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Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006

MenQuadfi

Common name: Meningococcal Group A, C, W and Y conjugate vaccine

Procedure no.: EMA/PAM/0000250392

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**
☐	CHMP Rapporteur AR	31 March 2025	31 March 2025
☐	CHMP comments	14 April 2025	14 April 2025
☐	Updated CHMP Rapporteur AR	16 April 2025	16 April 2025
☒	CHMP outcome	25 April 2025	25 April 2025

Table of contents

1. Introduction 4

2. Scientific discussion 4

2.1. Information on the development program 4
2.2. Information on the pharmaceutical formulation used in the study 4
2.3. Clinical aspects 4
2.3.1. Introduction 4
2.3.2. Clinical study 4
Description 4
Methods 5
Results 13
2.3.3. Discussion on clinical aspects 26

3. CHMP's overall conclusion and recommendation 29

Fulfilled: 29

1. Introduction

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

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that Study MET55: *Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adults, Adolescents, and Children in India and Healthy Adolescents and Children in the Republic of South Africa* is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

The formulation of the MenACWY 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).

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- MET55 - Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adults, Adolescents, and Children in India and Healthy Adolescents and Children in the Republic of South Africa

2.3.2. Clinical study

MET55 - Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Adults, Adolescents, and Children in India and Healthy Adolescents and Children in the Republic of South Africa

Description

This was a Phase 3, modified double-blind, randomised, parallel-group, active-controlled, step-wise, multi-centre study to compare and describe the immunogenicity and safety of MenACYW conjugate vaccine when administered as a single dose in healthy adults, adolescents, and children in India and a modified double-blind, randomised, parallel-group, active-controlled, multi-centre study to compare and describe the immunogenicity and safety of MenACYW conjugate vaccine when administered as a single dose in healthy adolescents and children in Republic of South Africa (RSA).

Approximately 1332 healthy adults, adolescents, and children were planned to be assigned into 1 of 3 cohorts (Cohort Ia, Cohort Ib, or Cohort II) and randomised 1:1 to the following 8 groups within those cohorts (a total of 866 planned participants in India and a total of 466 planned participants in RSA) as follows:

Cohort Ia (Adults aged 18 to 55 years; 200 participants in India; 1 vaccination):

- Group 1 (MenACYW conjugate vaccine; 100 participants)
- Group 2 (Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Sanofi Pasteur Inc, Swiftwater, PA, USA)]; 100 participants)

Cohort Ib (Adults aged ≥ 56 years; 200 participants in India; 1 vaccination):

- Group 3 (MenACYW conjugate vaccine; 100 participants)
- Group 4 (Quadri Meningo [MenPS A,C,Y & W135]: Meningococcal Polysaccharide Vaccine [Group A, C, Y & W135] [Bio-Med Pvt. Ltd., Uttar Pradesh, India] or any locally available licensed meningococcal vaccine indicated for the participant's age; 100 participants)

Cohort II (healthy children and adolescents aged 2 to 17 years; 466 participants in India and 466 in RSA; 1 vaccination):

- Group 5 (MenACYW conjugate vaccine, India; 233 participants)
- Group 6 (Menactra, India; 233 participants)
- Group 7 (MenACYW conjugate vaccine, RSA; 233 participants)
- Group 8 (Menactra, RSA; 233 participants)

The recruitment in ages 2 to 17 years was stratified to ensure an equal distribution into 2 subgroups (2 to 9 years and 10 to 17 years) in both countries. This was done to ensure distribution of participants across the complete age range.

Methods

Study participants

Inclusion Criteria

An individual must fulfil all of the following criteria to be eligible for study enrolment:

1) Age in the defined range on the day of inclusion

For Adults: Aged ≥ 18 years on the day of inclusion

For Children and Adolescents: Aged 2 to 17 years on the day of inclusion

2) Z-score of ≥ -2 SD on the Weight-for-height table of the World Health Organization (WHO) Child Growth Standards

For Children: Children aged 2 to 5 years must have a Z-score of ≥ -2 SD on the Weight-for-height table of the WHO Child Growth Standards

3) Informed consent obtained

For Adults: Informed Consent Form has been signed and dated by the subject and by an independent witness, if required by local regulations

