
	Post-Dose (D31)	200	99.4	(85.6 ; 115)	221	166	(139 ; 198)	421	130	(116 ; 147)

N: number of participants in PPAS
M: number of participants with available data for the relevant endpoint

Table 12: Summary of hSBA titres >=1:4 and >=1:8 before and 30 days after a single dose of meningococcal conjugate vaccine - PPAS

			MenACYW 12-23 months of age (N=200)			MenACYW 24 months of age and above (N=221)			MenACYW All (N=421)		
Serogroup	**Timepoint**	**hSBA Titers**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
A	Pre-Dose (D01)	>=1:4	159/200	79.5	(73.2 ; 84.9)	208/221	94.1	(90.2 ; 96.8)	367/421	87.2	(83.6 ; 90.2)
		>=1:8	50/200	25.0	(19.2 ; 31.6)	132/221	59.7	(52.9 ; 66.3)	182/421	43.2	(38.4 ; 48.1)
	Post-Dose (D31)	>=1:4	195/200	97.5	(94.3 ; 99.2)	197/221	89.1	(84.3 ; 92.9)	392/421	93.1	(90.3 ; 95.3)
		>=1:8	187/200	93.5	(89.1 ; 96.5)	187/221	84.6	(79.2 ; 89.1)	374/421	88.8	(85.4 ; 91.7)
C	Pre-Dose (D01)	>=1:4	33/200	16.5	(11.6 ; 22.4)	142/221	64.3	(57.6 ; 70.6)	175/421	41.6	(36.8 ; 46.4)
		>=1:8	17/200	8.5	(5.0 ; 13.3)	85/221	38.5	(32.0 ; 45.2)	102/421	24.2	(20.2 ; 28.6)
	Post-Dose (D31)	>=1:4	200/200	100	(98.2 ; 100)	221/221	100	(98.3 ; 100)	421/421	100	(99.1 ; 100)
		>=1:8	200/200	100	(98.2 ; 100)	221/221	100	(98.3 ; 100)	421/421	100	(99.1 ; 100)
Y	Pre-Dose (D01)	>=1:4	42/200	21.0	(15.6 ; 27.3)	78/221	35.3	(29.0 ; 42.0)	120/421	28.5	(24.2 ; 33.1)
		>=1:8	31/200	15.5	(10.8 ; 21.3)	58/221	26.2	(20.6 ; 32.6)	89/421	21.1	(17.3 ; 25.4)
	Post-Dose (D31)	>=1:4	199/200	99.5	(97.2 ; 100)	219/221	99.1	(96.8 ; 99.9)	418/421	99.3	(97.9 ; 99.9)
		>=1:8	197/200	98.5	(95.7 ; 99.7)	219/221	99.1	(96.8 ; 99.9)	416/421	98.8	(97.3 ; 99.6)
W	Pre-Dose (D01)	>=1:4	14/200	7.0	(3.9 ; 11.5)	114/221	51.6	(44.8 ; 58.3)	128/421	30.4	(26.0 ; 35.0)
		>=1:8	8/200	4.0	(1.7 ; 7.7)	71/221	32.1	(26.0 ; 38.7)	79/421	18.8	(15.1 ; 22.8)
	Post-Dose (D31)	>=1:4	199/200	99.5	(97.2 ; 100)	221/221	100	(98.3 ; 100)	420/421	99.8	(98.7 ; 100)
		>=1:8	197/200	98.5	(95.7 ; 99.7)	221/221	100	(98.3 ; 100)	418/421	99.3	(97.9 ; 99.9)

N: number of participants in PPAS
n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
Percentages are based on M.

Table 13: Number and percentage of participants with >= 4-fold rise of hSBA titre from pre-dose 1 to 30 days after vaccination - PPAS

	MenACYW 12-23 months of age (N=200)			MenACYW 24 months of age and above (N=221)			MenACYW All (N=421)		
Serogroup	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
A	163/200	81.5	(75.4 ; 86.6)	147/221	66.5	(59.9 ; 72.7)	310/421	73.6	(69.1 ; 77.8)
C	199/200	99.5	(97.2 ; 100)	216/221	97.7	(94.8 ; 99.3)	415/421	98.6	(96.9 ; 99.5)
Y	193/200	96.5	(92.9 ; 98.6)	211/221	95.5	(91.8 ; 97.8)	404/421	96.0	(93.6 ; 97.6)
W	189/200	94.5	(90.4 ; 97.2)	211/221	95.5	(91.8 ; 97.8)	400/421	95.0	(92.5 ; 96.9)

n: number of participants with valid serology results for the particular serogroup and who met the criterion
M: number of participants with valid serology results for the particular serogroup
N: number of participants in PPAS; percentages are based on M

Table 14: hSBA antibody titres against meningococcal serogroup A before and 30 days after a single dose of meningococcal conjugate vaccine by age sub-groups - PPAS

