Amsterdam, 13 November 2025
EMADOC-1700519818-2353917
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/0000291488

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	N/A
☐	Updated CHMP Rapporteur AR	6 November 2025	N/A
☒	CHMP outcome	13 November 2025	13 November 2025

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1. Introduction

On 7 August 2025, the MAH (Sanofi Winthrop Industrie) submitted a completed paediatric study for MenQuadfi, in accordance with Article 46 of Regulation (EC) No 1901/2006, 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 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.

The MAH stated that study MEQ00075 "Phase I Open-Label, Age De-escalation Safety and Immunogenicity Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adolescents, Children, Toddlers, and Infants in China" is a stand-alone study, is not 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.

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 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 (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 MEQ00075 – Phase I Open-Label, Age De-escalation Safety and Immunogenicity Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adolescents, Children, Toddlers, and Infants in China.

2.3.2. Clinical study

Description

Study MEQ00075 is a Phase I, open-label, age de-escalation study conducted in China (1 centre [1 satellite site of 1 main site]), to describe the safety and immunogenicity of MenACYW conjugate vaccine (MenQuadfi) and two locally licensed meningococcal vaccines (i.e., Green Bamboo's and Royal's MenAC conjugate vaccines) in adolescents, children, toddlers and infants aged 3 months to 17 years.

MEQ00075 was conducted from 12 August 2023 (first participant first visit) to 22 October 2024 (last participant last contact). Last participant last visit was 25 May 2024.

Database lock for the provided CSR (Final Report Version 1.0, dated 1 July 2025) was 13 March 2025.

Methods

Study design

Approximately 300 healthy adolescents, children, toddlers, and infants were planned to be assigned into 1 of 5 cohorts (Cohorts I to V) and randomised 1:1 to the following 10 groups within those cohorts as follows:

Cohort I (adolescents aged 7 to 17 years, 1 vaccination)

- Group 1 (MenACYW conjugate vaccine; 30 participants)
- Group 2 (Green Bamboo's MenAC conjugate vaccine; 30 participants)

Cohort II (children aged 2 to 6 years, 1 vaccination)

- Group 3 (MenACYW conjugate vaccine; 30 participants)
- Group 4 (Royal's MenAC conjugate vaccine; 30 participants)

Cohort III (toddlers aged 12 to 23 months, 1 vaccination)

- Group 5 (MenACYW conjugate vaccine; 30 participants)
- Group 6 (Royal's MenAC conjugate vaccine; 30 participants)

Cohort IV (infants aged 6 to 11 months, 2 vaccinations)

- Group 7 (MenACYW conjugate vaccine; 30 participants)
- Group 8 (Royal's MenAC conjugate vaccine; 30 participants)

Cohort V (infants aged 3 to 5 months, 3 vaccinations)

- Group 9 (MenACYW conjugate vaccine; 30 participants)
- Group 10 (Green Bamboo's MenAC conjugate vaccine; 30 participants)

Blood sampling:

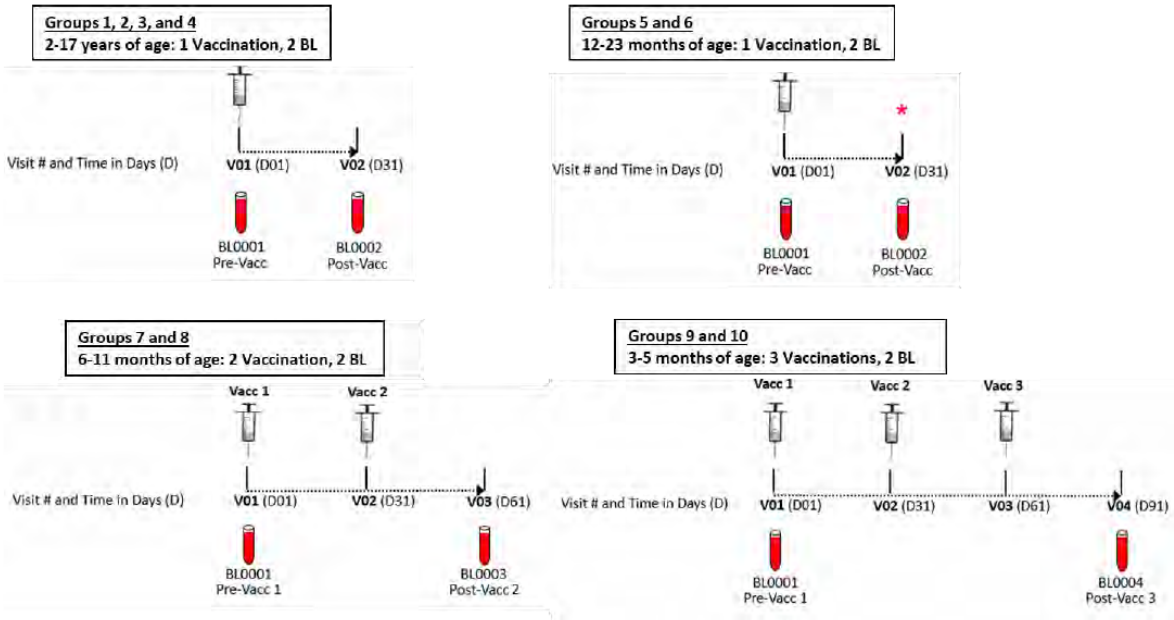
All participants were to provide a total of 2 blood samples for immunogenicity assessment. The first blood sample was to be provided at baseline (pre-vaccination) and the second blood sample was to be provided at 30 to 37 days post the last vaccination.

Table 1: Vaccination and blood sampling schedule

Cohort	Age of participant	Group	Vaccine Administered	Vaccination	Blood draw time point	Blood volume (per blood draw)
Cohort I	7 to 17 years	Group 1	MenACYW conjugate	1 dose	Pre-vaccination, 30 days post-vaccination	3 mL
		Group 2	Green Bamboo's MenAC conjugate	1 dose		2 mL
Cohort II	2 to 6 years	Group 3	MenACYW conjugate	1 dose	Pre-vaccination, 30 days post-vaccination	3 mL
		Group 4	Royal's MenAC conjugate	1 dose		2 mL
Cohort III	12 to 23 months	Group 5	MenACYW conjugate	1 dose	Pre-vaccination, 30 days post-vaccination	3 mL
		Group 6	Royal's MenAC conjugate	1 dose[a]		2 mL
Cohort IV	6 to 11 months	Group 7	MenACYW conjugate	2 doses separated by 30 days	Pre-vaccination, 30 days after the last vaccination	3 mL
		Group 8	Royal's MenAC conjugate	2 doses separated by 30 days		2 mL
Cohort V	3 to 5 months	Group 9	MenACYW conjugate	3 doses separated by 30 days	Pre-vaccination, 30 days after the last vaccination	3 mL
		Group 10	Green Bamboo's MenAC conjugate	3 doses separated by 30 days		2 mL

a At the discretion of parent(s)/legally acceptable representative(s), an additional dose (open-label) of Royal's MenAC conjugate vaccine was be offered to participant in Group 6 after the study procedure on the last visit of blood sampling (Visit 2), to comply with product's approved vaccination schedule. This second dose of Royal's vaccine was not part of the study assessment and needed to be administered at least 31 days after the study vaccination (first dose).

Table 2: Presentation of vaccination and blood draws by age group



Abbreviations: BL: blood sample; D: study day; V: visit; Vacc: vaccination

* At the discretion of the participant/parent(s)/legally acceptable representative(s), an additional dose of Royal's MenAC conjugate vaccine was offered by the Sponsor to participants in Group 6 after the study procedure on the last visit of blood sampling (Visit 2), to comply with product's approved vaccination schedule. This second dose of Royal's vaccine was not part of the study assessment and needs to be administered at least 31 days after the study vaccination (first dose).

Collection of safety data:

Safety data were to be collected as follows: Immediate adverse event (AE) information was to be collected within 30 minutes after each vaccination; solicited AE information was to be collected for 7 days after each vaccination; unsolicited AE information was to be collected for 30 days after each vaccination; serious adverse event (SAE) information was to be collected throughout the duration of the study.

Of note, adverse events of special interest (AESIs) were not to be collected in Study MEQ00075. However, if events that were collected as AESIs in past clinical trials occur, including generalized seizures (febrile or non-febrile), Kawasaki disease, Guillain-Barré syndrome, and idiopathic thrombocytopenic purpura, they were to be reported as SAEs throughout the trial.

Study participants

As per Protocol version 4.0 dated 10 Jan 2024:

Inclusion Criteria

1. *For participants 6 months through 17 years:* Aged 6 months to 17 years on the day of inclusion (6 months to 17 years" means from the day of the 6th month after birth to the day before the 18th birthday).

   For participants 3 through 5 months of age: Aged 3 months to 5 months on the day of inclusion (3 to 5 months" means from the day of the 3rd month after birth to the day before the 6th month after birth).

2. *For participants 3 through 23 months of age:* Born at full term of pregnancy (≥37 weeks) or born after a gestation period of 27 through 36 weeks and medically stable as assessed by the Investigator, based on the following definition: "Medically stable" refers to the condition of premature infants who do not require significant medical support or ongoing management for debilitating disease and who have demonstrated a clinical course of sustained recovery by the time they receive the first dose of study intervention.
3. *For participants 12 through 17 years of age* (This criterion also applies to female participants who are under 12 years of age but are post-menarche.): A female participant is eligible to participate if she is not pregnant or breastfeeding and one of the following conditions applies:

    a. 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

    b. Is of childbearing potential and agrees to use an effective contraceptive method or abstinence from at least 4 weeks prior to the first study intervention administration until at least 12 weeks after the last study intervention administration.

    A female participant of childbearing potential must have a negative highly sensitive pregnancy test (urine or serum as required by local regulation) on the day of any dose of study intervention.
4. Assent form or informed consent form has been signed and dated by the participant (based on local regulations), and if applicable informed consent form has been signed and dated by the parent(s) or another legally acceptable representative.
5. Participants or participant and parent/legally acceptable representative are able to attend all scheduled visits and to comply with all trial procedures.

<u>Exclusion Criteria</u>

1. 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).
2. History of meningococcal infection, confirmed either serologically, or microbiologically.
3. History of any neurologic disorders, including any seizures and progressive neurologic disorders.
4. History of Guillain-Barré syndrome.
5. History of an Arthus-type hypersensitivity reaction after a previous dose of tetanus toxoid-containing vaccine.
6. At high risk for meningococcal infection during the trial (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).

7. Known systemic hypersensitivity to any of the vaccine components, or history of a life-threatening reaction to the vaccines used in the trial or to a vaccine containing any of the same substances.
8. Self-reported thrombocytopenia, contraindicating intramuscular vaccination.
9. Bleeding disorder, or receipt of anticoagulants in the 3 weeks preceding inclusion, contraindicating intramuscular vaccination.
10. Chronic illness that, in the opinion of the Investigator, is at a stage where it might interfere with trial 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).
11. Moderate or severe acute illness/infection (according to Investigator judgement) or febrile illness (axillary temperature ≥37.3°C [99.14°F] for participants >14 years, axillary temperature ≥37.5°C [99.5°F] for participants ≤14 years). A prospective participant should not be included in the study until the condition has resolved or the febrile event has subsided.
12. Alcohol, prescription drug, or substance abuse that, in the opinion of the Investigator, might interfere with the study conduct or completion.
13. *For participants in Cohorts I or II:* receipt of any vaccine in the 4 weeks preceding the trial vaccination or planned receipt of any vaccine in the 4 weeks following trial vaccination.

    For participants in Cohorts III, IV, or V: receipt of any vaccine in the 2 weeks preceding the trial vaccination or planned receipt of any vaccine in the 2 weeks prior to or following trial vaccination.

    "Any vaccine" includes routine paediatric vaccines, influenza vaccine, and COVID-19 vaccines, if they are available at the time of this study.
14. Participants aged 3 through 5 months with vaccination history of any meningococcal vaccine;

    Participants aged 6 through 23 months who received any other meningococcal vaccine except the meningococcal group A polysaccharide vaccine included in the National Immunization Program (NIP), and the time since last vaccination of meningococcal group A polysaccharide vaccine was 6 months or less;

    For participants ≥2 years, the time since last vaccination of meningococcal vaccine was 2 years or less.
15. Receipt of immune globulins, blood or blood-derived products in the past 3 months.
16. Receipt of oral or injectable antibiotic therapy within 72 hours prior to the first blood draw.
17. Participation at the time of study enrolment (or in the 4 weeks preceding the trial vaccination) or planned participation during the present trial period in another clinical trial investigating a vaccine, drug, medical device, or medical procedure.
18. Deprived of freedom by an administrative or court order, or in an emergency setting, or hospitalized involuntarily.
19. 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.

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

Treatments

Table 3: Study interventions administered

Intervention Name	MenACYW conjugate vaccine: Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine (Sanofi Pasteur Inc., Swiftwater, PA, USA)	MenAC conjugate vaccine: (Royal (Wuxi) Bio-Pharmaceutical Co., LTD, China)	MenAC conjugate vaccine: (Green Bamboo Biopharmaceutical Co., LTD, China)
Intervention description	Conjugate vaccine	Conjugate vaccine	Conjugate vaccine
Marketing authorization status	Not approved in China	Approved in China and used in accordance with the terms of the marketing authorizations	Approved in China and used in accordance with the terms of the marketing authorizations
Use	Investigational	Active comparator	Active comparator
IMP or NIMP	IMP	IMP	IMP
Type	Vaccine	Vaccine	Vaccine
Dose Form	Liquid solution	Lyophilized powder	Suspension
Unit Dose Strength(s)	Each dose of MenACYW conjugate vaccine contained the following components: Meningococcal capsular polysaccharides: Serogroup A: 10 µg Serogroup C: 10 µg Serogroup W: 10 µg Serogroup Y: 10 µg Tetanus toxoid protein carrier approximately 55 µg[a]	Each dose of MenAC conjugate vaccine contained the following components: Meningococcal capsular polysaccharides: Serogroup A: no less than 10 µg Serogroup C: no less than 10 µg Tetanus toxoid protein carrier	Each dose of MenAC conjugate vaccine contained the following components: Meningococcal capsular polysaccharides: Serogroup A: 10 µg Serogroup C: 10 µg Tetanus toxoid protein carrier
Excipients/ Diluent	Sodium acetate buffered saline solution	lactose Sterile and pyrogen-free PBS	Aluminum Hydroxide/NaCl
Dosage Level(s)	0.5 mL per dose	0.5 mL per dose	0.5 mL per dose
Number of Doses/ Dosing Interval	For children aged: • 2 years through 17 years: 1 dose • 12 months through 23 months: 1 dose • 6 months through 11 months: 2 doses with a 1-month interval • 3 through 5 months: 3 doses with a 1-month interval	For children aged: • 2 through 15 years: 1 dose • 6 months through 24 months: 2 doses with a 1-month interval	For children aged: • >36 months: 1 dose • 3 through 12 months: 3 doses with a 1-month interval
Route of Administration	IM injection	IM injection	IM injection
Site of Administration	Deltoid muscle in the upper arm	Deltoid muscle in the upper arm	Deltoid muscle in the upper arm
Injection Site Side	Left or right	Left or right	Left or right
Sourcing	Provided by the Sponsor	Provided by the Sponsor	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.	Each study intervention was provided in an individual box. Each study intervention bore one fixed label and each box bore two detachable labels and one fixed label containing the dose number. All were labeled as required per country requirement.	Each study intervention was provided in an individual box. Each study intervention bore one fixed label and each box bore two detachable labels and one fixed label containing the dose number. All were labeled as required per country requirement.
Current/Former Name(s) or Alias(es)	MenQuadfi®	Brand name: Not Available	Brand name: Mening A Con®
Batch Number	VA030490	VA031644, VA033140, VA034878	VA031441, VA034879
Storage Conditions	Study interventions were to be stored in a refrigerator at a temperature ranging from +2°C to +8°C. The study interventions must not be frozen. Keep out light for Royal and Green Bamboo products.		