For Children and Adolescents: Assent Form has been signed and dated by the subject (for subjects 7 to 17 years of age), and Informed Consent Form has been signed and dated by the parent(s) or legally acceptable representative and by an independent witness, if required by local regulations

4) Able to attend all scheduled visits and to comply with all study procedures

For Adults: Able to attend all scheduled visits and to comply with all study procedures

For Children and Adolescents: Subjects and parent / legally acceptable representative are able to attend all scheduled visits and to comply with all study procedures

Exclusion Criteria

An individual fulfilling any of the following criteria is to be excluded from study enrolment:

1) Subject is pregnant, or lactating, or of childbearing potential and not using an effective method of contraception or abstinence from at least 4 weeks prior to vaccination until at least 4 weeks after vaccination. To be considered of non-childbearing potential, a female must be pre-menarche, or post-menopausal for at least 1 year, or surgically sterile.

2) Participation at the time of study enrolment (or in the 4 weeks preceding the study vaccination) or planned participation during the present study period in another clinical study investigating a vaccine, drug, medical device, or medical procedure.

3) Receipt of any vaccine in the 4 weeks (28 days) preceding the study vaccination or planned receipt of any vaccine in the 4 weeks following vaccination except for oral poliovirus vaccine (OPV) in India, received during national immunization days. In India, OPV may be received with a gap of at least 2 weeks before the study vaccine. This exception includes monovalent and bivalent OPV.

4) Previous vaccination against meningococcal disease with either the study vaccine or another vaccine (ie, mono- or polyvalent, polysaccharide, or conjugate meningococcal vaccine containing serogroups A, C,Y, or W; or meningococcal B serogroup containing vaccine)

5) Receipt of immune globulins, blood or blood-derived products in the past 3 months

6) Known or suspected congenital or acquired immune-deficiency; 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)

7) History of meningococcal infection, confirmed either clinically, serologically, or microbiologically

8) At high risk for meningococcal infection during the study (specifically, but not limited to, subjects with persistent complement deficiency, with anatomic or functional asplenia, or subjects traveling to countries with high endemic or epidemic disease)

9) Known systemic hypersensitivity to latex or to any of the vaccine components, or history of a life-threatening reaction to the vaccine(s) used in the study or to a vaccine containing any of the same substances

10) Verbal report of thrombocytopenia, as reported by the subject or the subject's parent / legally acceptable representative, contraindicating intramuscular (IM) vaccination in the Investigator's opinion

11) Bleeding disorder, or receipt of anticoagulants in the 3 weeks preceding inclusion, contraindicating IM vaccination in the Investigator's opinion

12) Personal history of Guillain-Barré syndrome (GBS)

13) Personal history of an Arthus-like reaction after vaccination with a tetanus toxoid-containing vaccine within 10 years of the proposed study vaccination

14) Deprived of freedom by an administrative or court order, or in an emergency setting, or hospitalised involuntarily

15) Current alcohol abuse or drug addiction

16) Chronic illness that, in the opinion of the Investigator, is at a stage where it might interfere with study conduct or completion

17) Any condition which, in the opinion of the Investigator, might interfere with the evaluation of the study objectives

18) Moderate or severe acute illness/infection (according to Investigator judgment) on the day of vaccination, febrile illness (temperature ≥ 38.0°C), persistent diarrhea, vomiting. A prospective subject should not be included in the study until the condition has resolved or the febrile event has subsided.

19) Receipt of oral or injectable antibiotic therapy within 72 hours prior to the first blood draw

20) 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 (ie, parent, spouse, natural or adopted child) of the Investigator or employee with direct involvement in the proposed study

Treatments

Table 1: Study interventions, dose, mode of administration, and batch numbers

Investigational Product:	**MenACYW conjugate vaccine:** Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine (Sanofi Pasteur Inc., Swiftwater, PA, USA)
Form:	Liquid solution
Dose:	0.5 mL/dose
Route:	IM
Batch Numbers:	[redacted]
Control Product 1:	**Menactra:** Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Sanofi Pasteur Inc, Swiftwater, PA, USA)
Form:	Sterile aqueous solution
Dose:	0.5 mL/dose
Route:	IM
Batch Numbers:	[redacted]
Control Product 2:	**Quadri Meningo (MenPS A, C, Y & W135):** Meningococcal Polysaccharide Vaccine (Group A, C, Y & W135) (Bio-Med Pvt. Ltd., Uttar Pradesh, India)
Form:	Lyophilisate for reconstitution with diluent to yield a solution for injection
Dose:	0.5 mL/dose
Route:	IM
Batch Numbers:	[redacted]