	MenACYW 12-23 months of age (N=200)	MenACYW Children 2 to 9 years of age (N=59)	MenACYW Adolescents 10 to 17 years of age (N=59)	MenACYW Adults 18 to 55 years of age (N=52)	MenACYW Older adults 56 years and above (N=51)	MenACYW 24 months of age and above (N=221)
D01						
Available data (M)	200	59	59	52	51	221
< 1:4 (LLOQ)						
n (%)	41 (20.5)	3 (5.1)	3 (5.1)	3 (5.8)	4 (7.8)	13 (5.9)
>= 1:4						
n (%)	159 (79.5)	56 (94.9)	56 (94.9)	49 (94.2)	47 (92.2)	208 (94.1)
(95% CI)	(73.2 ; 84.9)	(85.9 ; 98.9)	(85.9 ; 98.9)	(84.1 ; 98.8)	(81.1 ; 97.8)	(90.2 ; 96.8)
>= 1:8						
n (%)	50 (25.0)	27 (45.8)	40 (67.8)	33 (63.5)	32 (62.7)	132 (59.7)
(95% CI)	(19.2 ; 31.6)	(32.7 ; 59.2)	(54.4 ; 79.4)	(49.0 ; 76.4)	(48.1 ; 75.9)	(52.9 ; 66.3)
Titers						
Geometric Mean Titers (GMT)	4.44	5.83	8.69	8.33	8.00	7.58
(95% CI)	(4.00 ; 4.92)	(4.97 ; 6.83)	(6.87 ; 11.0)	(6.28 ; 11.0)	(6.25 ; 10.2)	(6.76 ; 8.51)
Median	4.00	4.00	8.00	8.00	8.00	8.00
Q1 ; Q3	4.00 ; 5.66	4.00 ; 8.00	4.00 ; 16.0	4.00 ; 11.3	4.00 ; 8.00	4.00 ; 8.00
Min ; Max	2.00 ; 1024	2.00 ; 64.0	2.00 ; 128	2.00 ; 512	2.00 ; 64.0	2.00 ; 512
Log10: Mean (SD)	0.647 (0.320)	0.765 (0.264)	0.939 (0.392)	0.920 (0.440)	0.903 (0.381)	0.880 (0.376)
D31						
Available data (M)	200	59	59	52	51	221
< 1:4 (LLOQ)						
n (%)	5 (2.5)	0	7 (11.9)	7 (13.5)	10 (19.6)	24 (10.9)
>= 1:4						
n (%)	195 (97.5)	59 (100)	52 (88.1)	45 (86.5)	41 (80.4)	197 (89.1)
(95% CI)	(94.3 ; 99.2)	(93.9 ; 100)	(77.1 ; 95.1)	(74.2 ; 94.4)	(66.9 ; 90.2)	(84.3 ; 92.9)
>= 1:8						
n (%)	187 (93.5)	55 (93.2)	49 (83.1)	44 (84.6)	39 (76.5)	187 (84.6)
(95% CI)	(89.1 ; 96.5)	(83.5 ; 98.1)	(71.0 ; 91.6)	(71.9 ; 93.1)	(62.5 ; 87.2)	(79.2 ; 89.1)
Titers						
Geometric Mean Titers (GMT)	39.0	46.6	41.0	61.5	29.5	43.2
(95% CI)	(32.9 ; 46.2)	(33.6 ; 64.7)	(26.8 ; 62.6)	(36.0 ; 105)	(17.3 ; 50.2)	(34.6 ; 54.1)
Median	32.0	32.0	64.0	64.0	32.0	64.0
Q1 ; Q3	16.0 ; 128	16.0 ; 64.0	16.0 ; 128	16.0 ; 256	8.00 ; 128	16.0 ; 128
Min ; Max	2.00 ; 1024	4.00 ; 1024	2.00 ; 1024	2.00 ; 2048	2.00 ; 1024	2.00 ; 2048
Log10: Mean (SD)	1.59 (0.527)	1.67 (0.546)	1.61 (0.707)	1.79 (0.835)	1.47 (0.820)	1.64 (0.733)
D31 / D01						
Available data (M)	200	59	59	52	51	221
>=4-fold rise from pre-vaccination to post-vaccination						
n (%)	163 (81.5)	46 (78.0)	35 (59.3)	36 (69.2)	30 (58.8)	147 (66.5)
(95% CI)	(75.4 ; 86.6)	(65.3 ; 87.7)	(45.7 ; 71.9)	(54.9 ; 81.3)	(44.2 ; 72.4)	(59.9 ; 72.7)
Seroresponse*						
n (%)	163 (81.5)	46 (78.0)	35 (59.3)	36 (69.2)	30 (58.8)	147 (66.5)
(95% CI)	(75.4 ; 86.6)	(65.3 ; 87.7)	(45.7 ; 71.9)	(54.9 ; 81.3)	(44.2 ; 72.4)	(59.9 ; 72.7)
S-						
n/M1	126/150	30/32	16/19	13/19	11/19	70/89
%	84.0	93.8	84.2	68.4	57.9	78.7
(95% CI)	(77.1 ; 89.5)	(79.2 ; 99.2)	(60.4 ; 96.6)	(43.4 ; 87.4)	(33.5 ; 79.7)	(68.7 ; 86.6)
S+						
n/M2	37/50	16/27	19/40	23/33	19/32	77/132
%	74.0	59.3	47.5	69.7	59.4	58.3
(95% CI)	(59.7 ; 85.4)	(38.8 ; 77.6)	(31.5 ; 63.9)	(51.3 ; 84.4)	(40.6 ; 76.3)	(49.4 ; 66.8)
Titers						
Geometric Mean Titers Ratio (GMTR)	7.62	7.72	4.61	7.19	3.49	5.51
(95% CI)	(6.42 ; 9.05)	(5.45 ; 11.0)	(2.98 ; 7.12)	(4.31 ; 12.0)	(2.04 ; 5.98)	(4.39 ; 6.91)
Median	8.00	8.00	4.00	8.00	4.00	8.00
Q1 ; Q3	4.00 ; 16.0	4.00 ; 16.0	1.00 ; 16.0	2.00 ; 32.0	0.500 ; 8.00	2.00 ; 16.0
Min ; Max	0.250 ; 128	0.500 ; 256	0.250 ; 256	0.125 ; 256	0.125 ; 256	0.125 ; 256
Log10: Mean (SD)	0.882 (0.534)	0.888 (0.582)	0.663 (0.726)	0.857 (0.798)	0.543 (0.830)	0.741 (0.743)