Abbreviations: IM: intramuscular; IMP: investigational medicinal product; NIMP: non-investigational medicinal product; PBS: phosphate buffered saline

a Tetanus toxoid protein quantity is approximate and dependent on the PS-to-protein ratio for the conjugates used in each formulation.

Duration of study intervention:

The duration of participation was approximately 180 days for participants aged 12 months to 17 years, 210 days for participants aged 6 to 11 months, and 240 days for participants aged 3 to 5 months. The study included a 6-month safety follow-up.

Objectives

Primary

Safety

To describe the safety profile of MenACYW conjugate vaccine and the safety profiles of the control vaccines (i.e., locally licensed MenAC conjugate vaccines: Royal or Green Bamboo).

Key Secondary

Immunogenicity

1. To describe the antibody responses against meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine and against serogroups A and C for Green Bamboo's MenAC conjugate vaccine following the administration of a single dose of the corresponding vaccine in children and adolescents 7 through 17 years of age (Cohort I [Groups 1 and 2]).
2. To describe the antibody responses against meningococcal serogroups A, C, Y and W for MenACYW conjugate vaccine and against serogroups A and C for Royal's MenAC conjugate vaccine following the administration of a single dose of the corresponding vaccine in children 2 through 6 years of age (Cohort II [Groups 3 and 4]).
3. To describe the antibody responses against meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine and against serogroups A and C for Royal's MenAC conjugate vaccine following the administration of a single dose of the corresponding vaccine in toddlers 12 through 23 months of age (Cohort III [Groups 5 and 6]).
4. To describe the antibody responses against meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine and against serogroups A and C for Royal's conjugate vaccine following the administration of two doses of the corresponding vaccine in infants 6 through 11 months of age (1-month interval between doses) (Cohort IV [Groups 7 and 8]).
5. To describe the antibody responses against meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine and against serogroups A and C for Green Bamboo's MenAC conjugate vaccine following the administration of three doses of the corresponding vaccine in infants 3 through 5months of age (1-month interval between doses) (Cohort V [Groups 9 and 10]).
6. To describe the immunogenicity of MenACYW conjugate vaccine and the immunogenicity of the control vaccines (i.e., locally licensed MenAC conjugate vaccines: Royal or Green Bamboo) to meningococcal serogroups A, C, Y, and W before and 30 days after the administration of 1, 2, or 3 doses of the corresponding vaccine.

Other Secondary

1. To describe the seropositivity (rSBA titres ≥1:8) and antibody responses of rSBA titres ≥1:128 to meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine (Sanofi Pasteur)

and to meningococcal serogroups A and C for MenAC conjugate vaccine (Green Bamboo) following the administration of a single dose of the corresponding vaccine: Groups 1 and 2.

2. To describe the seropositivity (rSBA titres ≥1:8) and antibody responses of rSBA titres ≥1:128 to meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine (Sanofi Pasteur) and to meningococcal serogroups A and C for MenAC conjugate vaccine (Royal) following the administration of a single dose of the corresponding vaccine: Groups 3 and 4.
3. To describe the seropositivity (rSBA titres ≥1:8) and antibody responses of rSBA titres ≥1:128 to meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine (Sanofi Pasteur) and to meningococcal serogroups A and C for MenAC conjugate vaccine (Royal) following the administration of a single dose[a] of the corresponding vaccine: Groups 5 and 6.
4. To describe the seropositivity (rSBA titres ≥1:8) and antibody responses of rSBA titres ≥1:128 to meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine (Sanofi Pasteur) and to meningococcal serogroups A and C for MenAC conjugate vaccine (Royal) following the administration of 2 doses of the corresponding vaccine: Groups 7 and 8.
5. To describe the seropositivity (rSBA titres ≥1:8) and antibody responses of rSBA titres≥1:128) to meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine (Sanofi Pasteur) and to meningococcal serogroups A and C for MenAC conjugate vaccine (Green Bamboo) following the administration of 3 doses of the corresponding vaccine: Groups 9 and 10.

[a] At the discretion of the parent(s)/legally acceptable representative(s), an additional dose of Royal's MenAC conjugate vaccine was to be offered by the Sponsor to participants in Group 6 after the study procedure on the last visit of blood sampling, to comply with product's approved vaccination schedule. This second dose of Royal's vaccine was not part of the study assessment and needs to be administered at least 31 days after the study vaccination (first dose).

Outcomes/endpoints

Primary

Safety

The following endpoints will be used for the evaluation of safety:

- Presence of any unsolicited systemic AEs reported in the 30 minutes after each and any study vaccination.
- Presence of solicited injection site reactions (pre-listed in the participant's DC and CRF) up to 7 days after each and any study vaccination.
- Presence of solicited systemic reactions (pre-listed in the participant's DC and CRF) up to 7 days after each and any study vaccination.
- Presence of unsolicited AEs up to 30 days after each and any study vaccination.
- Presence of SAEs, throughout the trial, i.e., from Visit 1 (first vaccination) to 6 months after the last study vaccination.

Depending on the items, the endpoints recorded or derived could include: nature (MedDRA preferred term), time of onset, duration/number of days of occurrence, intensity, relationship to the study vaccine, whether the AE led to early termination from the study, outcome, and seriousness criterion.

Key Secondary

Immunogenicity

1. Vaccine seroresponse of meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine or of serogroups A and C for Green Bamboo's MenAC conjugate vaccine measured using rSBA in serum specimens collected on D01 (pre-vaccination) and D31 (30 days [+7 days] after vaccination with the corresponding study vaccine) rSBA vaccine seroresponse to meningococcal serogroups A, C, Y, and W is defined as follows:
    - 30 days post vaccination rSBA titres ≥1:8 for participants with pre vaccination rSBA titres <1:8, or
    - At least 4-fold increase in rSBA titres from pre to 30 days post vaccination for participants with pre vaccination rSBA titres ≥1:8.
2. Vaccine seroresponse of meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine or of serogroups A and C for Royal's MenAC conjugate vaccine measured using rSBA in serum specimens collected on D01 (pre-vaccination) and D31 (30 days [+7 days] after vaccination with the corresponding study vaccine).
3. Vaccine seroresponse of meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine or of serogroups A and C for Royal's MenAC conjugate vaccine measured using rSBA in serum specimens collected on D01 (pre-vaccination) and D31 (30 days [+7 days] after vaccination with the corresponding study vaccine).
4. Vaccine seroresponse of meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine or of serogroups A and C for Royal's MenAC conjugate vaccine measured using rSBA in serum specimens collected on D01 (pre-vaccination) and D31 (30 days [+7 days] after vaccination with the corresponding study vaccine).
5. Vaccine seroresponse of meningococcal serogroups A, C, Y, and W for MenACYW conjugate vaccine or of serogroups A and C for Green Bamboo's MenAC conjugate vaccine measured using rSBA in serum specimens collected on D01 (pre-vaccination) and D91 (30 days [+7 days] after the third vaccination with the corresponding study vaccine).
6. :
    - Antibody titres in terms of GMTs against meningococcal serogroups A, C, Y, and W measured by rSBA 30 days after one dose of MenACYW conjugate vaccine in Group 1 and antibody titres in terms of GMTs against meningococcal serogroups A and C measured by rSBA 30 days after one dose of Green Bamboo's vaccine in Group 2 (participants 2 through 17 years of age; 1 dose of vaccine).
    - Antibody titres in terms of GMTs against meningococcal serogroups A, C, Y, and W measured by rSBA 30 days after one dose of MenACYW conjugate vaccine in Group 3 and against meningococcal serogroups A and C measured by rSBA 30 days after one dose of Royal's vaccine in Group 4 (participants 2 through 6 years of age, 1 dose of vaccine).
    - Antibody titres in terms of GMTs against meningococcal serogroups A, C, Y, and W measured by rSBA 30 days after one dose of MenACYW conjugate vaccine in Group 5 and antibody titres in terms of GMTs against meningococcal serogroups A and C measured by rSBA 30 days after one dose of Royal's vaccine in Group 6 (participants 12 through 23 months of age, 1 dose of vaccine).

- Antibody titres in terms of GMTs against meningococcal serogroups A, C, Y, and W measured by rSBA 30 days after the last dose of MenACYW conjugate vaccine in Group 7 and antibody titres in terms of GMTs against meningococcal serogroups A and C measured by rSBA 30 days after the last dose of Royal's vaccine in Group 8 (participants 6 through 11 months of age, 2 doses of vaccines 30 days apart).
- Antibody titres in terms of GMTs against meningococcal serogroups A, C, Y, and W measured by rSBA 30 days after last dose of MenACYW conjugate vaccine in Group 9 and antibody titres in terms of GMTs against meningococcal serogroups A and C measured by rSBA 30 days after the last dose of Green Bamboo's vaccine in Group 10 (participants 3 through 5 months of age, 3 doses of vaccine, 30 days apart).

Other Secondary

1. Antibody titres against meningococcal serogroups A, C, Y, and W in Group 1 and against meningococcal serogroups A and C in Group 2 measured by rSBA titre ≥1:8, ≥1:128 on D31 (+7 days).
2. Antibody titres against meningococcal serogroups A, C, Y, and W in Group 3 and against meningococcal serogroups A and C in Group 4 measured by rSBA titre ≥1:8, ≥1:128 on D31 (+7 days).
3. Antibody titres against meningococcal serogroups A, C, Y, and W in Group 5 and against meningococcal serogroups A and C in Group 6 measured by rSBA titre ≥1:8, ≥1:128 on D31 (+7 days).
4. Antibody titres against meningococcal serogroups A, C, Y, and W in Group 7 and against meningococcal serogroups A and C in Group 8 measured by rSBA titre ≥1:8, ≥1:128 on D61 (+7 days).
5. Antibody titres against meningococcal serogroups A, C, Y, and W in Group 9 and against meningococcal serogroups A and C in Group 10 measured by rSBA titre ≥1:8, ≥1:128 on D91 (+7 days).

Sample size

As per Protocol version 4.0 dated 10 Jan 2024:

In total 300 participants will be enrolled, 30 in each group. All analyses will be descriptive. The number of participants in each group was not hypothesis driven. No formal sample size calculations were performed.

Randomisation and blinding (masking)

All participants were centrally assigned to randomised study intervention using an Interactive Response Technology.

As this was an open-label study, there was no blinding.

Statistical Methods

As per Protocol version 4.0 dated 10 Jan 2024:

Analysis Sets

Participant Analysis Set	Description
Overall Safety Analysis Set for Any Dose (SafAS)	Participants who have received at least one dose of the study vaccine and have any safety data available.
Safety Analysis Set for the Single Dose or the First Dose (SafAS1)	Participants who have received at least one dose of the study vaccine at Visit 1 and have any safety data available.
Safety Analysis Set for the Second Dose (SafAS2)	Participants who have received at least one dose of the study vaccine at Visit 2 and have any safety data available.
Safety Analysis Set for the Third Dose (SafAS3)	Participants who have received at least one dose of the study vaccine at Visit 3 and have any safety data available.
Full analysis set (FAS)	The FAS is defined as the participants who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result.

Per-protocol analysis set (PPAS)	The PPAS is a subset of the FAS. The participants presenting with at least one of the following relevant protocol deviations will be excluded from the PPAS:
	• Participant did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria
	• Participant did not complete the study vaccination schedule
	• Participant received a vaccine other than the one that he/she was randomized to receive
	• Preparation and/or administration of study vaccine was not done as per-protocol
	• Participant did not receive study vaccine in the proper time window
	  ○ Groups 7 and 8
	  ▪ Visit 2: Visit 1 + 30 days (+7 days)
	  ○ Groups 9 and 10
	  ▪ Visit 2: Visit 1 + 30 days (+7 days)
	  ▪ Visit 3: Visit 2 + 30 days (+7 days)
	• Participant did not provide post-dose serology sample at V02, V03 or V04 if applicable in the proper time window or a post-dose serology sample at V02, V03 or V04 if applicable was not drawn
	  ○ Groups 1 to 6
	  ▪ Visit 2: Visit 1 + 30 days (+7 days)
	  ○ Groups 7 and 8
	  ▪ Visit 3: Visit 2 + 30 days (+7 days)
	  ○ Groups 9 and 10
	  ▪ Visit 4: Visit 3 + 30 days (+7 days)
	• Participant received a protocol-prohibited therapy/medication/vaccine
	• Participant had other protocol violation that affected the participant's immune response, as determined by the clinical team prior to locking the database
	In addition to the reasons listed above, participants will also be excluded from the PPAS if their post-vaccination serology sample at V02, V03 or V04 if applicable did not produce a valid test result (ie, results for all antigens are missing).
	In the event of a local or national immunization program with any other vaccine as needed, including any COVID-19 vaccine, participants who receive such a vaccine at any time during the study will not be withdrawn from the study.

Statistical Analyses

Primary Endpoint

No statistical hypothesis will be tested.

Safety results will be described for participants in all vaccine groups after each and any study vaccination during the reported periods. The main parameters for the safety endpoints will be described by 95% confidence intervals (CIs) based on exact Clopper-Pearson method.

Safety analysis will include but is not limited to:

- The number and percentage of participants reporting any immediate unsolicited systemic AEs occurring within 30 minutes after study vaccination by study group.
- The number and percentage of participants reporting any solicited injection site reactions and solicited systemic reactions occurring within 7 days after study vaccination by study group for intensity, time of onset, days of occurrence and action taken.
- The number and percentage of participants reporting any unsolicited non-serious AE occurring up to 30 days after study vaccination by study group, by intensity, time of onset, duration and by Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT), as well as by relationship to the study vaccine.
- The number and percentage of participants reporting an AE leading to study discontinuation by study group, within 30 days after study vaccination, respectively.
- The number and percentage of participants reporting at least one SAEs by study group, seriousness criterion, outcome and by MedDRA SOC and PT, as well as by relationship to the study vaccine.

Adverse events and SAEs will be also described according to the relationship status to the vaccine (adverse event related to the vaccination/ adverse event not related to the vaccination).

The SafAS will be used for safety analysis. Specific SafAS will be used after each study vaccination. All participants will have their safety data analysed after each study vaccination according to the vaccine they actually received, and after any study vaccination according to the first vaccine that they have received.