Abbreviations: IM, intramuscular; mL, milliliter

Objective(s)

Table 2: Objectives and endpoints of study MET55

Primary Objective:	To demonstrate the non-inferiority of immunogenicity of a single dose of MenACYW conjugate vaccine compared to Menactra® in adolescents and children aged 2 to 17 years in terms of hSBA titers in India and RSA
Primary Endpoint:	hSBA antibody titers ≥ 1:8 against meningococcal serogroups A, C, Y, and W measured by hSBA assessed at D30 (+14 days) after vaccination in adolescents and children aged 2 to 17 years in India and RSA ([Group 5 + Group 7 who received MenACYW conjugate vaccine] versus [Group 6 + Group 8 who received Menactra])
Secondary Objectives:	1) To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in adults aged 18 to 55 years in India 2) To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Quadri Meningo™ in adults aged ≥ 56 years in India 3) To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India and RSA 4) To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India 5) To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in RSA
Secondary Endpoints:	1) Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in adults aged 18 to 55 years in India (Group 1 versus Group 2) 2) Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Quadri Meningo in adults aged ≥ 56 years in India (Group 3 versus Group 4) 3) Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India and RSA ([Group 5 + Group 7] versus [Group 6 + Group 8]) 4) Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India (Group 5 versus Group 6) 5) Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in RSA (Group 7 versus Group 8)

Observational Objectives:	***Immunogenicity*** To describe the antibody titers to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in the children and adolescents aged 2 to 17 years by age groups (2 to 9 years of age and 10 to 17 years of age) in India and RSA combined and separated by India only or RSA only
	Safety 1) To describe the safety profile of MenACYW conjugate vaccine and that of licensed Menactra in adults aged 18 to 55 years in India 2) To describe the safety profile of MenACYW conjugate vaccine and that of licensed Quadri Meningo in adults aged ≥ 56 years in India 3) To describe the safety profile of MenACYW conjugate vaccine and that of licensed Menactra in children and adolescents aged 2 to 17 years in India and RSA
Observational Endpoints:	***Immunogenicity*** Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA and rSBA (in a subset*) before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years by age groups (2 to 9 years of age and 10 to 17 years of age) ***Safety*** These endpoints were for all the safety objectives: • Occurrence, nature (MedDRA preferred term), duration, intensity, and relationship to vaccination of any unsolicited systemic AEs reported in the 30 minutes after vaccination • Occurrence, time of onset, number of days of occurrence, intensity, action taken, and whether the reaction led to early termination from the study, of solicited (prelisted in the subject's diary card and CRB) injection site reactions occurring up to D07 after vaccination • Occurrence, time of onset, number of days of occurrence, intensity, action taken, and whether the reaction led to early termination from the study, of solicited (prelisted in the subject's diary card and CRB) systemic reactions occurring up to D07 after vaccination • Occurrence, nature (MedDRA preferred term), time of onset, duration, intensity, action taken, relationship to vaccination (for systemic AEs only), and whether the event led to early termination from the study, of unsolicited AEs up to D30 after vaccination • Occurrence, nature (MedDRA preferred term), time of onset, duration, seriousness criteria, relationship to vaccination, outcome, and whether the event led to early termination from the study, of SAEs (including AESIs) throughout the study

Abbreviations: AE, adverse event; AESI, adverse event of special interest; CRB, case report book; D, Day. hSBA, serum bactericidal assay using human complement; MedDRA, Medical Dictionary for Regulatory Activities; rSBA, serum bactericidal assay using baby rabbit complement; RSA, Republic of South Africa; SAE, serious adverse event

*rSBA data were generated in a subset of subjects as follows:

- Groups 1, 2, 3, and 4: 50 subjects each
- Groups 5, 6, 7, and 8: 100 subjects each

Outcomes/endpoints

See included table on Objectives and endpoints above.