N: number of participants in PPAS by age sub-groups. n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
Q1 and Q3 are the first and third quartiles
*hSBA vaccine seroresponse is defined as a post-vaccination titer >= 1:16 for participants with pre-vaccination hSBA titer < 1:8, or a post-vaccination titer >= 4-fold increase at post baseline for participants with pre-vaccination hSBA titer >= 1:8
S-: Proportion of participants with a pre-vaccination titer < 1:8 to a post-vaccination titer >= 1:16
S+: Proportion of participants with a pre-vaccination titer >= 1:8 and >= 4-fold increase of the titer
M, M1, and M2: number of participants with valid serology results for the particular serogroup and time point (Remark: M1+M2=M)

Safety results

Solicited adverse event (AE) information was collected for vaccination day and 7 days after vaccination (D01-D08); unsolicited AE information was collected from Visit 1 (D01) to Visit 2 (D31 [+14 days]), and serious adverse event (SAE) information (including adverse events of special interest [AESIs]) was collected throughout the study period.

Per Protocol version 1.0 dated 29 March 2021, an AESI is an event for which ongoing monitoring and rapid communication by the Investigator to the Sponsor must be done. The following SAEs will be captured as serious AESIs throughout the study:

- Generalized seizures (febrile and non-febrile)
- Kawasaki disease
- Guillain-Barré syndrome
- Idiopathic thrombocytopenic purpura (ITP)

These events have been listed as AESIs based on the feedback received from the European Union regulators for the MenACYW conjugate vaccine.

Table 15: Safety overview after MenACYW conjugate vaccine dose received at V01 - SafAS

	MenACYW 12-23 months of age (N=223)			MenACYW 24 months of age and above (N=223)			MenACYW All (N=446)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection									
Immediate unsolicited AE	0/223	0	(0 ; 1.6)	1/223	0.4	(0 ; 2.5)	1/446	0.2	(0 ; 1.2)
Immediate unsolicited AR	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
Solicited reaction within solicited period after vaccine injection									
Solicited injection site reaction	29/223	13.0	(8.9 ; 18.1)	29/223	13.0	(8.9 ; 18.1)	58/446	13.0	(10.0 ; 16.5)
Solicited systemic reaction	34/223	15.2	(10.8 ; 20.6)	24/223	10.8	(7.0 ; 15.6)	58/446	13.0	(10.0 ; 16.5)
Within 30 days after vaccine injection									
Unsolicited AE	50/223	22.4	(17.1 ; 28.5)	12/223	5.4	(2.8 ; 9.2)	62/446	13.9	(10.8 ; 17.5)
Unsolicited AR	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
Unsolicited non-serious AE	48/223	21.5	(16.3 ; 27.5)	11/223	4.9	(2.5 ; 8.7)	59/446	13.2	(10.2 ; 16.7)
Unsolicited non-serious AR	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
Unsolicited non-serious injection site AE	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
Unsolicited non-serious injection site AR	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
Unsolicited non-serious systemic AE	48/223	21.5	(16.3 ; 27.5)	11/223	4.9	(2.5 ; 8.7)	59/446	13.2	(10.2 ; 16.7)
Unsolicited non-serious systemic AR	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
AE leading to study discontinuation	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
SAE	3/223	1.3	(0.3 ; 3.9)	2/223	0.9	(0.1 ; 3.2)	5/446	1.1	(0.4 ; 2.6)
Death	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
AESI	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
During the Study									
SAE	3/223	1.3	(0.3 ; 3.9)	2/223	0.9	(0.1 ; 3.2)	5/446	1.1	(0.4 ; 2.6)
Death	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)
AESI	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)	0/446	0	(0 ; 0.8)

N: number of participants in SafAS
n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint; Percentages are based on M.
AR: Reactions related to the study vaccine; SAE: Serious adverse event; AESI: Adverse event of special interest