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

Secondary Endpoints

No statistical hypothesis will be tested.

Descriptive analyses on immunogenicity endpoints of A, C, Y and W serogroups (for participants in Groups 1, 3, 5, 7, and 9) or A and C serogroups (for participants in Groups 2, 4, 6, 8, and 10) measured using rSBA providing a blood sample at corresponding time points will include but not be limited to:

- GMT and 95% CI.
- Geometric mean of individual titre ratio (post-vaccination compared to pre-vaccination) and 95% CI.

- Percentage of participants with rSBA vaccine seroresponse defined as rSBA titres ≥1:8 at 30 days post-vaccination for participants with pre-vaccination rSBA titres <1:8, or at least 4-fold increase in rSBA titres from pre- to 30 days post-vaccination for participants with pre-vaccination rSBA titres ≥1:8 and 95% CI.
- Percentage of participants with titre ≥1:8 and ≥1:128 and 95% CI.
- Titre distribution and reverse cumulative distribution curves (RCDCs).

In general, the 95% CIs of point estimates will be calculated using the normal approximation for quantitative data assuming they are log-normally distributed, and the Clopper-Pearson method based on the exact binomial distribution for percentages.

The rSBA geometric mean titre ratio (GMTR) and difference in the vaccine seroresponse rates between investigational MenACYW conjugate vaccine and local vaccine for serogroups A and C in each age group will be calculated and their 95% CIs will be provided. The CIs of GMTRs will be calculated using the log10 transformed titres for the difference and then antilog transformations will be applied to the results of the calculation to provide the results in terms of GMTs. The CIs of the difference in the seroresponse rates will be computed using the Wilson Score method without continuity correction. These comparisons are descriptive.

Immunogenicity analysis will be performed on the full analysis set (FAS) and the per-protocol analysis set (PPAS). All participants will be analysed according to the vaccine group to which they were randomised.

Interim Analyses

The statistical analysis will be performed in 2 steps:

- The first statistical analysis will be done once all participants in Cohorts 1 and 2 have completed the 6-month follow-up, and all safety and immunogenicity data are available.
- The final statistical analysis will be done once all participants in Cohorts 3, 4 and 5 have completed the 6-month follow-up, and all safety and immunogenicity data are available. In the final statistical analysis, all cohorts will be included.

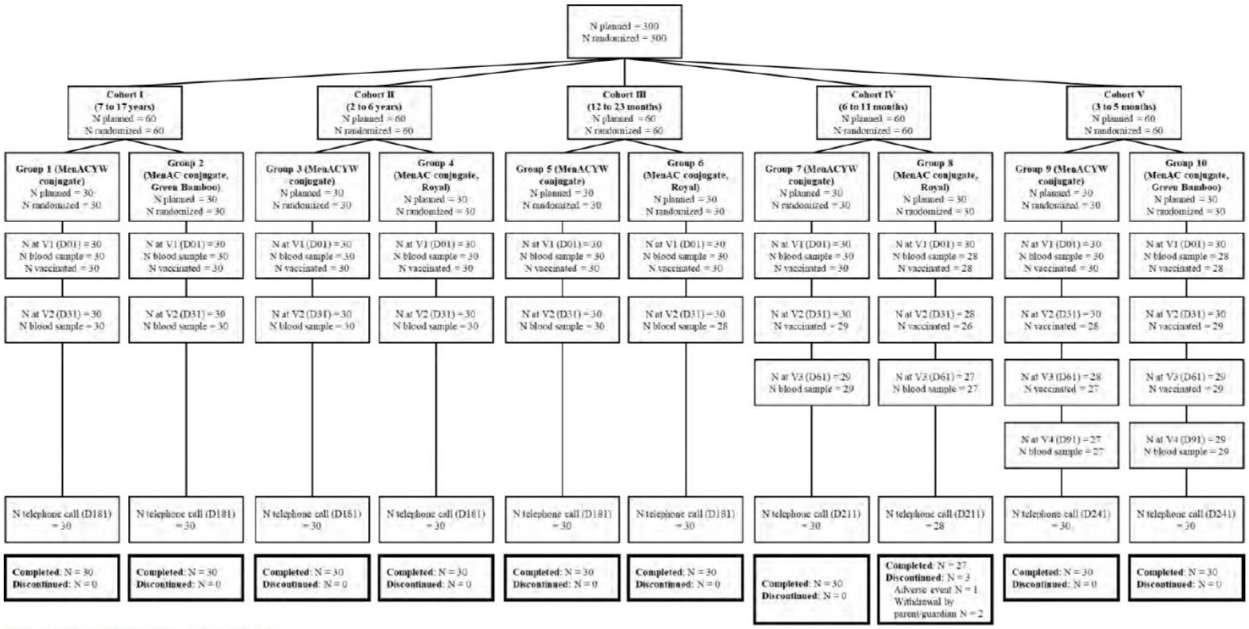
No statistical adjustment is necessary for these analyses because no hypotheses will be tested.

In addition, this study will include 4 early safety data reviews.

Results

Participant flow

Table 4: Participant disposition flow chart



Abbreviations: D: day; N; number; V: visit

Table 5: Duration of the study - All enrolled study participants

	Earliest (DDMMMYYYY)	Latest (DDMMMYYYY)	Duration (days)
Cohort I			
Visit V01 (D01)	12AUG2023	12AUG2023	
Visit V02 (D31)	11SEP2023	18SEP2023	
Active phase termination date	11SEP2023	18SEP2023	
Active phase duration			38
6-month follow-up telephone call (D181)	08FEB2024	20FEB2024	
Follow-up duration			163
Study duration			193
Mean study participant duration (SD)			187 (5.4)
Cohort II			
Visit V01 (D01)	17SEP2023	23SEP2023	
Visit V02 (D31)	17OCT2023	30OCT2023	
Active phase termination date	17OCT2023	30OCT2023	
Active phase duration			44
6-month follow-up telephone call (D181)	15MAR2024	21MAR2024	
Follow-up duration			157
Study duration			187
Mean study participant duration (SD)			181 (0.0)
Cohort III			
Visit V01 (D01)	28OCT2023	18NOV2023	
Visit V02 (D31)	27NOV2023	12JAN2024	
Active phase termination date	27NOV2023	12JAN2024	
Active phase duration			77
6-month follow-up telephone call (D181)	26APR2024	16MAY2024	
Follow-up duration			172
Study duration			202
Mean study participant duration (SD)			183 (1.1)
Cohort IV			
Visit V01 (D01)	25NOV2023	23DEC2023	
Visit V02 (D31)	27DEC2023	29JAN2024	
Visit V03 (D61)	26JAN2024	12MAR2024	
Active phase termination date	27NOV2023	12MAR2024	
Active phase duration			109
6-month follow-up telephone call (D211)	24JUN2024	03AUG2024	
Follow-up duration			251
Study duration			253
Mean study participant duration (SD)			209 (39.1)
Cohort V			
Visit V01 (D01)	24DEC2023	25JAN2024	
Visit V02 (D31)	23JAN2024	06MAR2024	
Visit V03 (D61)	25FEB2024	06JUN2024	
Visit V04 (D91)	26MAR2024	25MAY2024	
Active phase termination date	07FEB2024	06JUN2024	
Active phase duration			166
6-month follow-up telephone call (D241)	23AUG2024	22OCT2024	
Follow-up duration			259
Study duration			304
Mean study participant duration (SD)			249 (9.0)

Duration (days): Latest period date - earliest period date + 1

Mean study participant duration: the mean of study participant durations defined as Maximum (Last visit date, Termination date, Follow-up date) - V01 date + 1

Active phase duration (days) = Max of all participants (Last visit date, Last Termination date) - Min of all participants (V01 date) + 1

Follow-up duration (days) = Max of all participants (Follow-up date) - Min of all participants (Termination date) + 1

Study duration (days) = Max of all participants (Last visit date, Termination date, Follow-up date) - Min of all participants (V01 date) + 1

Table 6: Disposition by randomised group - All randomised study participants

Timepoint		Cohort I 7-17 years		Cohort II 2-6 years		Cohort III 12-23 months		Cohort IV 6-11 months		Cohort V 3-5 months		
		Group 1 (N=30) n (%)	Group 2 (N=30) n (%)	Group 3 (N=30) n (%)	Group 4 (N=30) n (%)	Group 5 (N=30) n (%)	Group 6 (N=30) n (%)	Group 7 (N=30) n (%)	Group 8 (N=30) n (%)	Group 9 (N=30) n (%)	Group 10 (N=30) n (%)	All (N=300) n (%)
V01 (D01)	Randomized	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	300 (100)
	BL performed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	298 (99.3)
	Received MenACYW	30 (100)	0	30 (100)	0	30 (100)	0	30 (100)	0	30 (100)	0	150 (50.0)
	Received Green Bamboo's MenAC	0	30 (100)	-	-	-	-	-	-	0	30 (100)	60 (20.0)
	Received Royal's MenAC	-	-	0	30 (100)	0	30 (100)	0	28 (93.3)	-	-	88 (29.3)
V02 (D31)	Present at visit	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	298 (99.3)
	BL performed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	-	-	-	-	178 (59.3)
	Received MenACYW	-	-	-	-	-	-	29 (96.7)	0	28 (93.3)	0	57 (19.0)
	Received Green Bamboo's MenAC	-	-	-	-	-	-	-	-	0	29 (96.7)	29 (9.7)
	Received Royal's MenAC	-	-	-	-	-	-	0	26 (86.7)	-	-	26 (8.7)
V03 (D61)	Present at visit	-	-	-	-	-	-	29 (96.7)	27 (90.0)	28 (93.3)	29 (96.7)	113 (37.7)
	BL performed	-	-	-	-	-	-	29 (96.7)	27 (90.0)	-	-	56 (18.7)
	Received MenACYW	-	-	-	-	-	-	-	-	27 (90.0)	0	27 (9.0)
	Received Green Bamboo's MenAC	-	-	-	-	-	-	-	-	0	29 (96.7)	29 (9.7)
V04 (D91)	Present at visit	-	-	-	-	-	-	-	-	27 (90.0)	29 (96.7)	56 (18.7)
	BL performed	-	-	-	-	-	-	-	-	27 (90.0)	29 (96.7)	56 (18.7)
	Completed the Active Phase	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	27 (90.0)	30 (100)	30 (100)	297 (99.0)
Follow-up	TC performed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	298 (99.3)
	Completed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	298 (99.3)

n: number of study participants fulfilling the item listed

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate; Group 5: MenACYW conjugate Group 6: Royal's MenAC conjugate; Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate; Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Protocol deviations

Overall, there were 55 (18.3%) participants with at least 1 major protocol deviation: 2 (6.7%) participants in Group 1, 4 (13.3%) in Group 2, 5 (16.7%) in Group 3, 1 (3.3%) in Group 4, 0 in Group 5, 3 (10.0%) in Group 6, 6 (20.0%) in Group 7, 9 (30.0%) in Group 8, 12 (40.0%) in Group 9, and 13 (43.3%) in Group 10.

Table 7: Major and critical protocol deviations by randomised group - All randomised study participants

	Cohort I 7-17 years		Cohort II 2-6 years		Cohort III 12-23 months		Cohort IV 6-11 months		Cohort V 3-5 months		
	Group 1 (N=30) n (%)	Group 2 (N=30) n (%)	Group 3 (N=30) n (%)	Group 4 (N=30) n (%)	Group 5 (N=30) n (%)	Group 6 (N=30) n (%)	Group 7 (N=30) n (%)	Group 8 (N=30) n (%)	Group 9 (N=30) n (%)	Group 10 (N=30) n (%)	All (N=300) n (%)
Study participants with at least one major or critical protocol deviation	2 (6.7)	4 (13.3)	5 (16.7)	1 (3.3)	1 (3.3)	3 (10.0)	6 (20.0)	9 (30.0)	12 (40.0)	13 (43.3)	56 (18.7)
Study participants with at least one major protocol deviation	2 (6.7)	4 (13.3)	5 (16.7)	1 (3.3)	0	3 (10.0)	6 (20.0)	9 (30.0)	12 (40.0)	13 (43.3)	55 (18.3)
A female participant (aged 12-17y) is eligible to participate if she is not pregnant or breastfeeding and applies: non-childbearing potential OR agrees to use an effective contraceptive method	2 (6.7)	4 (13.3)	0	0	0	0	0	0	0	0	6 (2.0)
Participants aged 3 to 5m with vaccination history of any meningococcal vaccine (MV);Received any other MV except the MPSV-A with<=6m interval(aged 6 to 23m) or other MV<=2y interval (aged>=2y)	0	0	1 (3.3)	0	0	0	0	0	0	0	1 (0.3)
Protocol prohibited therapy/medication/vaccine/ administered	0	0	4 (13.3)	1 (3.3)	0	0	1 (3.3)	2 (6.7)	0	1 (3.3)	9 (3.0)
Study physical visit, phone call or safety contact not performed	0	0	0	0	0	0	1 (3.3)	1 (3.3)	3 (10.0)	1 (3.3)	6 (2.0)
Study physical visit, phone call or safety contact not performed within the protocol-specified time window	0	0	0	0	0	3 (10.0)	5 (16.7)	3 (10.0)	7 (23.3)	7 (23.3)	25 (8.3)
Assessment (physical examination and Vital signs) not performed	0	0	0	0	0	0	1 (3.3)	0	3 (10.0)	0	4 (1.3)
Planned sample (serology blood samples) not Performed	0	0	0	0	0	2 (6.7)	0	0	0	0	2 (0.7)
Planned sample (Urine pregnancy test) not Performed	2 (6.7)	4 (13.3)	0	0	0	0	0	0	0	0	6 (2.0)
Planned sample (serology blood samples) not Performed within the protocol-specified time window	0	0	0	0	0	1 (3.3)	0	1 (3.3)	0	0	2 (0.7)
IMP not administered	0	0	0	0	0	0	1 (3.3)	1 (3.3)	3 (10.0)	1 (3.3)	6 (2.0)
IMP administered but not within the protocol-specified time window	0	0	0	0	0	0	4 (13.3)	4 (13.3)	9 (30.0)	11 (36.7)	28 (9.3)
IMP administered still under a protocol-specified temporary contraindication (other than prohibited therapy/medication/vaccine)	0	0	3 (10.0)	1 (3.3)	0	0	1 (3.3)	1 (3.3)	0	1 (3.3)	7 (2.3)
Failure to report safety case to sponsor within the protocol-specified time window	0	0	0	0	0	0	1 (3.3)	0	3 (10.0)	2 (6.7)	6 (2.0)
Failure to follow protocol safety requirements	0	0	0	0	0	0	0	2 (6.7)	0	0	2 (0.7)
Study participants with at least one critical protocol deviation	0	0	0	0	1 (3.3)	0	0	0	0	0	1 (0.3)
History of any neurologic disorders, including any seizures and progressive neurologic disorders.	0	0	0	0	1 (3.3)	0	0	0	0	0	1 (0.3)

n: number of study participants fulfilling the item listed

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate; Group 5: MenACYW conjugate

Group 6: Royal's MenAC conjugate; Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate; Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Recruitment

Study initiation date:

12 August 2023 (first participant first visit)

Study completion:

22 October 2024 (last participant last contact)

Database lock date: 13 March 2025

Baseline data

Overall, the proportion of male versus female participants enrolled in the study was similar (47.3% versus 52.7%), with a male/female sex ratio of 0.90. Similar proportions were observed for all groups except for Group 1, where there were fewer males than females (26.7% versus 73.3%, male/female ratio: 0.36).