Sample size

Calculation of Sample Size:

Approximately 1332 subjects will be enrolled. An estimated 15% drop-out rate (only ages 2 – 17 years) from enrolment will result in approximately 1190 subjects in the per-protocol population available for immunogenicity analyses.

For the Primary Objective:

With 396 evaluable subjects in the combined group (Gr5 + Gr7) and 396 evaluable subjects in the combined group (Gr6 + Gr8), the study will have 90% power using Farrington and Manning's method to declare the non-inferiority of the combined group (Gr5+ Gr7) versus the combined group (Gr6 + Gr8) based on A, C, Y, W antibodies in adolescents and children aged 2 to 17 years (assuming 15% drop-out rate for each group). The power is calculated with the assumption that the estimate from the investigational group equals that of the control group.

Table 3: Power of the study based on the primary objective of non-inferiority in children and adolescents aged 2 to 17 years

Antigen	Estimated* MenACYW	Estimated Menactra®	Non-inferiority	Power
A	76%	76%	10%	91%
C	94.5%	94.5%	10%	> 99.9%
Y	89%	89%	10%	> 99.9%
W	95%	95%	10%	> 99.2%
Overall				90%

Note: Evaluable subjects:

Combined group (Gr5 + Gr7) = 396 subjects

Combined group (Gr 6 + Gr8) = 396 subjects

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

* Estimated seroresponses are based on the results of a study (50) conducted in India in subjects aged 2 to 75 years. The estimates were the average of overall rates of 2 age groups (2 to 10 years and 11 to 18 years). Borrow et al. reported that incidence rates vary in RSA by province but are currently low overall (0.36/100 000 in 2014) with the majority of disease caused by MenW, followed by MenB. Approximately 66-77% of disease is caused by MenA, C, Y, or W. Due to any lack of published data from RSA it is assumed that the response in subjects aged 2-17 years will be similar between India and RSA. Additionally, any variability should balance itself out due to the wider age range.

Randomisation and blinding (masking)

For India, subjects will be assigned to 1 of 3 cohorts and randomised 1:1 to the groups within those cohorts.

On the day of enrolment, subjects in India (aged 18 to ≥ 56 years) who meet the inclusion/exclusion criteria and provide consent will be randomly assigned to Group 1 or Group 2 (Cohort 1a: subjects aged 18 to 55 years) or to Group 3 or Group 4 (Cohort 1b: subjects aged ≥ 56 years).

Cohort II will consist of adolescents and children aged 2 to 17 years from India and RSA. For India, subjects or subject's parent / legally authorised representative (LAR) who sign the recording form and provide consent will be randomly assigned to Group 5 or Group 6.

For RSA, subjects who sign the study Assent Form (for subjects aged 7 – 17 years) and whose parent / LAR signs the informed consent form will be randomly assigned to Group 7 or Group 8.

The recruitment in ages 2 to 17 years will be stratified to ensure an equal distribution into 2 subgroups (2 to 9 years and 10 to 17 years) in both of the countries. This will be done to ensure distribution of subjects across the 2 to 17 year age range.

Site staff will connect to the Interactive Response Technology (IRT) system, enter the identification and security information, and confirm a minimal amount of data in response to IRT system prompts. The IRT system will then provide at least the subject number and vaccine dose number. The IRT system will also be used to allocate subjects in the rSBA)serum bactericidal assay using rabbit complement) subset as follows:

- Groups 1 – 4: 50 subjects each
- Groups 5 - 8: 100 subjects each

The full detailed procedures for randomization are described in the Operating Guidelines. If the subject is not eligible to participate in the study, then the information will only be recorded on the subject recruitment log. Subject numbers that are assigned by the IRT system will consist of a string. Subject numbers should not be reassigned for any reason. The randomization codes will be kept securely in the IRT system.

Statistical Methods

Clinical data will be analysed under the responsibility of the Biostatistics Platform of the Sponsor. A SAP will be written and peer reviewed before any analyses. In accordance with the protocol, the SAP will describe all analyses to be performed by the Sponsor and all the conventions to be taken.