Table 16: Summary of solicited reactions within 7 days after MenACYW conjugate vaccine dose received at V01 - SafAS

	MenACYW 12-23 months of age (N=223)			MenACYW 24 months of age and above (N=223)			MenACYW All (N=446)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Solicited reaction	48/223	21.5	(16.3 ; 27.5)	39/223	17.5	(12.7 ; 23.1)	87/446	19.5	(15.9 ; 23.5)
Grade 3 solicited reaction	8/223	3.6	(1.6 ; 6.9)	2/223	0.9	(0.1 ; 3.2)	10/446	2.2	(1.1 ; 4.1)
Solicited injection site reaction	29/223	13.0	(8.9 ; 18.1)	29/223	13.0	(8.9 ; 18.1)	58/446	13.0	(10.0 ; 16.5)
Grade 3 injection site reaction	3/223	1.3	(0.3 ; 3.9)	0/223	0	(0 ; 1.6)	3/446	0.7	(0.1 ; 2.0)
Solicited systemic reaction	34/223	15.2	(10.8 ; 20.6)	24/223	10.8	(7.0 ; 15.6)	58/446	13.0	(10.0 ; 16.5)
Grade 3 systemic reaction	5/223	2.2	(0.7 ; 5.2)	2/223	0.9	(0.1 ; 3.2)	7/446	1.6	(0.6 ; 3.2)

N: number of participants in SafAS
n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
Percentages are based on M.

Table 17: Solicited injection site reactions after MenACYW conjugate vaccine dose received at V01, by maximum intensity during the solicited period - SafAS

		MenACYW 12-23 months of age (N=223)			MenACYW 24 months of age and above (N=223)			MenACYW All (N=446)		
Participants experiencing at least one:	**Maximum intensity:**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Injection site Tenderness	Any	26/223	11.7	(7.8 ; 16.6)	NA	NA	NA	26/223	11.7	(7.8 ; 16.6)
	Grade 1	25/223	11.2	(7.4 ; 16.1)	NA	NA	NA	25/223	11.2	(7.4 ; 16.1)
	Grade 2	1/223	0.4	(0 ; 2.5)	NA	NA	NA	1/223	0.4	(0 ; 2.5)
	Grade 3	0/223	0	(0 ; 1.6)	NA	NA	NA	0/223	0	(0 ; 1.6)
Injection site Pain	Any	NA	NA	NA	23/223	10.3	(6.7 ; 15.1)	23/223	10.3	(6.7 ; 15.1)
	Grade 1	NA	NA	NA	22/223	9.9	(6.3 ; 14.6)	22/223	9.9	(6.3 ; 14.6)
	Grade 2	NA	NA	NA	1/223	0.4	(0 ; 2.5)	1/223	0.4	(0 ; 2.5)
	Grade 3	NA	NA	NA	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)
Injection site Erythema	Any	13/223	5.8	(3.1 ; 9.8)	11/223	4.9	(2.5 ; 8.7)	24/446	5.4	(3.5 ; 7.9)
	Grade 1	10/223	4.5	(2.2 ; 8.1)	10/223	4.5	(2.2 ; 8.1)	20/446	4.5	(2.8 ; 6.8)
	Grade 2	1/223	0.4	(0 ; 2.5)	1/223	0.4	(0 ; 2.5)	2/446	0.4	(0.1 ; 1.6)
	Grade 3	2/223	0.9	(0.1 ; 3.2)	0/223	0	(0 ; 1.6)	2/446	0.4	(0.1 ; 1.6)
Injection site Swelling	Any	9/223	4.0	(1.9 ; 7.5)	5/223	2.2	(0.7 ; 5.2)	14/446	3.1	(1.7 ; 5.2)
	Grade 1	5/223	2.2	(0.7 ; 5.2)	5/223	2.2	(0.7 ; 5.2)	10/446	2.2	(1.1 ; 4.1)
	Grade 2	2/223	0.9	(0.1 ; 3.2)	0/223	0	(0 ; 1.6)	2/446	0.4	(0.1 ; 1.6)
	Grade 3	2/223	0.9	(0.1 ; 3.2)	0/223	0	(0 ; 1.6)	2/446	0.4	(0.1 ; 1.6)

N: number of participants in SafAS
n: number of participants experiencing the endpoint listed in the first two columns
M: number of participants with available data for the relevant endpoint; Percentages are based on M
NA: Not Applicable

Table 18: Solicited systemic reactions after MenACYW conjugate vaccine dose received at V01, by maximum intensity during the solicited period - SafAS