Table 8: Baseline demographics by randomised group - All randomised study participants

	Cohort I 7-17 years		Cohort II 2-6 years		Cohort III 12-23 months		Cohort IV 6-11 months		Cohort V 3-5 months		
	Group 1 (N=30) n (%)	Group 2 (N=30) n (%)	Group 3 (N=30) n (%)	Group 4 (N=30) n (%)	Group 5 (N=30) n (%)	Group 6 (N=30) n (%)	Group 7 (N=30) n (%)	Group 8 (N=30) n (%)	Group 9 (N=30) n (%)	Group 10 (N=30) n (%)	All (N=300) n (%)
Sex: n (%)											
Male	8 (26.7)	13 (43.3)	17 (56.7)	14 (46.7)	16 (53.3)	16 (53.3)	16 (53.3)	17 (56.7)	13 (43.3)	12 (40.0)	142 (47.3)
Female	22 (73.3)	17 (56.7)	13 (43.3)	16 (53.3)	14 (46.7)	14 (46.7)	14 (46.7)	13 (43.3)	17 (56.7)	18 (60.0)	158 (52.7)
Missing	0	0	0	0	0	0	0	0	0	0	0
Sex ratio: Male/Female	0.36	0.76	1.31	0.88	1.14	1.14	1.14	1.31	0.76	0.67	0.90
Age (years)											
M	30	30	30	30	-	-	-	-	-	-	120
Mean (SD)	10.4 (1.7)	11.4 (2.4)	5.1 (1.2)	5.1 (1.1)	-	-	-	-	-	-	8.0 (3.4)
Min ; Max	7 ; 13	8 ; 16	2 ; 6	3 ; 6	-	-	-	-	-	-	2 ; 16
Median	10.0	11.0	5.5	5.0	-	-	-	-	-	-	6.5
Q1 ; Q3	9.0 ; 12.0	10.0 ; 14.0	5.0 ; 6.0	5.0 ; 6.0	-	-	-	-	-	-	5.0 ; 11.0
Age (months)											
M	-	-	-	-	30	30	30	30	30	30	180
Mean (SD)	-	-	-	-	20.7 (2.3)	19.4 (2.9)	7.0 (1.4)	6.9 (1.3)	4.0 (0.8)	4.1 (0.8)	10.4 (7.2)
Min ; Max	-	-	-	-	13 ; 23	12 ; 23	6 ; 11	6 ; 11	3 ; 5	3 ; 5	3 ; 23
Median	-	-	-	-	21.0	20.0	6.0	6.0	4.0	4.0	6.0
Q1 ; Q3	-	-	-	-	19.0 ; 23.0	17.0 ; 21.0	6.0 ; 8.0	6.0 ; 7.0	3.0 ; 5.0	3.0 ; 5.0	5.0 ; 19.0

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

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate; Group 5: MenACYW conjugate

Group 6: Royal's MenAC conjugate; Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate; Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Number analysed

Table 9: Safety analysis set by vaccination group - All randomised study participants

	Cohort I 7-17 years		Cohort II 2-6 years		Cohort III 12-23 months		Cohort IV 6-11 months		Cohort V 3-5 months		Randomized but not	
	Group 1 (N=30) n (%)	Group 2 (N=30) n (%)	Group 3 (N=30) n (%)	Group 4 (N=30) n (%)	Group 5 (N=30) n (%)	Group 6 (N=30) n (%)	Group 7 (N=30) n (%)	Group 8 (N=30) n (%)	Group 9 (N=30) n (%)	Group 10 (N=30) n (%)	vaccinated (N=2) n (%)	All (N=300) n (%)
Overall Safety Analysis Set for Any Dose	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	0	298 (99.3)
Safety Analysis Set for the Single Dose or the First Dose	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	0	298 (99.3)
Solicited injection site safety assessed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	0	298 (99.3)
Solicited systemic safety assessed	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	30 (100)	30 (100)	0	298 (99.3)
Safety Analysis Set for the Second Dose	-	-	-	-	-	-	29 (96.7)	26 (86.7)	28 (93.3)	29 (96.7)	0	112 (37.3)
Solicited injection site safety assessed	-	-	-	-	-	-	29 (96.7)	26 (86.7)	28 (93.3)	29 (96.7)	0	112 (37.3)
Solicited systemic safety assessed	-	-	-	-	-	-	29 (96.7)	26 (86.7)	28 (93.3)	29 (96.7)	0	112 (37.3)
Safety Analysis Set for the Third Dose	-	-	-	-	-	-	-	-	27 (90.0)	29 (96.7)	0	56 (18.7)
Solicited injection site safety assessed	-	-	-	-	-	-	-	-	27 (90.0)	29 (96.7)	0	56 (18.7)
Solicited systemic safety assessed	-	-	-	-	-	-	-	-	27 (90.0)	29 (96.7)	0	56 (18.7)

n: number of study participants experiencing the endpoint

Safety endpoints are considered assessed if at least one data has been collected, unsolicited adverse events are never missing as all study participants had a 30-minute surveillance period after each injection

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate; Group 5: MenACYW conjugate

Group 6: Royal's MenAC conjugate; Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate; Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Table 10: Immunogenicity analysis sets by randomised group - All randomised study participants

	Cohort I 7-17 years		Cohort II 2-6 years		Cohort III 12-23 months		Cohort IV 6-11 months		Cohort V 3-5 months		
	Group 1 (N=30) n (%)	Group 2 (N=30) n (%)	Group 3 (N=30) n (%)	Group 4 (N=30) n (%)	Group 5 (N=30) n (%)	Group 6 (N=30) n (%)	Group 7 (N=30) n (%)	Group 8 (N=30) n (%)	Group 9 (N=30) n (%)	Group 10 (N=30) n (%)	All (N=300) n (%)
Full Analysis Set	30 (100)	30 (100)	30 (100)	30 (100)	30 (100)	28 (93.3)	29 (96.7)	27 (90.0)	27 (90.0)	29 (96.7)	290 (96.7)
Participants with at least one criterion for exclusion from FAS	0	0	0	0	0	2 (6.7)	1 (3.3)	3 (10.0)	3 (10.0)	1 (3.3)	10 (3.3)
Not injected	0	0	0	0	0	0	0	2 (6.7)	0	0	2 (0.7)
Post-vaccination sample did not produce valid result	0	0	0	0	0	2 (6.7)	1 (3.3)	3 (10.0)	3 (10.0)	1 (3.3)	10 (3.3)
Per Protocol Analysis Set	28 (93.3)	26 (86.7)	25 (83.3)	29 (96.7)	29 (96.7)	27 (90.0)	25 (83.3)	21 (70.0)	19 (63.3)	18 (60.0)	247 (82.3)
Participants with at least one criterion for exclusion from PPAS	2 (6.7)	4 (13.3)	5 (16.7)	1 (3.3)	1 (3.3)	3 (10.0)	5 (16.7)	9 (30.0)	11 (36.7)	12 (40.0)	53 (17.7)
Participant did not meet all protocol-specified inclusion criteria or met at least one of the protocol-specified exclusion criteria	2 (6.7)	4 (13.3)	1 (3.3)	0	1 (3.3)	0	0	0	0	0	8 (2.7)
Participant did not complete the study vaccination schedule	0	0	0	0	0	0	1 (3.3)	4 (13.3)	3 (10.0)	1 (3.3)	9 (3.0)
Participant received a vaccine other than the one that he/she was randomized to receive	0	0	0	0	0	0	0	0	0	0	0
Preparation and/or administration of study vaccine was not done as per-protocol	0	0	3 (10.0)	1 (3.3)	0	0	1 (3.3)	1 (3.3)	0	1 (3.3)	7 (2.3)
Participant did not receive study vaccine in the proper time window	0	0	0	0	0	0	4 (13.3)	4 (13.3)	9 (30.0)	11 (36.7)	28 (9.3)
Participant did not provide post-dose serology sample in the proper time window or a post-dose serology sample was not drawn	0	0	0	0	0	3 (10.0)	1 (3.3)	4 (13.3)	3 (10.0)	1 (3.3)	12 (4.0)
Participant received a protocol-prohibited therapy/medication/vaccine	0	0	4 (13.3)	1 (3.3)	0	0	1 (3.3)	2 (6.7)	0	1 (3.3)	9 (3.0)
Post-vaccination serology sample did not produce a valid test result	0	0	0	0	0	2 (6.7)	1 (3.3)	3 (10.0)	3 (10.0)	1 (3.3)	10 (3.3)
Other protocol violation	0	0	0	0	0	0	0	0	0	0	0

n: number of study participants fulfilling the item listed

Note: a study participant may be associated with more than one criterion

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate; Group 5: MenACYW conjugate

Group 6: Royal's MenAC conjugate; Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate; Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Efficacy results

Key secondary immunogenicity objectives

rSBA meningococcal seroresponse in Cohort I (7 to 17 YoA) after single dose of the corresponding vaccine

Table 11: Comparison of rSBA vaccine seroresponse at D31 for Group 1 versus Group 2 of Cohort I - Per-Protocol Analysis Set

	Group 1 (N=28)			Group 2 (N=26)			Group 1 - Group 2	
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	Difference (%)	(95% CI)
A	23/28	82.1	(63.1 ; 93.9)	5/26	19.2	(6.6 ; 39.4)	62.91	(37.18 ; 77.56)
C	27/28	96.4	(81.7 ; 99.9)	8/26	30.8	(14.3 ; 51.8)	65.66	(41.80 ; 80.23)
Y	25/28	89.3	(71.8 ; 97.7)	-	-	-	-	-
W	27/28	96.4	(81.7 ; 99.9)	-	-	-	-	-

n: number of participants with titers that meet the rSBA vaccine seroresponse criteria; rSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:8; 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.

M: number of participants with available data for the relevant endpoint at both pre-vaccination and post-vaccination time points

N: number of participants in per-protocol analysis set; Percentages are based on M.

95% CI of the single proportion calculated from the exact binomial method. 95% CI of the difference calculated from the Wilson Score method without continuity correction

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate

rSBA meningococcal seroresponse in Cohort II (2 to 6 YoA) after single dose of the corresponding vaccine

Table 12: Comparison of rSBA vaccine seroresponse at D31 for Group 3 versus Group 4 of Cohort II - Per-Protocol Analysis Set

	Group 3 (N=25)			Group 4 (N=29)			Group 3 - Group 4	
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	Difference (%)	(95% CI)
A	22/25	88.0	(68.8 ; 97.5)	24/29	82.8	(64.2 ; 94.2)	5.24	(-15.14 ; 24.24)
C	25/25	100	(86.3 ; 100)	29/29	100	(88.1 ; 100)	0.00	(-13.32 ; 11.70)
Y	23/25	92.0	(74.0 ; 99.0)	-	-	-	-	-
W	24/25	96.0	(79.6 ; 99.9)	-	-	-	-	-

n: number of participants with titers that meet the rSBA vaccine seroresponse criteria; rSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:8; 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.

M: number of participants with available data for the relevant endpoint at both pre-vaccination and post-vaccination time points

N: number of participants in per-protocol analysis set; Percentages are based on M.

95% CI of the single proportion calculated from the exact binomial method. 95% CI of the difference calculated from the Wilson Score method without continuity correction

Group 3: MenACYW conjugate; Group 4: Royal>s MenAC conjugate

rSBA meningococcal seroresponse in Cohort III (12 to 23 MoA) after single dose of the corresponding vaccine

Table 13: Comparison of rSBA vaccine seroresponse at D31 for Group 5 versus Group 6 of Cohort III - Per-Protocol Analysis Set

		Group 5 (N=29)			Group 6 (N=27)		Group 5 - Group 6	
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	Difference (%)	(95% CI)
A	28/29	96.6	(82.2 ; 99.9)	24/27	88.9	(70.8 ; 97.6)	7.66	(-7.87 ; 24.85)
C	29/29	100	(88.1 ; 100)	27/27	100	(87.2 ; 100)	0.00	(-11.70 ; 12.46)
Y	26/29	89.7	(72.6 ; 97.8)	-	-	-	-	-
W	27/29	93.1	(77.2 ; 99.2)	-	-	-	-	-

n: number of participants with titers that meet the rSBA vaccine seroresponse criteria; rSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:8; 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.
M: number of participants with available data for the relevant endpoint at both pre-vaccination and post-vaccination time points
N: number of participants in per-protocol analysis set; Percentages are based on M.
95% CI of the single proportion calculated from the exact binomial method. 95% CI of the difference calculated from the Wilson Score method without continuity correction
Group 5: MenACYW conjugate; Group 6: Royal's MenAC conjugate

rSBA meningococcal seroresponse in Cohort IV (6 to 11 MoA) after 2 doses of the corresponding vaccine

Table 14: Comparison of rSBA vaccine seroresponse at D61 for Group 7 versus Group 8 of Cohort IV - Per-Protocol Analysis Set

		Group 7 (N=25)			Group 8 (N=21)		Group 7 - Group 8	
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	Difference (%)	(95% CI)
A	24/25	96.0	(79.6 ; 99.9)	16/21	76.2	(52.8 ; 91.8)	19.81	(-0.57 ; 41.34)
C	25/25	100	(86.3 ; 100)	21/21	100	(83.9 ; 100)	0.00	(-13.32 ; 15.46)
Y	22/25	88.0	(68.8 ; 97.5)	-	-	-	-	-
W	24/25	96.0	(79.6 ; 99.9)	-	-	-	-	-

n: number of participants with titers that meet the rSBA vaccine seroresponse criteria; rSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:8; 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.
M: number of participants with available data for the relevant endpoint at both pre-vaccination and post-vaccination time points
N: number of participants in per-protocol analysis set; Percentages are based on M.
95% CI of the single proportion calculated from the exact binomial method. 95% CI of the difference calculated from the Wilson Score method without continuity correction
Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate

rSBA meningococcal seroresponse in Cohort V (3 to 5 MoA) after 3 doses of the corresponding vaccine

Table 15: Comparison of rSBA vaccine seroresponse at D91 for Group 9 versus Group 10 of Cohort V - Per-Protocol Analysis Set