		MenACYW 12-23 months of age (N=223)			MenACYW 24 months of age and above (N=223)			MenACYW All (N=446)		
Participants experiencing at least one:	**Maximum intensity:**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Vomiting	Any	6/223	2.7	(1.0 ; 5.8)	NA	NA	NA	6/223	2.7	(1.0 ; 5.8)
	Grade 1	4/223	1.8	(0.5 ; 4.5)	NA	NA	NA	4/223	1.8	(0.5 ; 4.5)
	Grade 2	2/223	0.9	(0.1 ; 3.2)	NA	NA	NA	2/223	0.9	(0.1 ; 3.2)
	Grade 3	0/223	0	(0 ; 1.6)	NA	NA	NA	0/223	0	(0 ; 1.6)
Crying abnormal	Any	13/223	5.8	(3.1 ; 9.8)	NA	NA	NA	13/223	5.8	(3.1 ; 9.8)
	Grade 1	9/223	4.0	(1.9 ; 7.5)	NA	NA	NA	9/223	4.0	(1.9 ; 7.5)
	Grade 2	3/223	1.3	(0.3 ; 3.9)	NA	NA	NA	3/223	1.3	(0.3 ; 3.9)
	Grade 3	1/223	0.4	(0 ; 2.5)	NA	NA	NA	1/223	0.4	(0 ; 2.5)
Drowsiness	Any	7/223	3.1	(1.3 ; 6.4)	NA	NA	NA	7/223	3.1	(1.3 ; 6.4)
	Grade 1	7/223	3.1	(1.3 ; 6.4)	NA	NA	NA	7/223	3.1	(1.3 ; 6.4)
	Grade 2	0/223	0	(0 ; 1.6)	NA	NA	NA	0/223	0	(0 ; 1.6)
	Grade 3	0/223	0	(0 ; 1.6)	NA	NA	NA	0/223	0	(0 ; 1.6)
Appetite lost	Any	17/223	7.6	(4.5 ; 11.9)	NA	NA	NA	17/223	7.6	(4.5 ; 11.9)
	Grade 1	15/223	6.7	(3.8 ; 10.9)	NA	NA	NA	15/223	6.7	(3.8 ; 10.9)
	Grade 2	1/223	0.4	(0 ; 2.5)	NA	NA	NA	1/223	0.4	(0 ; 2.5)
	Grade 3	1/223	0.4	(0 ; 2.5)	NA	NA	NA	1/223	0.4	(0 ; 2.5)
Irritability	Any	11/223	4.9	(2.5 ; 8.7)	NA	NA	NA	11/223	4.9	(2.5 ; 8.7)
	Grade 1	4/223	1.8	(0.5 ; 4.5)	NA	NA	NA	4/223	1.8	(0.5 ; 4.5)
	Grade 2	6/223	2.7	(1.0 ; 5.8)	NA	NA	NA	6/223	2.7	(1.0 ; 5.8)
	Grade 3	1/223	0.4	(0 ; 2.5)	NA	NA	NA	1/223	0.4	(0 ; 2.5)
Fever	Any	16/172	9.3	(5.4 ; 14.7)	6/180	3.3	(1.2 ; 7.1)	22/352	6.3	(4.0 ; 9.3)
	Grade 1	7/172	4.1	(1.7 ; 8.2)	3/180	1.7	(0.3 ; 4.8)	10/352	2.8	(1.4 ; 5.2)
	Grade 2	7/172	4.1	(1.7 ; 8.2)	1/180	0.6	(0 ; 3.1)	8/352	2.3	(1.0 ; 4.4)
	Grade 3	2/172	1.2	(0.1 ; 4.1)	2/180	1.1	(0.1 ; 4.0)	4/352	1.1	(0.3 ; 2.9)
Headache	Any	NA	NA	NA	11/223	4.9	(2.5 ; 8.7)	11/223	4.9	(2.5 ; 8.7)
	Grade 1	NA	NA	NA	8/223	3.6	(1.6 ; 6.9)	8/223	3.6	(1.6 ; 6.9)
	Grade 2	NA	NA	NA	3/223	1.3	(0.3 ; 3.9)	3/223	1.3	(0.3 ; 3.9)
	Grade 3	NA	NA	NA	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)
Malaise	Any	NA	NA	NA	13/223	5.8	(3.1 ; 9.8)	13/223	5.8	(3.1 ; 9.8)
	Grade 1	NA	NA	NA	10/223	4.5	(2.2 ; 8.1)	10/223	4.5	(2.2 ; 8.1)
	Grade 2	NA	NA	NA	3/223	1.3	(0.3 ; 3.9)	3/223	1.3	(0.3 ; 3.9)
	Grade 3	NA	NA	NA	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)
Myalgia	Any	NA	NA	NA	15/223	6.7	(3.8 ; 10.9)	15/223	6.7	(3.8 ; 10.9)
	Grade 1	NA	NA	NA	14/223	6.3	(3.5 ; 10.3)	14/223	6.3	(3.5 ; 10.3)
	Grade 2	NA	NA	NA	1/223	0.4	(0 ; 2.5)	1/223	0.4	(0 ; 2.5)
	Grade 3	NA	NA	NA	0/223	0	(0 ; 1.6)	0/223	0	(0 ; 1.6)

N: number of participants in SafAS
n: number of participants experiencing the endpoint listed in the first two columns
M: number of participants with available data for the relevant endpoint;
Percentages are based on M
NA: Not Applicable

2.3.3. Discussion on clinical aspects

Design and conduct

Study MEQ00074 was a Phase III, open-label study to evaluate immunogenicity and safety of a single dose of MenQuadfi in 447 enrolled participants in Vietnam, of which 446 participants (99.8%) actually received MenQuadfi. The study population was analysed depended on participants' allocation to one of two age groups: 12 to 23 months of age (designated Toddlers as per protocol) or 24 months of age and above. Of note, MenQuadfi is approved in the EU for individuals aged 12 months and older and thus in the enrolled age groups. The MAH enrolled a minimum of 20 participants per one of the 4 sub-groups (Children 2 to 9 years of age, Adolescents 10 to 17 years of age, Adults 18 to 55 years of age, and Older adults 56 years and above) of the 24 months of age and above group to ensure that all of these subgroups were represented.

The study period was from 18 January 2024 (first participant first visit) to 31 March 2024 (last participant last visit). Mean study participant duration was 41 days (SD: 3.2). It is noted that the study

report of this paediatric study (MEQ00074) was not submitted within 6 months after study completion as required with Article 46 of Regulation (EC) No. 1901/2006, as amended, since the last visit of the last participant was on 31 March 2024, according to the CSR. It is also unclear why the database lock (17 April 2025) was almost one year after the last contact with the last participant. However, given the negligible impact of this study on the overall benefit-risk balance of MenQuadfi, no issue is made.

The MAH noted that this study was a single-centre study including 1 main centre with 3 satellite sites, and participant enrolment was conducted in 2 satellite sites (Centre 0003 and Centre 0004), whereas in the third satellite site sample processing was carried out. The proportions of participants of each age group in the two centres differed: n=89 (39.9%) of those aged 12-23 months and n=101 participants (45.1%) of those aged 24 months and above in Centre 0003 vs n=134 participants (60.1%) of those aged 12-23 months and n=123 participants (54.9%) of those aged 24 months and above in Centre 0004. However, no concern is raised in this regard.

Receipt of any vaccine in the 4 weeks preceding the 1st study vaccination or planned receipt of any vaccine in the 4 weeks following study vaccination (except for monovalent pandemic and multivalent influenza vaccines) or previous vaccination against meningococcal vaccine containing Serogroups A, C, W, or Y or meningococcal B serogroup-containing vaccine was not allowed; additionally, participants with history of any *N. meningitidis* infection, confirmed either clinically, serologically, or microbiologically and who were at high risk for meningococcal disease during the study were excluded.

There were more female than male participants in both age groups, n=118 females (52.9%) and n=105 males (47.1%) in the 12-23 months of age group and n=130 females (58.0%) and n=94 males (42.0%) in the 24 months of age and above group. The mean age in the 12-23 months of age group was 17.6 months (SD: 3.20) whereas in the 24 months of age and above group was 28.9 years (SD:23.3). No concern is raised on that aspect.

At least 1 major protocol deviation was reported for n= 23 participants (10.3%) in the 12-23 months of age group and n=2 participants (0.9%) in the 24 months of age and above group, mostly due to due to administration of protocol prohibited therapy/medication/vaccine: n=21 (9.4%) and n=2 (0.9%) in the 12-23 months of age group and the 24 months of age and above group, respectively. This is of no concern as this is not unexpected, in particular for the toddler population.

Data was analysed descriptively. Immunogenicity was evaluated by measuring hSBA (human complement serum bactericidal assay) antibody titres against meningococcal Serogroups A, C, Y, and W at baseline (before vaccination) at Day 1 (Visit 1) and at Day 31 (Visit 2, +14 days) after vaccination. Titres were presented as GMTs, percentages of participants with titres ≥ 4-fold rise from pre-vaccination to postvaccination, percentages of participants with hSBA titres ≥ 1:4 and ≥ 1:8, and percentages of participants with hSBA vaccine seroresponse (seroresponse was defined as a post-vaccination titre of ≥ 1:16 for a participant with a pre-vaccination titre < 1:8, or a post-vaccination titre of at least 4-fold greater than the pre-vaccination titre for a participant with a pre-vaccination titre ≥ 1:8). Apparently, immunogenicity of non-meningococcal vaccines was not evaluated.

The sample size was oriented on safety evaluation with an anticipated 10% non-adherence rate to have at least 400 participants overall and at least 200 participants per age group in order to provide a probability of approximately 95% of observing any AE (at least 1 occurrence) with a true incidence of 0.75% in the overall study population, and a probability of approximately 95% of observing any AE (at least 1 occurrence) with a true incidence of 1.5% in each of the two age groups.

All immunogenicity analyses were performed on the full analysis set (FAS), defined as the participants who received the study vaccine and had a valid post-vaccination serology result, and the PPAS, a

subset of the FAS, excluding participants presenting with at least 1 relevant protocol deviations. All safety analyses were performed on the Safety Analysis Set (SafAS), which included participants who received the study vaccine and had any safety data available.

Immunogenicity data analyses

Titres after a single vaccination with MenQuadfi against Serogroups C, Y, and W, hSBA titres in both groups, 12-23 months of age and 24 months of age and older, were of similar magnitude. However, titres against Serogroup A were higher in the 12-23 months of age group than in the 24 months of age and older group, e.g., as regards seroresponse rate: 81.5% (95% CI: 75.4%; 86.6%) vs 66.5% (95% CI: 59.9%; 72.7%), respectively.