		Group 9 (N=19)			Group 10 (N=18)		Group 9 - Group 10	
Serogroup	n/M	%	(95% CI)	n/M	%	(95% CI)	Difference (%)	(95% CI)
A	18/19	94.7	(74.0 ; 99.9)	2/18	11.1	(1.4 ; 34.7)	83.63	(54.54 ; 92.73)
C	19/19	100	(82.4 ; 100)	7/18	38.9	(17.3 ; 64.3)	61.11	(33.03 ; 79.69)
Y	19/19	100	(82.4 ; 100)	-	-	-	-	-
W	19/19	100	(82.4 ; 100)	-	-	-	-	-

n: number of participants with titers that meet the rSBA vaccine seroresponse criteria; rSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:8; 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.
M: number of participants with available data for the relevant endpoint at both pre-vaccination and post-vaccination time points
N: number of participants in per-protocol analysis set; Percentages are based on M.
95% CI of the single proportion calculated from the exact binomial method. 95% CI of the difference calculated from the Wilson Score method without continuity correction
Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

rSBA antibody titres in terms of GMTs in each cohort

Table 16: Comparison of rSBA GMTs at D31 for Group 1 versus Group 2 of Cohort I - Per-Protocol Analysis Set

		Group 1 (N=28)			Group 2 (N=26)		Group 1 / Group 2	
Serogroup	M	GMT	(95% CI)	M	GMT	(95% CI)	GMT Ratio	(95% CI)
A	28	742	(517 ; 1066)	26	60.7	(29.1 ; 126)	12.2	(5.60 ; 26.7)
C	28	565	(370 ; 864)	26	3.89	(1.89 ; 8.03)	145	(64.9 ; 324)
Y	28	353	(205 ; 609)	-	-	-	-	-
W	28	238	(163 ; 346)	-	-	-	-	-

M: number of participants with available data for the relevant endpoint.
N: number of participants in per-protocol analysis set
95% CI calculated using calculation for normal distribution on log10 (titer) following by antilog transformation
Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate

Table 17: Comparison of rSBA GMTs at D31 for Group 3 versus Group 4 of Cohort II - Per-Protocol Analysis Set

		Group 3 (N=25)			Group 4 (N=29)		Group 3 / Group 4	
Serogroup	M	GMT	(95% CI)	M	GMT	(95% CI)	GMT Ratio	(95% CI)
A	25	572	(400 ; 817)	29	349	(243 ; 502)	1.64	(0.992 ; 2.70)
C	25	695	(463 ; 1042)	29	433	(325 ; 577)	1.60	(0.997 ; 2.58)
Y	25	294	(209 ; 413)	-	-	-	-	-
W	25	118	(74.7 ; 186)	-	-	-	-	-

M: number of participants with available data for the relevant endpoint.
N: number of participants in per-protocol analysis set
95% CI calculated using calculation for normal distribution on log10 (titer) following by antilog transformation

Table 18: Comparison of rSBA GMTs at D31 for Group 5 versus Group 6 of Cohort III - Per-Protocol Analysis Set

		Group 5 (N=29)			Group 6 (N=27)		Group 5 / Group 6	
Serogroup	M	GMT	(95% CI)	M	GMT	(95% CI)	GMT Ratio	(95% CI)
A	29	256	(160 ; 409)	27	91.7	(42.0 ; 200)	2.79	(1.17 ; 6.69)
C	29	550	(407 ; 744)	27	284	(199 ; 404)	1.94	(1.23 ; 3.05)
Y	29	54.1	(36.4 ; 80.5)	-	-	-	-	-
W	29	36.9	(21.5 ; 63.6)	-	-	-	-	-

M: number of participants with available data for the relevant endpoint.
N: number of participants in per-protocol analysis set
95% CI calculated using calculation for normal distribution on log10 (titer) following by antilog transformation
Group 5: MenACYW conjugate; Group 6: Royal's MenAC conjugate

Table 19: Comparison of rSBA GMTs at D61 for Group 7 versus Group 8 of Cohort IV - Per-Protocol Analysis Set

		Group 7 (N=25)			Group 8 (N=21)		Group 7 / Group 8	
Serogroup	M	GMT	(95% CI)	M	GMT	(95% CI)	GMT Ratio	(95% CI)
A	25	89.3	(47.8 ; 167)	21	40.3	(13.0 ; 125)	2.21	(0.664 ; 7.38)
C	25	211	(151 ; 295)	21	47.6	(34.4 ; 65.8)	4.43	(2.80 ; 7.02)
Y	25	39.9	(23.4 ; 68.1)	-	-	-	-	-
W	25	45.9	(28.5 ; 73.8)	-	-	-	-	-

M: number of participants with available data for the relevant endpoint.
N: number of participants in per-protocol analysis set
95% CI calculated using calculation for normal distribution on log10 (titer) following by antilog transformation
Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate

Table 20: Comparison of rSBA GMTs at D91 for Group 9 versus Group 10 of Cohort V - Per-Protocol Analysis Set

		Group 9 (N=19)			Group 10 (N=18)		Group 9 / Group 10	
Serogroup	M	GMT	(95% CI)	M	GMT	(95% CI)	GMT Ratio	(95% CI)
A	19	82.6	(34.3 ; 199)	18	1.71	(0.786 ; 3.74)	48.2	(15.4 ; 150)
C	19	159	(112 ; 227)	18	3.30	(1.58 ; 6.89)	48.3	(22.3 ; 105)
Y	19	128	(91.6 ; 179)	-	-	-	-	-
W	19	82.6	(55.1 ; 124)	-	-	-	-	-

M: number of participants with available data for the relevant endpoint.
N: number of participants in per-protocol analysis set
95% CI calculated using calculation for normal distribution on log10 (titer) following by antilog transformation
Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Other secondary immunogenicity objectives

rSBA antibody titres ≥1:8 and ≥1:128 in each cohort

Table 21: Number and percentage of participants with rSBA titre >= 1:8 and >= 1:128 of Cohort I - Per-Protocol Analysis Set

			Cohort I 7-17 years					
			Group 1 (N=28)			Group 2 (N=26)		
Serogroup	Time Point	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D01	>=1:8	24/28	85.7	(67.3 ; 96.0)	22/26	84.6	(65.1 ; 95.6)
		>=1:128	16/28	57.1	(37.2 ; 75.5)	12/26	46.2	(26.6 ; 66.6)
	D31	>=1:8	28/28	100	(87.7 ; 100)	22/26	84.6	(65.1 ; 95.6)
		>=1:128	27/28	96.4	(81.7 ; 99.9)	13/26	50.0	(29.9 ; 70.1)
C	D01	>=1:8	2/28	7.1	(0.9 ; 23.5)	2/26	7.7	(0.9 ; 25.1)
		>=1:128	1/28	3.6	(0.1 ; 18.3)	0/26	0	(0 ; 13.2)
	D31	>=1:8	28/28	100	(87.7 ; 100)	10/26	38.5	(20.2 ; 59.4)
		>=1:128	28/28	100	(87.7 ; 100)	2/26	7.7	(0.9 ; 25.1)
Y	D01	>=1:8	19/28	67.9	(47.6 ; 84.1)	-	-	-
		>=1:128	4/28	14.3	(4.0 ; 32.7)	-	-	-
	D31	>=1:8	27/28	96.4	(81.7 ; 99.9)	-	-	-
		>=1:128	26/28	92.9	(76.5 ; 99.1)	-	-	-
W	D01	>=1:8	9/28	32.1	(15.9 ; 52.4)	-	-	-
		>=1:128	0/28	0	(0 ; 12.3)	-	-	-
	D31	>=1:8	28/28	100	(87.7 ; 100)	-	-	-
		>=1:128	25/28	89.3	(71.8 ; 97.7)	-	-	-

n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
N: number of participants in per-protocol analysis set
Percentages are based on M
Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate

Table 22: Number and percentage of participants with rSBA titre >= 1:8 and >= 1:128 of Cohort II - Per-Protocol Analysis Set

			Cohort II 2-6 years					
			Group 3 (N=25)			Group 4 (N=29)		
Serogroup	Time Point	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D01	>=1:8	18/25	72.0	(50.6 ; 87.9)	20/29	69.0	(49.2 ; 84.7)
		>=1:128	5/25	20.0	(6.8 ; 40.7)	8/29	27.6	(12.7 ; 47.2)
	D31	>=1:8	25/25	100	(86.3 ; 100)	29/29	100	(88.1 ; 100)
		>=1:128	24/25	96.0	(79.6 ; 99.9)	27/29	93.1	(77.2 ; 99.2)
C	D01	>=1:8	4/25	16.0	(4.5 ; 36.1)	2/29	6.9	(0.8 ; 22.8)
		>=1:128	1/25	4.0	(0.1 ; 20.4)	0/29	0	(0 ; 11.9)
	D31	>=1:8	25/25	100	(86.3 ; 100)	29/29	100	(88.1 ; 100)
		>=1:128	25/25	100	(86.3 ; 100)	29/29	100	(88.1 ; 100)
Y	D01	>=1:8	23/25	92.0	(74.0 ; 99.0)	-	-	-
		>=1:128	3/25	12.0	(2.5 ; 31.2)	-	-	-
	D31	>=1:8	25/25	100	(86.3 ; 100)	-	-	-
		>=1:128	24/25	96.0	(79.6 ; 99.9)	-	-	-
W	D01	>=1:8	4/25	16.0	(4.5 ; 36.1)	-	-	-
		>=1:128	0/25	0	(0 ; 13.7)	-	-	-
	D31	>=1:8	24/25	96.0	(79.6 ; 99.9)	-	-	-
		>=1:128	18/25	72.0	(50.6 ; 87.9)	-	-	-

n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
N: number of participants in per-protocol analysis set
Percentages are based on M
Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate

Table 23: Number and percentage of participants with rSBA titre >= 1:8 and >= 1:128 of Cohort III - Per-Protocol Analysis Set

			Cohort III 12-23 months					
			Group 5 (N=29)			Group 6 (N=27)		
Serogroup	Time Point	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D01	>=1:8	3/29	10.3	(2.2 ; 27.4)	3/27	11.1	(2.4 ; 29.2)
		>=1:128	1/29	3.4	(0.1 ; 17.8)	1/27	3.7	(0.1 ; 19.0)
	D31	>=1:8	29/29	100	(88.1 ; 100)	24/27	88.9	(70.8 ; 97.6)
		>=1:128	23/29	79.3	(60.3 ; 92.0)	17/27	63.0	(42.4 ; 80.6)
C	D01	>=1:8	0/29	0	(0 ; 11.9)	0/27	0	(0 ; 12.8)
		>=1:128	0/29	0	(0 ; 11.9)	0/27	0	(0 ; 12.8)
	D31	>=1:8	29/29	100	(88.1 ; 100)	27/27	100	(87.2 ; 100)
		>=1:128	29/29	100	(88.1 ; 100)	24/27	88.9	(70.8 ; 97.6)
Y	D01	>=1:8	3/29	10.3	(2.2 ; 27.4)	-	-	-
		>=1:128	1/29	3.4	(0.1 ; 17.8)	-	-	-
	D31	>=1:8	28/29	96.6	(82.2 ; 99.9)	-	-	-
		>=1:128	10/29	34.5	(17.9 ; 54.3)	-	-	-
W	D01	>=1:8	0/29	0	(0 ; 11.9)	-	-	-
		>=1:128	0/29	0	(0 ; 11.9)	-	-	-
	D31	>=1:8	27/29	93.1	(77.2 ; 99.2)	-	-	-
		>=1:128	8/29	27.6	(12.7 ; 47.2)	-	-	-

n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
N: number of participants in per-protocol analysis set
Percentages are based on M
Group 5: MenACYW conjugate; Group 6: Royal's MenAC conjugate

Table 24: Number and percentage of participants with rSBA titre >= 1:8 and >= 1:128 of Cohort IV - Per-Protocol Analysis Set

			Cohort IV 6-11 months					
			Group 7 (N=25)			Group 8 (N=21)		
Serogroup	Time Point	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D01	>=1:8	1/25	4.0	(0.1 ; 20.4)	0/21	0	(0 ; 16.1)
		>=1:128	0/25	0	(0 ; 13.7)	0/21	0	(0 ; 16.1)
	D61	>=1:8	24/25	96.0	(79.6 ; 99.9)	16/21	76.2	(52.8 ; 91.8)
		>=1:128	14/25	56.0	(34.9 ; 75.6)	9/21	42.9	(21.8 ; 66.0)
C	D01	>=1:8	0/25	0	(0 ; 13.7)	0/21	0	(0 ; 16.1)
		>=1:128	0/25	0	(0 ; 13.7)	0/21	0	(0 ; 16.1)
	D61	>=1:8	25/25	100	(86.3 ; 100)	21/21	100	(83.9 ; 100)
		>=1:128	21/25	84.0	(63.9 ; 95.5)	3/21	14.3	(3.0 ; 36.3)
Y	D01	>=1:8	1/25	4.0	(0.1 ; 20.4)	-	-	-
		>=1:128	0/25	0	(0 ; 13.7)	-	-	-
	D61	>=1:8	23/25	92.0	(74.0 ; 99.0)	-	-	-
		>=1:128	6/25	24.0	(9.4 ; 45.1)	-	-	-
W	D01	>=1:8	0/25	0	(0 ; 13.7)	-	-	-
		>=1:128	0/25	0	(0 ; 13.7)	-	-	-
	D61	>=1:8	24/25	96.0	(79.6 ; 99.9)	-	-	-
		>=1:128	7/25	28.0	(12.1 ; 49.4)	-	-	-

n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
N: number of participants in per-protocol analysis set
Percentages are based on M
Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate

Table 25: Number and percentage of participants with rSBA titre >= 1:8 and >= 1:128 of Cohort V - Per-Protocol Analysis Set

			Cohort V 3-5 months					
			Group 9 (N=19)			Group 10 (N=18)		
Serogroup	Time Point	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D01	>=1:8	0/19	0	(0 ; 17.6)	1/18	5.6	(0.1 ; 27.3)
		>=1:128	0/19	0	(0 ; 17.6)	0/18	0	(0 ; 18.5)
	D91	>=1:8	18/19	94.7	(74.0 ; 99.9)	2/18	11.1	(1.4 ; 34.7)
		>=1:128	9/19	47.4	(24.4 ; 71.1)	2/18	11.1	(1.4 ; 34.7)
C	D01	>=1:8	0/19	0	(0 ; 17.6)	1/18	5.6	(0.1 ; 27.3)
		>=1:128	0/19	0	(0 ; 17.6)	0/18	0	(0 ; 18.5)
	D91	>=1:8	19/19	100	(82.4 ; 100)	7/18	38.9	(17.3 ; 64.3)
		>=1:128	16/19	84.2	(60.4 ; 96.6)	0/18	0	(0 ; 18.5)
Y	D01	>=1:8	1/19	5.3	(0.1 ; 26.0)	-	-	-
		>=1:128	0/19	0	(0 ; 17.6)	-	-	-
	D91	>=1:8	19/19	100	(82.4 ; 100)	-	-	-
		>=1:128	14/19	73.7	(48.8 ; 90.9)	-	-	-
W	D01	>=1:8	0/19	0	(0 ; 17.6)	-	-	-
		>=1:128	0/19	0	(0 ; 17.6)	-	-	-
	D91	>=1:8	19/19	100	(82.4 ; 100)	-	-	-
		>=1:128	10/19	52.6	(28.9 ; 75.6)	-	-	-

n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint
N: number of participants in per-protocol analysis set
Percentages are based on M
Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

Safety results

Safety data were collected as follows:

- immediate unsolicited systemic AEs within 30 minutes of each vaccination,
- solicited AEs within 7 days after each vaccination,
- unsolicited AEs within 30 days after each vaccination,
- SAEs throughout the study period from Visit 1 until the end of the 6-month follow-up period after the last vaccination.

Table 26: Safety overview after vaccine injection of Cohort I to II - SafAS

	Cohort I 7-17 years						Cohort II 2-6 years					
	Group 1 (N=30)			Group 2 (N=30)			Group 3 (N=30)			Group 4 (N=30)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection												
Immediate unsolicited AE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Immediate unsolicited AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Solicited reaction within solicited period after vaccine injection	8/30	26.7	(12.3 ; 45.9)	10/30	33.3	(17.3 ; 52.8)	11/30	36.7	(19.9 ; 56.1)	5/30	16.7	(5.6 ; 34.7)
Solicited injection site reaction	7/30	23.3	(9.9 ; 42.3)	9/30	30.0	(14.7 ; 49.4)	9/30	30.0	(14.7 ; 49.4)	5/30	16.7	(5.6 ; 34.7)
Solicited systemic reaction	3/30	10.0	(2.1 ; 26.5)	2/30	6.7	(0.8 ; 22.1)	5/30	16.7	(5.6 ; 34.7)	2/30	6.7	(0.8 ; 22.1)
Within 30 days after vaccine injection												
Unsolicited AE	6/30	20.0	(7.7 ; 38.6)	7/30	23.3	(9.9 ; 42.3)	11/30	36.7	(19.9 ; 56.1)	10/30	33.3	(17.3 ; 52.8)
Unsolicited AR	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	2/30	6.7	(0.8 ; 22.1)	2/30	6.7	(0.8 ; 22.1)
Unsolicited non-serious AE	6/30	20.0	(7.7 ; 38.6)	7/30	23.3	(9.9 ; 42.3)	10/30	33.3	(17.3 ; 52.8)	10/30	33.3	(17.3 ; 52.8)
Unsolicited non-serious AR	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	2/30	6.7	(0.8 ; 22.1)	2/30	6.7	(0.8 ; 22.1)
Unsolicited non-serious injection site AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Unsolicited non-serious systemic AE	6/30	20.0	(7.7 ; 38.6)	7/30	23.3	(9.9 ; 42.3)	10/30	33.3	(17.3 ; 52.8)	10/30	33.3	(17.3 ; 52.8)
Unsolicited non-serious systemic AR	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	2/30	6.7	(0.8 ; 22.1)	2/30	6.7	(0.8 ; 22.1)
AE leading to study discontinuation	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	0/30	0	(0 ; 11.6)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During 6-month follow-up period												
SAE	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	3/30	10.0	(2.1 ; 26.5)	3/30	10.0	(2.1 ; 26.5)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During the study												
SAE	0/30	0	(0 ; 11.6)	1/30	3.3	(0.1 ; 17.2)	4/30	13.3	(3.8 ; 30.7)	3/30	10.0	(2.1 ; 26.5)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)

n: number of participants experiencing the endpoint listed in the first column; M: number of participants with available data for the relevant endpoint

N: number of participants in SafAS; Percentages are based on M; AR: Reactions related to study vaccine

Group 1: MenACYW conjugate; Group 2: Green Bamboo's MenAC conjugate; Group 3: MenACYW conjugate; Group 4: Royal's MenAC conjugate

Table 27: Safety overview after vaccine injection of Cohort III - SafAS

	Cohort III 12-23 months					
	Group 5 (N=30)			Group 6 (N=30)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection						
Immediate unsolicited AE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Immediate unsolicited AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Solicited reaction within solicited period after vaccine injection	9/30	30.0	(14.7 ; 49.4)	6/30	20.0	(7.7 ; 38.6)
Solicited injection site reaction	2/30	6.7	(0.8 ; 22.1)	2/30	6.7	(0.8 ; 22.1)
Solicited systemic reaction	7/30	23.3	(9.9 ; 42.3)	6/30	20.0	(7.7 ; 38.6)
Within 30 days after vaccine injection						
Unsolicited AE	15/30	50.0	(31.3 ; 68.7)	15/30	50.0	(31.3 ; 68.7)
Unsolicited AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Unsolicited non-serious AE	13/30	43.3	(25.5 ; 62.6)	14/30	46.7	(28.3 ; 65.7)
Unsolicited non-serious AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Unsolicited non-serious injection site AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Unsolicited non-serious systemic AE	13/30	43.3	(25.5 ; 62.6)	14/30	46.7	(28.3 ; 65.7)
Unsolicited non-serious systemic AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
AE leading to study discontinuation	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
SAE	4/30	13.3	(3.8 ; 30.7)	2/30	6.7	(0.8 ; 22.1)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During 6-month follow-up period						
SAE	5/30	16.7	(5.6 ; 34.7)	7/30	23.3	(9.9 ; 42.3)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During the study						
SAE	7/30	23.3	(9.9 ; 42.3)	8/30	26.7	(12.3 ; 45.9)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)

n: number of participants experiencing the endpoint listed in the first column; M: number of participants with available data for the relevant endpoint
N: number of participants in SafAS; Percentages are based on M; AR: Reactions related to study vaccine
Group 5: MenACYW conjugate; Group 6: Royal's MenAC conjugate

Table 28: Safety overview after any vaccine injections of Cohort IV - SafAS

	Cohort IV 6-11 months					
	Group 7 (N=30)			Group 8 (N=28)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection						
Immediate unsolicited AE	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Immediate unsolicited AR	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Solicited reaction within solicited period after vaccine injection	18/30	60.0	(40.6 ; 77.3)	9/28	32.1	(15.9 ; 52.4)
Solicited injection site reaction	3/30	10.0	(2.1 ; 26.5)	1/28	3.6	(0.1 ; 18.3)
Solicited systemic reaction	17/30	56.7	(37.4 ; 74.5)	8/28	28.6	(13.2 ; 48.7)
Within 30 days after vaccine injection						
Unsolicited AE	26/30	86.7	(69.3 ; 96.2)	23/28	82.1	(63.1 ; 93.9)
Unsolicited AR	2/30	6.7	(0.8 ; 22.1)	1/28	3.6	(0.1 ; 18.3)
Unsolicited non-serious AE	25/30	83.3	(65.3 ; 94.4)	23/28	82.1	(63.1 ; 93.9)
Unsolicited non-serious AR	2/30	6.7	(0.8 ; 22.1)	1/28	3.6	(0.1 ; 18.3)
Unsolicited non-serious injection site AR	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Unsolicited non-serious systemic AE	25/30	83.3	(65.3 ; 94.4)	23/28	82.1	(63.1 ; 93.9)
Unsolicited non-serious systemic AR	2/30	6.7	(0.8 ; 22.1)	1/28	3.6	(0.1 ; 18.3)
AE leading to study discontinuation	0/30	0	(0 ; 11.6)	1/28	3.6	(0.1 ; 18.3)
SAE	4/30	13.3	(3.8 ; 30.7)	7/28	25.0	(10.7 ; 44.9)
Related SAE	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Death	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
During 6-month follow-up period						
SAE	9/30	30.0	(14.7 ; 49.4)	8/28	28.6	(13.2 ; 48.7)
Related SAE	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Death	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
During the study						
SAE	13/30	43.3	(25.5 ; 62.6)	14/28	50.0	(30.6 ; 69.4)
Related SAE	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)
Death	0/30	0	(0 ; 11.6)	0/28	0	(0 ; 12.3)

n: number of participants experiencing the endpoint listed in the first column; M: number of participants with available data for the relevant endpoint
N: number of participants in SafAS; Percentages are based on M; AR: Reactions related to study vaccine
Group 7: MenACYW conjugate; Group 8: Royal's MenAC conjugate

Table 29: Safety overview after any vaccine injections of Cohort V - SafAS

	Cohort V 3-5 months					
	Group 9 (N=30)			Group 10 (N=30)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection						
Immediate unsolicited AE	0/30	0	(0 ; 11.6)	2/30	6.7	(0.8 ; 22.1)
Immediate unsolicited AR	0/30	0	(0 ; 11.6)	2/30	6.7	(0.8 ; 22.1)
Solicited reaction within solicited period after vaccine injection	19/30	63.3	(43.9 ; 80.1)	14/30	46.7	(28.3 ; 65.7)
Solicited injection site reaction	1/30	3.3	(0.1 ; 17.2)	3/30	10.0	(2.1 ; 26.5)
Solicited systemic reaction	19/30	63.3	(43.9 ; 80.1)	12/30	40.0	(22.7 ; 59.4)
Within 30 days after vaccine injection						
Unsolicited AE	28/30	93.3	(77.9 ; 99.2)	25/30	83.3	(65.3 ; 94.4)
Unsolicited AR	4/30	13.3	(3.8 ; 30.7)	5/30	16.7	(5.6 ; 34.7)
Unsolicited non-serious AE	28/30	93.3	(77.9 ; 99.2)	25/30	83.3	(65.3 ; 94.4)
Unsolicited non-serious AR	4/30	13.3	(3.8 ; 30.7)	5/30	16.7	(5.6 ; 34.7)
Unsolicited non-serious injection site AR	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Unsolicited non-serious systemic AE	28/30	93.3	(77.9 ; 99.2)	25/30	83.3	(65.3 ; 94.4)
Unsolicited non-serious systemic AR	4/30	13.3	(3.8 ; 30.7)	5/30	16.7	(5.6 ; 34.7)
AE leading to study discontinuation	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
SAE	10/30	33.3	(17.3 ; 52.8)	6/30	20.0	(7.7 ; 38.6)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During 6-month follow-up period						
SAE	7/30	23.3	(9.9 ; 42.3)	8/30	26.7	(12.3 ; 45.9)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
During the study						
SAE	15/30	50.0	(31.3 ; 68.7)	14/30	46.7	(28.3 ; 65.7)
Related SAE	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)
Death	0/30	0	(0 ; 11.6)	0/30	0	(0 ; 11.6)

n: number of participants experiencing the endpoint listed in the first column; M: number of participants with available data for the relevant endpoint
N: number of participants in SafAS; Percentages are based on M; AR: Reactions related to study vaccine
Group 9: MenACYW conjugate; Group 10: Green Bamboo's MenAC conjugate

2.3.3. Discussion on clinical aspects

Design and conduct

It is noted that the study report of this paediatric study (MEQ00075) 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 contact of the last participant was on 22 October 2024, according to the CSR. It is also unclear why the database lock (dated 13 March 2025) was approximately 6 months after the last contact with the last participant, albeit the 6-month follow-up period was already included in the study period (12 August 2023 to 22 October 2024). However, given the negligible impact of this study on the overall benefit-risk balance of MenQuadfi, no issue is made.

Study MEQ00075 was a Phase I, randomised, open-label, age de-escalation study conducted in a single centre in China and intended to evaluate safety and immunogenicity of MenQuadfi and two locally licensed meningococcal serogroups A and C vaccines (i.e., Green Bamboo's MenAC conjugate vaccine and Royal's MenAC conjugate vaccine) in approximately 300 healthy adolescents, children, toddlers, and infants, aged 3 months to 17 years. The participants were assigned to 1 of 5 cohorts (Cohorts I to V), depending on their age, and randomised 1:1 to receive either MenQuadfi (MenACYW conjugate vaccine) or one of the locally licensed meningococcal vaccines resulting in totally 10 groups with 30 participants each: Cohort I (aged 7 to 17 years, 1 vaccination, Group 1 MenQuadfi, Group 2

Green Bamboo's), Cohort II (aged 2 to 6 years, 1 vaccination, Group 3 MenQuadfi, Group 4 Royal's), Cohort III (aged 12 to 23 months, 1 vaccination, Group 5 MenQuadfi, Group 6 Royal's), Cohort IV (aged 6 to 11 months, 2 vaccinations, Group 7 MenQuadfi, Group 8 Royal's), Cohort V (aged 3 to 5 months, 3 vaccinations, Group 9 MenQuadfi, Group 10 Green Bamboo's). In this regard it is noted that neither of the aforementioned applied comparator vaccines is authorised in the EU.

Different dose regimens/vaccination schedules were investigated, depending on the age of the subjects at enrolment and thus their respective cohort. Cohorts I, II, and III, which included participants above 12 months of age received one vaccination at Visit 1, which is in accordance with the currently approved posology of MenQuadfi in the EU (1 single dose for primary vaccination + 1 single dose for booster vaccination for individuals aged 12 months and older). Cohort IV, which included subjects aged 6 to 11 months, received 2 vaccinations (at Visit 1 and Visit 2, 1 month apart). Cohort V, which included subjects aged 3 to 5 months, received 3 vaccinations (at Visit 1, Visit 2, and Visit 3, 1 month apart respectively). MenQuadfi is authorised for individuals aged 12 months and older; a type II variation procedure to extend the indication to individuals aged 6 weeks to below 12 months is currently ongoing. Consequently, there is no approved posology for individuals below the age of 12 months for MenQuadfi at the moment.

In total, 300 subjects were randomised, with 30 subjects in each of the 10 groups. Eligibility criteria seemed overall acceptable. Participants had to be either naïve as regards meningococcal vaccination (Cohort V, aged 3 to 5 months), or had received only the Group A meningococcal polysaccharide vaccine (MPV-A) included in National Immunization Program (NIP) within 6 months prior to study participation (Cohorts III and IV, aged 6 to 23 months), or had received the last meningococcal vaccination more than 2 years prior to study participation (Cohorts I and II, aged 2 to 17 years). Vaccination with other vaccines (e.g., routine paediatric vaccines, influenza vaccine, and COVID-19 vaccine) was allowed if not 4 weeks before or after receipt of trial vaccination for Cohort I and II or 2 weeks before and after receipt of trial vaccination for Cohort III, IV, and V. Apparently, immunogenicity of non-meningococcal vaccines was not evaluated.

At least 1 major protocol deviation was reported for 55 subjects (18.3 %): 2 (6.7%) participants in Group 1, 4 (13.3%) in Group 2, 5 (16.7%) in Group 3, 1 (3.3%) in Group 4, 0 in Group 5, 3 (10.0%) in Group 6, 6 (20.0%) in Group 7, 9 (30.0%) in Group 8, 12 (40.0%) in Group 9, and 13 (43.3%) in Group 10. The most frequently reported major protocol deviations were "IMP administered but not within the protocol-specified time window", which was reported for 28 (9.3%) participants, and "Study physical visit, phone call or safety contact not performed within the protocol-specified time window", which was reported for 25 (8.3%) participants. This is all not considered concerning, considering that such deviations are expected in trials including the paediatric population. Male/female ratio varied to some extent but only in considerable extent for Cohort I, in which the male/female ratio of Group 1 was 0.36 and Group 2 was 0.76.