Likewise, MenQuadfi elicited hSBA titres ≥ 1:8, which can be considered as seroprotection titre, against Serogroups C, Y, and Y in almost all study participants of both age groups. However, in the 12-23 months of age group, hSBA titres ≥ 1:8 against Serogroup A were achieved by 93.5% (95% CI: 89.1%; 96.5%) of participants in contrast to the 24 months of age and older age group where the percentage of participants with hSBA titres ≥ 1:8 against Serogroup A was lower in comparison with 84.6% (95% CI: 79.2%; 89.1%).

Of note, percentages of participants with hSBA titres ≥ 1:4 and ≥ 1:8 at baseline before vaccination were higher for Serogroup A than for Serogroups C, Y, and W in both age groups, e.g., for those aged 12-23 months of age, the percentage of participants with hSBA titres ≥ 1:4 was 79.5% (95% CI: 73.2; 84.9) at Day 1 and percentage of participants with hSBA titres ≥ 1:8 was 25.0% (95% CI: 19.2%; 31.6%). This indicates that immunity against Serogroup A had been acquired in this population to some extent, prior to enrolment in the study, and consequently, the actual immune responses (and their elicitation by MenQuadfi) against Serogroup A could be overestimated, in particular for those aged 12-23 months of age.

Taken together, the observations reported are deemed to be likely a consequence of several factors combined, i.e., the weaker elicitation of titres against Serogroup A (compared to Serogroups C, Y, and W), the fact that the immune system's responsiveness decreases with age (which is also demonstrated by the analyses per age sub-group) but also the prior immunity towards Serogroup A. However, it must be noted that since the sample size was oriented on safety evaluation and not on immunogenicity investigation and no hypotheses were formulated or tested in this regard, a comprehensive data interpretation is limited to some extent.

Safety data analyses

Immediate unsolicited systemic AEs were collected within 30 minutes after each vaccination. Solicited reactions within solicited period after vaccine injection (within 7 days, from Day 1 to Day 8) were further distinguished in injection site reactions and systemic reactions. Unsolicited AEs were collected from Visit 1 (Day 1) to Visit 2 (Day 31 [+14 days]) and were further distinguished in unsolicited adverse events and unsolicited adverse reactions (i.e., considered related). Serious adverse event (SAE) information (including adverse events of special interest [AESIs]) was collected throughout the study period. An AESI was defined as an event for which ongoing monitoring and rapid communication by the Investigator to the Sponsor must be done, and included Generalized seizures (febrile and non-febrile), Kawasaki disease, Guillain-Barré syndrome, and Idiopathic thrombocytopenic purpura (ITP). This is all acceptable.

Immediate unsolicited AEs reported within 30 minutes of vaccination

There were no immediate unsolicited AEs reported within 30 minutes of vaccination for the 12-23 months of age group. In contrast, one subject (0.4%) experienced an immediate unsolicited AE within 30 minutes of vaccination (high blood pressure in a 46-year-old male participant), which was assessed as not related to the vaccine by the Investigator to which can be agreed.

Solicited reactions within 7 days following vaccination

Incidence of solicited reactions was reportedly higher in the 12-23 months of age group than the 24 months of age and older group: n=48 participants (21.5%) vs n=39 participants (17.5%), respectively. Although the number and percentage of participants with at least 1 solicited injection site reaction was the same (13%, n=29), the number and percentage of participants with at least 1 solicited systemic reaction were higher in the 12-23 months of age group than the 24 months of age and older group: 15.2% (n=34) vs 10.8% (n=24), respectively. In the 12-23 months of age group, tenderness was the most frequently solicited injection site reaction (n=36, 11.7%), followed by erythema (n=13, 5.8%) and swelling (n=9, 4.0%). In contrast, in the 24 months of age and older group, injection site pain was the most frequently solicited injection site reaction (n=23, 10.3%), followed by erythema (n=11, 4.9%) and swelling (n=5, 2.2%). According to the submitted data, in the 12-23 months of age group, Grade 3 solicited injection site reactions were reported in n=3 participants (1.3) but also Grade 3 solicited administration site reactions consisted of both erythema and swelling reported by 2 participants (0.9% each), which is confusing; however, none of those ongoing at Day 9. For the 24 months of age and older group, no solicited administration site reactions were ongoing on Day 9 and there were no Grade 3 solicited administration site reactions reported. The most frequently reported solicited systemic reaction in the in the 12-23 months of age group was appetite lost (n=17, 7.6%), followed by fever (n=16, 9.3%), abnormal crying (n=13, 5.8%), and irritability (n=11, 4.9%), whereas in the 24 months of age and older group, the most frequently reported solicited systemic reaction was myalgia (n=15, 6.7%), followed by malaise (n=13, 5.8%), headache (n=11, 4.9%), and fever (n=6, 3.3%).