Data was analysed descriptively. The primary objective and endpoint aimed at the evaluation of safety. Secondary objectives and endpoints evaluated immunogenicity by measuring rSBA (rabbit complement serum bactericidal assay) antibody titres against meningococcal serogroups A, C, Y, and W, which were expressed as seroresponse (defined as 30 days post vaccination rSBA titres ≥1:8 for participants with pre vaccination rSBA titres <1:8, or at least 4-fold increase in rSBA titres from pre to 30 days post vaccination for participants with pre vaccination rSBA titres ≥1:8), Geometric mean titres (GMT) or percentages of subjects with rSBA antibody titres ≥1:8 and ≥1:128. Application of only rSBA, instead of hSBA, or both, is not considered optimal as analyses based on hSBA titres are better established as correlate of protection.

As regards sample size, the number of participants in each group was not hypothesis driven and no formal sample size calculations were performed. All immunogenicity analyses were performed on the full analysis set (FAS), defined as the participants who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result, and the per-protocol analysis set (PPAS), a subset of the FAS excluding participants with relevant protocol deviations. Safety was analysed using the Safety Analysis Set for Any Dose (SafAS), which included participants who have received at least one dose of the study vaccine and have any safety data available, and additionally, SafAS1, SafAS2, and SafAS3, each including participants who have received at least one dose of the study vaccine at Visit 1, 2, or 3, respectively, and have any safety data available.

Immunogenicity data analyses

Comparative data

Comparative immunogenicity data are only available for serogroups A and C, as a result of the application of comparators that include only these serogroups.

Cohort I (7-17 yoa, single dose, comparator Green Bamboo's)

In Cohort I, rSBA seroresponse titres at Day 31 after vaccination were significantly higher in Group 1 (MenQuadfi) than in Group 2 (comparator Green Bamboo's): 82.1% (95% CI: 63.1%; 93.9%) vs 19.2% (95% CI: 6.6%; 39.4%) for Serogroup A, and 96.4% (95% CI: 81.7%; 99.9%) vs 30.8% (95% CI: 14.3%; 51.8%) for Serogroup C, Group 1 vs Group 2 (PPAS), respectively. This was corroborated by rSBA GMTs at Day 31: 742 (95% CI: 517; 1066) vs 60.7 (95% CI: 29.1; 126) for Serogroup A, and 565 (95% CI: 370; 864) vs 3.89 (95% CI: 1.89; 8.03) for Serogroup C, Group 1 vs Group 2 (PPAS), respectively.

In Cohort II (2-6 yoa, single dose, comparator Royal's)

In Cohort II, rSBA seroresponse titres at Day 31 after vaccination were similar between Group 3 (MenQuadfi) and Group 4 (comparator Royal's): 88.0% (95% CI: 68.8%; 97.5%) vs 82.8% (95% CI: 64.2%; 94.2%) for Serogroup A, and 100% (95% CI: 86.3%; 100%) vs 100% (95% CI: 88.1%; 100%) for Serogroup C, Group 3 vs Group 4 (PPAS), respectively. However, rSBA GMTs at Day 31 were higher in Group 3 than in Group 4: 572 (95% CI: 400; 817) vs 349 (95% CI: 243; 502) for Serogroup A, and 695 (95% CI: 463; 1042) vs 433 (95% CI: 325; 577) for Serogroup C, Group 3 vs Group 4 (PPAS), respectively.

In Cohort III (12-23 moa, single dose, comparator Royal's)

In Cohort III, rSBA seroresponse titres at Day 31 after vaccination were higher in Group 5 (MenQuadfi) than in Group 6 (comparator Royal's) for Serogroup A: 96.6% (95% CI: 82.2%; 99.9%) vs 88.9% (95% CI: 70.8%; 97.6%), Group 5 vs Group 6 (PPAS), respectively. In contrast, for Serogroup C, rSBA seroresponse titres at Day 31 were similar between both groups: 100% (95% CI: 88.1%; 100%) vs 100% (95% CI: 87.2%; 100%), Group 5 vs Group 6 (PPAS), respectively. Notably, rSBA GMTs at Day 31 were higher in Group 5 than in Group 6 for both serogroups: Serogroup A: 256 (95% CI: 160; 409) vs 91.7 (95% CI: 42.0; 200); Serogroup C: 550 (95% CI: 407; 744) vs 284 (95% CI: 199; 404); Group 5 vs Group 6 (PPAS), respectively.

Cohort IV (6-11 moa, 2 doses, comparator Royal's)

In Cohort IV, rSBA seroresponse titres at Day 61 after vaccination were higher in Group 7 (MenQuadfi) than in Group 8 (comparator Royal's) for Serogroup A: 96.0% (95% CI: 79.6%; 99.9) vs 76.2% (95%

CI: 52.8%; 91.8), Group 7 vs Group 8 (PPAS), respectively. In contrast, for Serogroup C, rSBA seroresponse titres at Day 61 were similar between both groups: 100% (95% CI: 86.3%; 100%) vs 100% (95% CI: 83.9%; 100%), Group 7 vs Group 8 (PPAS), respectively. Of note, rSBA GMTs at Day 61 were higher in Group 7 than in Group 8 for both serogroups: Serogroup A: 89.3 (95% CI: 47.8; 167) vs 40.3 (95% CI: 13.0; 125); Serogroup C: 211 (95% CI: 151; 295) vs 47.6 (95% CI: 34.4; 65.8); Group 7 vs Group 8 (PPAS), respectively.

Cohort V (3-5 moa, 3 doses, comparator Green Bamboo's)

In Cohort V, rSBA seroresponse titres at Day 91 after vaccination were significantly higher in Group 9 (MenQuadfi) than in Group 10 (comparator Green Bamboo's): 94.7% (95% CI: 74.0%; 99.9%) vs 11.1% (95% CI: 1.4%; 34.7%) for Serogroup A, and 100% (95% CI: 82.4%; 100%) vs 38.9% (95% CI: 17.3%; 64.3%) for Serogroup C, Group 9 vs Group 10 (PPAS), respectively. This was corroborated by rSBA GMTs at Day 91: 82.6 (95% CI: 34.3; 199) vs 1.71 (95% CI: 0.786; 3.74) for Serogroup A, and 159 (95% CI: 112; 227) vs 3.30 (95% CI: 1.58; 6.89) for Serogroup C Group 9 vs Group 10 (PPAS), respectively.

Non-comparative data

Based on the provided data, elicitation of immune responses can be concluded for the majority of subjects in all cohorts for all serogroups. As regards Cohorts IV and IV, which included age cohorts below 12 months of age, rSBA seroresponse titres were for Cohort IV 88.0% (95% CI: 68.8%; 97.5%) for Serogroup Y and 96.0% (95% CI: 79.6%; 99.9%) for Serogroup W at Day 61 after 2 doses, and for Cohort V 100% (95% CI: 82.4%; 100%) for Serogroup Y and 100% (95% CI: 82.4%; 100%) for Serogroup W at Day 91 after 3 doses.

As regards serogroups A and C for which comparative analyses were possible, titres elicited by MenQuadfi were reportedly of higher magnitude than those elicited by the comparators. However, it is important to mention that multiple shortcomings impair interpretation of both the comparative and non-comparative immunogenicity data to a significant extent. Those are namely the open-label design, the limited sample size of 30 randomised subjects per group, the absence of an EU-authorised comparator, no hypothesis testing and descriptive data analyses only.

Safety data analyses

Immediate unsolicited systemic AEs were collected within 30 minutes after each vaccination, solicited (pre-defined) AEs (solicited reactions) within 7 days after each vaccination (further distinguished in injection site reactions and systemic reactions), unsolicited AEs within 30 days after each vaccination (further distinguished in unsolicited adverse events and unsolicited adverse reactions [i.e., considered related]), and SAEs throughout the study period from Visit 1 until the end of the 6-month follow-up period after the last vaccination, and analysed with different safety analysis sets (see above 'Design and conduct'), which is all acceptable.

Immediate unsolicited AEs within 30 minutes of each vaccination

Immediate unsolicited AEs within 30 minutes after vaccination were reported only in Group 10 (Green Bamboo's, Cohort V), one event (3.3%) of eyelid oedema after the first dose and one event (3.4%) of pallor after the second dose. Both events were Grade 1 and thus no concern is raised.

Solicited AEs (solicited reactions) within 7 days after each vaccination

Cohort I (7-17 yoa, single dose, comparator Green Bamboo's)

Solicited reactions were reported for 8 (26.7%) participants in Group 1 and 10 (33.3%) in Group 2; no Grade 3 or above solicited reactions were reported. Injection site pain was the most frequently reported solicited injection site reaction in both groups, with 23.3% (7 of 30) and 26.7% (8 of 30) of participants in Groups 1 and 2, respectively. Erythema, 10.0% (3 of 30) in Group 1 and 10.0% (3 of 30) in Group 2, and swelling 6.7% (2 of 30) in Group 1 and 10.0% (3 of 30) in Group 2, were less frequently reported. The most frequently reported solicited systemic reactions in either group were headache (6.7%, 2 of 30), malaise (6.7%, 2 of 30), and myalgia (6.7%, 2 of 30) in Group 1. In both groups, most solicited injection site reactions and most solicited systemic reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days; none ongoing at Day 8 were reported.

In Cohort II (2-6 yoa, single dose, comparator Royal's)

Solicited reactions were reported for 11 (36.7%) participants in Group 3 and 5 (16.7%) in Group 4 [Cohort II]; Grade 3 or above solicited injection site reactions were reported for 1 (3.3%) participant in Group 3 (injection site erythema). Injection site pain was the most frequently reported solicited injection site reaction in both groups, with 20.0% (6 of 30) and 10.0% (3 of 30) of participants in Groups 3 and 4, respectively. Erythema, 16.7% (5 of 30) in Group 3 and 6.7% (2 of 30) in Group 4, and swelling, 10.0% (3 of 30) in Group 3 and 10.0% (3 of 30) in Group 4, were less frequently reported. In both groups, most solicited injection site reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days; no solicited injection site reactions ongoing at Day 8 were reported. The most frequently reported solicited systemic reaction in either group was fever (10.0%, 3 of 30) in Group 3. In Group 3, most fever episodes started within Day 1 to Day 4 and resolved with medication after 4-7 days, most of the other solicited systemic reactions (i.e., headache, malaise, and myalgia) started within Day 1 to Day 4 and resolved spontaneously after 1-3 days. In Group 4, all solicited systemic reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days. All solicited systemic reactions had resolved by Day 8, except for a fever episode in a participant in Group 3 (Grade 2 from Day 8 post vaccination that lasted for 2 days and resolved with medication).

In Cohort III (12-23 moa, single dose, comparator Royal's)

Solicited reactions were reported for 9 (30.0%) participants in Group 5 and 6 (20.0%) in Group 6; no Grade 3 or above solicited reactions were reported. In Group 5, 6.7% (2 of 30) of participants experienced at least 1 injection site tenderness; none of the participants experienced any injection site erythema or injection site swelling. In Group 6, 3.3% (1 of 30) of participants experienced at least 1 injection site tenderness and 3.3% (1 of 30) of participants experienced at least 1 injection site erythema; no injection site swelling was reported in either group. In both groups, most solicited injection site reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days; no solicited injection site reactions ongoing at Day 8 were reported. The most frequently reported solicited systemic reactions were fever (16.7%, 5 of 30) in Group 5 and appetite lost (10.0%, 3 of 30) in Group 6. In both groups, most solicited systemic reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days. All solicited systemic reactions had resolved by Day 8, except for an appetite lost episode in a participant in Group 5 (Grade 2 from Day 5 post vaccination that lasted for 5 days and resolved spontaneously).

Cohort IV (6-11 moa, 2 doses, comparator Royal's)

Solicited reactions were reported for 18 (60.0%) participants in Group 7 after any vaccination (14 [46.7%] participants after the first dose and 9 [31.0%] after the second dose) and 9 (32.1%) in Group 8 after any vaccination (4 [14.3%] participants after the first dose and 5 [19.2%] after the second dose); Grade 3 or above solicited systemic reactions were reported for 1 (3.3%) participant in Group 7

after any vaccination (0 participants after the first dose and 1 [3.4%] after the second dose, i.e., vomiting that lasted for 2 days and resolved spontaneously) and 1 (3.6%) participant in Group 8 after any vaccination (0 participant after the first dose and 1 [3.8%] after the second dose, i.e., fever that lasted for 4 days and resolved with medication and hospitalization). The most frequently reported solicited injection site reaction after any vaccination was erythema (6.7%, 2 of 30) in Group 7 and tenderness (3.6%, 1 of 28) in Group 8. Tenderness and swelling were reported for 3.3% (1 of 30) and 3.3% (1 of 30), respectively, of participants in Group 7; no erythema or swelling was reported for participants in Group 8. In both groups, most solicited injection site reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days; no solicited injection site reactions ongoing at Day 8 were reported. The most frequently reported solicited systemic reaction in both groups was fever, with 43.3% (13 of 30) of participants in Group 7 and 17.9% (5 of 28) in Group 8. Most solicited systemic reactions after any vaccination had resolved by Day 8, except for fever in 3 participants (1 in Group 7 that lasted for 2 days and resolved with medication, and 2 in Group 8 of which one was Grade 3, and the other lasted for 2 days and resolved with medication) and appetite lost in 1 participant in Group 7 (Grade 2 from Day 1 that lasted for 35 days and resolved spontaneously).

Cohort V (3-5 moa, 3 doses, comparator Green Bamboo's)

Solicited reactions were reported for 19 (63.3%) participants in Group 9 after any vaccination (12 [40.0%] participants after the first dose, 9 [32.1%] after the second dose, and 2 [7.4%] after the third dose) and 14 (46.7%) in Group 10 after any vaccination (4 [13.3%] participants after the first dose, 6 [20.7%] after the second dose, and 8 [27.6%] after the third dose); Grade 3 or above solicited systemic reactions were reported for 3 (10.0%) participants in Group 9 after the first dose: 1 (3.3%) participant experienced fever from Day 1 that lasted for 4 days and resolved with medication, 1 (3.3%) participant experienced vomiting from Day 1 that lasted for 4 days and resolved spontaneously, and 1 (3.3%) participant experienced irritability from Day 4 that lasted for 2 days and resolved spontaneously. The most frequently reported solicited injection site reaction was injection site erythema (3.3%, 1 of 30) in Group 9 and injection site tenderness (6.7%, 2 of 30) and erythema (6.7%, 2 of 30) in Group 10. No tenderness or swelling was reported for participants in Group 9. Swelling was reported for 3.3% (1 of 30) of participants in Group 10. In both groups, all solicited injection site reactions started within Day 1 to Day 4 and resolved spontaneously after 1-3 days; no solicited injection site reactions ongoing at Day 8 were reported. The most frequently reported solicited systemic reaction after any vaccination in both groups was fever, with 33.3% (10 of 30) of participants in Group 9 and 26.7% (8 of 30) in Group 10. Most solicited systemic reactions after the first dose of vaccination had resolved by Day 8, except appetite lost in 1 participant in Group 9 (Grade 2 from Day 4 that lasted for 6 days and resolved spontaneously) and irritability in 1 participant in Group 10 (Grade 1 from Day 1 that lasted for 10 days and resolved spontaneously). Most solicited systemic reactions after the second dose of vaccination had resolved by Day 8, except vomiting and appetite lost, both reported in 1 participant in Group 10 (Grade 1 vomiting and a Grade 1 appetite lost from Day 8, both reactions lasted for 6 days and resolved spontaneously). Most solicited systemic reactions after the third dose of vaccination had resolved by Day 8, except fever in 1 participant in Group 9 (Grade 2 from Day 8 that lasted for 4 days and resolved with medication) and irritability in 1 participant in Group 10 (Grade 1 from Day 4 that lasted for 9 days and resolved spontaneously).