Unsolicited AEs

The number and percentage of unsolicited AEs differed between the 12-23 months of age group and the 24 months of age and older group with n= 50 (22.4%) and n=12 (5.4%), respectively. However, none of those were considered an unsolicited adverse reaction. In the 12-23 months of age group, most participants experienced upper respiratory tract infection (9.9%), followed by upper respiratory tract inflammation (4.5%), and pneumonia (2.7%), whereas, in the 24 months of age and older group pyrexia, upper respiratory tract infection, and hypertension were experienced in 0.9% of participants each, followed by food allergy, appendicitis, tonsillitis, rib fracture, hepatic enzyme increased, tendonitis, pleural effusion, and upper respiratory tract inflammation in 0.4% of participants each.

In the 12-23 months of age group, n=4 Grade 3 unsolicited AEs were reported for 3 participants (1.3%): One participant experienced pneumonia on Day 1 after administration, which required medication and hospitalization and resolved; this event was also evaluated as SAE. One participant reported 2 unsolicited AEs which were evaluated as Grade 3 intensity during at least 1 day, i.e., Pneumonia which started on Day 19 after administration and required medication and hospitalization and resolved (assessed as SAE), and an anaphylactic reaction which started on Day 28 after administration and required medication and hospitalization and resolved (the reaction was caused by antibiotics (ampicillin and sulbactam) used to treat pneumonia, assessed as SAE). One participant reported pneumonia on Day 23 after administration, which required medication and hospitalization and

resolved (this event was evaluated as Grade 3 intensity during at least 1 day and assessed as SAE). All were considered not related to the study vaccine by the Investigator, which can be agreed given the nature of the events.

In the 24 months of age and older group, n=3 Grade 3 unsolicited AEs were reported in 2 participants (0.9%): One participant reported appendicitis on Day 19 after administration, which required medication and hospitalization and resolved (this event was evaluated as Grade 3 intensity during at least 1 day and was assessed as SAE). One participant reported 2 unsolicited AEs that were evaluated as Grade 3 intensity during at least 1 day (rib fracture, which started on Day 20 after administration, required medication and hospitalization and resolved, assessed as SAE; and a pleural effusion, which started on Day 23 after administration, required medication and resolved, not assessed as SAE). Those were considered not related to the study vaccine by the Investigator; this judgment can be agreed to considering the nature of the events.

For both age groups, there were no AEs that caused participants to discontinue from the study within 30 days of vaccination and no deaths or AESIs during the study. All reported SAEs were unsolicited AEs and are addressed above.

In summary, although no significant concern arises from the observations reported, it is clearly noted that the open-label design does not allow for an adequate conclusion on safety, and the sample size is considered limited, additionally impairing interpretation.

3. CHMP's overall conclusion and recommendation

The MAH submitted data of Study MEQ00074 "A Phase III, open-label, single-centre study to describe the immunogenicity and safety of a single dose of MenACYW Conjugate Vaccine in participants aged 12 months and older in Vietnam", a stand-alone study that is not included in the MenQuadfi Paediatric Investigational Plan (PIP).

MenQuadfi is authorised for active immunisation of individuals from the age of 12 months and older against invasive meningococcal disease caused by *Neisseria (N.) meningitidis* serogroups A, C, W, and Y. Consequently, Study MEQ00074's population being entirely comprised of participants aged 12 months and older is covered by the currently effective EU Marketing Authorisation of MenQuadfi.

Of note, a type II variation intended to extend the indication to individuals aged 6 weeks to below 12 months is currently ongoing. However, Study MEQ00074 has not been included in the data package for that procedure. Moreover, the MAH has not submitted any amendments to the Product Information as part of this Article 46 procedure.

As regards immunogenicity, titres after a single vaccination with MenQuadfi against Serogroups C, Y, and W, hSBA titres in both groups, 12-23 months of age and 24 months of age and older, were of similar magnitude. In contrast, titres against Serogroup A were higher in the 12-23 months of age group than in the 24 months of age and older group.

Of note, percentages of participants with hSBA titres ≥ 1:4 and ≥ 1:8 at baseline before vaccination were higher for Serogroup A than for Serogroups C, Y, and W in both age groups, which indicates that immunity against Serogroup A had been acquired in this population to some extent, prior to enrolment in the study, and consequently, the actual immune responses (and their elicitation by MenQuadfi) against Serogroup A could be overestimated, in particular for those aged 12-23 months of age.

Taken together, the observation reported are deemed to be likely a consequence of several factors combined, i.e., the weaker elicitation of titres against Serogroup A (compared to Serogroups C, Y, and

W), the fact that the immune system's responsiveness decreases with age (which is also demonstrated by the analyses per age sub-group) but also the immunity towards Serogroup A prior to the study. However, it must be noted that since the sample size was oriented on safety evaluation and not on immunogenicity investigation and no hypotheses were formulated or tested in this regard, a comprehensive data interpretation is limited to some extent.

Concerning safety, although no significant concern arises from the observations reported, it is noted that the open-label design does not allow for an adequate conclusion on safety, and the sample size is considered limited, additionally impairing interpretation.

Overall, no concerns arise from the study results and the benefit-risk balance of MenQuadfi remains positive in the approved indication. No updates of the PI are necessary.

Fulfilled:

No regulatory action required.