<u>Unsolicited AEs within 30 days after each vaccination</u>

Cohort I (7-17 yoa, single dose, comparator Green Bamboo's)

Unsolicited AEs were reported for 20.0% (6 of 30) of participants in Group 1 and 23.3% (7 of 30) in Group 2, all were systemic. Participants most frequently experienced (at least 10% of participants in a

group) Rhinorrhoea (10.0% [3 of 30] in Group 1); no Grade 3 or above unsolicited AEs were reported in either group. In both groups, most unsolicited AEs started from ≥D16 and resolved after 1-3 days. As regards unsolicited adverse reactions (AR), one (3.3%) participant in Group 2 experienced rhinorrhoea, which started from Day 5 to Day 8 and resolved after 1-3 days, none of those were Grade 3 or higher.

In Cohort II (2-6 yoa, single dose, comparator Royal's)

Unsolicited AEs were reported for 36.7% (11 of 30) of participants in Group 3 and 33.3% (10 of 30) in Group 4, all were systemic. Participants most frequently experienced cough, 20.0% (6 of 30) in Group 3 and 13.3% (4 of 30) in Group 4, and rhinorrhoea, 10.0% (3 of 30) in Group 4. Two Grade 3 unsolicited AEs were reported in 2 (6.7%) participants in Group 3: Tonsillitis bacterial by 1 (3.3%) participant and upper respiratory tract infection by 1 (3.3%) participant. In Group 3, most unsolicited AEs started from Day 9 to Day 15 and resolved after 4-7 days; in Group 4, most unsolicited AEs started from ≥Day 16 and resolved after 1-3 days. 6.7% (2 of 30) of participants in Group 3 experienced at least 1 unsolicited AR within 30 days of vaccination (both cough), and 6.7% (2 of 30) of participants in Group 4 (vomiting, cough); none of those were Grade 3 or higher. In both groups, most unsolicited ARs started from Day 1 to Day 4 and resolved after 1-3 days.

In Cohort III (12-23 moa, single dose, comparator Royal's)

Unsolicited AEs were reported for 50.0% (15 of 30) of participants in Group 5 and 50.0% (15 of 30) in Group 6, all were systemic. Participants most frequently experienced cough: 20.0% (6 of 30) in Group 5 and 10.0% (3 of 30) in Group 6, rhinorrhoea: 10.0% (3 of 30) in Group 5 and 16.7% (5 of 30) in Group 6, pyrexia: 13.3% (4 of 30) in Group 6, and diarrhoea: 10.0% (3 of 30) in Group 5. Grade 3 or above unsolicited AEs were reported in 13.3% (4 of 30) of participants in Group 5 and 13.3% (4 of 30) in Group 6 and consisted of pneumonia: 6.7% (2 of 30, 2 events) in Group 5 and 6.7% (2 of 30, 2 events) in Group 6, diarrhoea: 3.3% (1 of 30, 1 event) in Group 6, pyrexia: 3.3% (1 of 30, 1 event) in Group 6, bronchitis: 3.3% (1 of 30, 1 event) in Group 5, gastroenteritis: 3.3% (1 of 30, 1 event) in Group 5, and pharyngitis: 3.3% (1 of 30, 1 event) in Group 5. In Group 5, most unsolicited AEs started from Day 9 to Day 15 and resolved after 1-3 days; in Group 4, most unsolicited AEs started from ≥Day 16 and resolved after 1-3 days. No unsolicited ARs were reported in either group.

Cohort IV (6-11 moa, 2 doses, comparator Royal's)

Unsolicited AE within 30 days of any vaccination were reported for 86.7% (26 of 30) of participants in Group 7 and 82.1% (23 of 28) of participants in Group 8, all were systemic. Participants most frequently experienced cough: 33.3% (10 of 30) in Group 7 and 42.9% (12 of 28) in Group 8, rhinorrhoea: 33.3% (10 of 30) in Group 7 and 42.9% (12 of 28) in Group 8, pyrexia: 40.0% (12 of 30) in Group 7 and 25.0% (7 of 28) in Group 8, bronchitis: 17.9% (5 of 28) in Group 8, influenza: 14.3% (4 of 28) in Group 8 and diarrhoea: 10.0% (3 of 30) in Group 7. Grade 3 or above unsolicited AEs were reported for 20.0% (6 of 30) of participants in Group 7 and 25.0% (7 of 28) participants in Group 8 and consisted of bronchitis: 3.3% (1 of 30, 1 event) in Group 7 and 14.3% (4 of 28, 4 events) in Group 8, pneumonia: 6.7% (2 of 30, 2 events) in Group 7 and 7.1% (2 of 28, 2 events) in Group 8, influenza: 3.3% (1 of 30, 1 event) in Group 7 and 7.1% (2 of 28, 2 events) in Group 8, pyrexia: 6.7% (2 of 30, 2 events) in Group 7, intestinal obstruction: 3.6% (1 of 28, 1 event) in Group 8, anaemia: 3.3% (1 of 30, 1 event) in Group 7, diarrhoea: 3.3% (1 of 30, 1 event) in Group 7, varicella: 3.3% (1 of 30, 1 event) in Group 7, and febrile convulsion: 3.3% (1 of 30, 1 event) in Group 7. Most unsolicited AEs started from ≥Day 16 in both groups and resolved after 1-3 days in Group 7 and after 4-7 days and 8 days or more in Group 8. 6.7% (2 of 30) of participants in Group 7 and 3.6% (1 of 28) of

participants in Group 8 experienced at least 1 unsolicited AR: Rhinorrhoea: 2 (6.7%) participants in Group 7 and 1 (3.6%) in Group 8, cough: 1 (3.3%) participant in Group 7 and 1 (3.6%) in Group 8, and diarrhoea: 1 (3.3%) participant in Group 7; none were Grade 3 or higher. In both groups, most unsolicited ARs started from Day 1 to Day 4 and resolved after 1-3 days.

Cohort V (3-5 moa, 3 doses, comparator Green Bamboo's)

Unsolicited AE within 30 days of any vaccination were reported for 93.3% (28 of 30) of participants in Group 9 and 83.3% (25 of 30) of participants in Group 10, all were systemic. Participants most frequently experienced cough: 53.3% (16 of 30) in Group 9 and 60.0% (18 of 30) in Group 10, rhinorrhoea: 33.3% (10 of 30) in Group 9 and 40.0% (12 of 30) in Group 10, pneumonia: 33.3% (10 in 30) in Group 9 and 13.3% (4 of 30) in Group 10, pyrexia: 26.7% (8 of 30) in Group 9 and 30.0% (9 of 30) in Group 10, diarrhoea: 16.7% (5 of 30) in Group 9, upper respiratory tract infection: 13.3% (4 of 30) in Group 9 and 10.0% (3 of 30) in Group 10, functional gastrointestinal disorder: 10.0% (3 of 30) in Group 9, bronchitis: 10.0% (3 of 30) in Group 9, and myocardial necrosis marker increased: 10.0% (3 of 30) in Group 10. Grade 3 or above unsolicited AEs were reported for 36.7% (11 of 30) of participants in Group 9 and 20.0% (6 of 30) in Group 10 and consisted of functional gastrointestinal disorder: 3.3% (1 of 30, 1 event) in Group 9, pyrexia: 3.3% (1 of 30, 1 event) in Group 9, bronchitis: 6.7% (2 of 30, 2 events) in Group 9, diarrhoea infectious: 3.3% (1 of 30, 1 event) in Group 10, herpangina: 3.3% (1 of 30, 1 event) in Group 9, influenza: 3.3% (1 of 30, 1 event) in Group 9, pneumonia: 30.0% (9 of 30, 10 events) in Group 9 and 13.3% (4 of 30, 4 events) in Group 10, tonsilitis bacterial: 3.3% (1 of 30, 1 event) in Group 9, upper respiratory tract infection bacterial: 3.3% (1 of 30, 1 event) in Group 9, and asthma: 3.3% (1 of 30, 1 event) in Group 10. In both groups, most unsolicited AEs started from ≥Day 16 and resolved after 1-3 days and 4-7 days. 13.3% (4 of 30) of participants in Group 9 and 16.7% (5 of 30) participants in Group 10 experienced at least 1 unsolicited AR: Cough: 2 (6.7%) participants in Group 9 and 2 (6.7%) in Group 10, rhinorrhoea: 1 (3.3%) participant in Group 9 and 1 (3.3%) in Group 10, eyelid oedema: 1 (3.3%) participant in Group 10, diarrhoea: 1 (3.3%) participant in Group 9, constipation: 1 (3.3%) participant in Group 10, dermatitis diaper: 1 (3.3%) participant in Group 10, rash: 1 (3.3%) participant in Group 10, and pallor: 1 (3.3%) participant in Group 10; none were Grade 3 or higher. In both groups, most unsolicited ARs started from Day 1 to Day 4 and resolved after 1-3 days.

Discontinuation due to AE

No AEs leading to study discontinuation within 30 days after any vaccination were reported in either group. In *Group* 8 (Cohort IV), one participant was diagnosed with Atrial septal defect on Day 33 and discontinued the study due to the event. However, this event was considered as not related to the study vaccine by the Investigator, which can be agreed to.

SAEs throughout the study period from Visit 1 until the end of the 6-month follow-up period after the last vaccination.

No deaths were reported in either group during the study.

Cohort I (7-17 yoa, single dose, comparator Green Bamboo's)

In Group 2, 1 participant (3.3%, 1 of 30) experienced blepharitis and febrile infection during the 6-month follow-up period. Both events were considered as not related to study vaccine by the Investigator, which can be agreed taking into account that those were not within 30 days after vaccination.

In Cohort II (2-6 yoa, single dose, comparator Royal's)

SAEs were reported for 13.3% (4 of 30) of participants in Group 3 (1 case each of appendicitis perforated, complicated appendicitis, febrile infection, pneumonia, and tonsilitis bacterial) and 10.0% (3 of 30) of participants in Group 4 (3 cases of bronchitis and 1 case each of influenza, pneumonia, and upper respiratory tract infection); none were considered as related to study vaccine by the Investigator, which can be followed considering that only 1 SAE (tonsilitis bacterial) was reported within 30 days after vaccination and that this case is deemed unrelated.

In Cohort III (12-23 moa, single dose, comparator Royal's)

SAEs were reported for 23.3% (7 of 30) of participants in Group 5 (5 cases of pneumonia, 2 cases each of bronchitis and pharyngitis, and 1 case each of gastroenteritis, gastrointestinal infection, influenza, and febrile convulsion) and 26.7% (8 of 30) of participants in Group 6 (5 cases each of bronchitis and pneumonia, 2 cases of influenza, and 1 case each of pyrexia, herpangina, and urticaria); none were considered related to study vaccine by the Investigator. This can be agreed to as the SAEs experienced within 30 days after vaccination were 2 cases of pneumonia and 1 case each of bronchitis, gastroenteritis, and pharyngitis (Group 5) and 2 cases of pneumonia (Group 6), and the SAEs experienced within 7 days after vaccination were bronchitis and pneumonia (Group 5, 2 participants, 1 case each).

Cohort IV (6-11 moa, 2 doses, comparator Royal's)

SAEs were reported for 43.3% (13 of 30) of participants in Group 7 (8 cases of pneumonia, 4 cases of tonsillitis bacterial, 2 cases of bronchitis, and 1 case each of functional gastrointestinal disorder, influenza, varicella, febrile convulsion, and urticaria) and 50.0% (14 of 28) of participants in Group 8 (6 cases of pneumonia, 4 cases of bronchitis, 3 cases of influenza, 2 cases of intestinal obstruction, and 1 case each of incarcerated inguinal hernia, herpangina, herpes pharyngitis, and tonsillitis bacterial); none were considered related to study vaccine by the Investigator. SAEs within 30 days after any vaccination were reported for 13.3% (4 of 30) of participants in Group 7 and 25.0% (7 of 28) in Group 8. SAEs within 7 days after any vaccination were reported for 10.0% (3 of 30) of participants in Group 7 and 3.6% (1 of 28) in Group 7. The case of febrile convulsion was experienced by participant (1560001-40031) 24 days after the first dose of MenQuadfi, who was diagnosed with respiratory adenovirus infection combined with acute bronchitis, febrile convulsion, and influenza A virus infection. The events resolved upon treatment and the participant continued in the trial and received the second dose. Hence, it is not objected to the relatedness judgments.

Cohort V (3-5 moa, 3 doses, comparator Green Bamboo's)

SAEs were reported for 50.0% (15 of 30) of participants in Group 9 (17 cases of pneumonia, 4 cases of bronchitis, 3 cases of herpangina, 1 case each of functional gastrointestinal disorder, gastroenteritis, hand-foot-and-mouth disease, influenza, tonsilitis bacterial, and upper respiratory tract infection bacterial) and 46.7% (14 of 30) of participants in Group 10 (9 cases of pneumonia, 3 cases of bronchitis, 2 cases each of hand-foot-and-mouth disease and herpangina, and 1 case each of diarrhoea infectious, gastroenteritis, and asthma); none were considered related to study vaccine by the Investigator, which can be agreed given the nature of these events.

In summary, although no significant concern arises from the observations reported, it is clearly noted that the sample size is deemed insufficient to conclude on safety adequately and the open-label setting adds even more concerns regarding interpretability.

3. CHMP's overall conclusion and recommendation

The MAH submitted data of Study MEQ00075 "Phase I Open-Label, Age De-escalation Safety and Immunogenicity Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adolescents, Children, Toddlers, and Infants in China", a stand-alone study that is not included in the MenQuadfi Paediatric Investigational Plan (PIP), as according to Article 46 of regulation (EC) No. 1901/2006, as amended, 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.

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. Hence, parts of the study population of MEQ00075 (Cohort IV, comprising participants aged 6 to 11 months; Cohort V, comprising participants aged 3 to 5 months) are not covered by the currently effective EU Marketing Authorisation of MenQuadfi.

The MAH has not submitted any amendments to the Product Information as part of this Article 46 procedure.

As regards immunogenicity, although rSBA antibody titres elicited by MenQuadfi were reportedly of higher magnitude than those elicited by the comparators, these results have to be interpreted with caution as the interpretability of that data is significantly impaired by several shortcomings, namely the open-label design, the limited sample size of 30 randomised subjects per group, the absence of EU-authorised comparators, the fact that no hypothesis was formulated or tested and data was analysed only descriptively.

Concerning safety, the low sample size is deemed insufficient to adequately conclude on safety and the open-label setting adds even more concerns regarding interpretability.

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.