Hypotheses and Statistical Methods for Primary Objective

Thirty days after the administration of MenACYW conjugate vaccine or Menactra, the percentages of subjects who achieve ≥ 1:8 in hSBA titres for meningococcal serogroups A, C, Y, and W in the combined group (Gr 5 + Gr 7) are non-inferior to the corresponding percentages in the combined group (Gr 6 + Gr8)

Null hypothesis (H0): p(G5 + G7) - p(G6 + 8) ≤ -10%

Alternative hypothesis (H1): p(G5 + G7) - p(G6 + G8) > -10%

where p(G5 + G7) and p(G6 + G8) are the percentages of subjects who achieve ≥ 1:8 in hSBA titres in the combined group (G5 + G7) and the combined groups (G6 +G8), respectively.

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

For the 4 non-inferiority hypotheses, the CI of the difference in proportions will be computed using the Wilson score method without continuity correction (48). The overall non-inferiority of this objective will be demonstrated if all 4 individual null hypotheses are rejected.

<u>Hypotheses and Statistical Methods for Secondary Objectives</u>

No hypotheses will be tested. Descriptive statistics will be presented.

Statistical Methods

Immunogenicity

Secondary Objectives 1 and 2:

Descriptive statistics will be provided for the antibody titres against meningococcal serogroups contained in MenACYW conjugate vaccine and Menactra in adults aged 18 to 55 years (Gr1 versus Gr2) or Quadri Meningo (or any locally available licensed meningococcal vaccine) in adults aged ≥ 56 years (Gr3 versus Gr4) in India.

Secondary Objectives 3, 4, and 5:

Descriptive statistics will be provided for the antibody titres against meningococcal serogroups contained in MenACYW conjugate vaccine and Menactra in adolescents and children aged 2 to 17 years in India and RSA combined ([Gr5 + Gr7] versus [Gr6 + Gr8]), India only (Gr5 versus Gr6), and RSA only (Gr7 versus Gr8).

In general, categorical variables in Cohorts Ia and Ib (in India) and II (in India and RSA) will be summarised and presented by frequency counts, percentages, and CIs. The 95% CIs of point estimates will be calculated using the normal approximation for quantitative data and the exact binomial distribution (Clopper-Pearson method) (49) for percentages.

Descriptive analyses on A, C, Y, and W serogroups on D0 and D30 (+14 days) using hSBA and rSBA (in a subset) a will be generated as follows:

Descriptive analyses of hSBA include but will not be limited to:

- Geometric mean titres (GMT) and 95% confidence interval (CI)
- Titre distribution and reverse cumulative distribution curves (RCDCs)
- Percentage of subjects with titre ≥ 1:4 and ≥ 1:8 and 95% CI
- Percentage of subjects with titre ≥ 4-fold rise from pre-vaccination to post-vaccination, and 95% CI
- Percentage of subjects with hSBA vaccine seroresponse and 95% CI

Safety

The Safety Analysis Set (SafAS) is defined as those subjects who have received at least 1 dose of the study vaccine and have any safety data available. All subjects will have their safety analyded according to the vaccine they actually received. Safety data recorded for a vaccine received out of the protocol design will be excluded from the analysis (and listed separately). Safety analyses will include but not be limited to the following:

- The number and percentage of subjects reporting any solicited injection site reactions and solicited systemic reactions occurring from D0 to D07 after vaccination will be summarised by study group for intensity, time of onset period, days of occurrence, and action taken
- Immediate unsolicited systemic AEs within 30 minutes and unsolicited AEs occurring up to D30 after vaccination will be summarised

- The number and percentage of subjects reporting any unsolicited non-serious AEs will be summarised by study group, intensity, time of onset period, duration, and by MedDRA preferred term and system organ class (SOC), as well as by relationship to the study vaccine
- The number and percentage of subjects reporting at least one of any SAEs will be summarised by study group, seriousness criterion, outcome, and by MedDRA preferred term and SOC, as well as by relationship to the study vaccine
- The number and percentage of subjects reporting at least one of any AESIs will be summarised throughout the study
- Exact (Clopper-Pearson) (49) 2-sided 95% CIs will be calculated for the percentages For exploratory purpose, main safety and immunogenicity parameters may be presented according to baseline HIV status in Groups 7 and 8. Further details will be included in the SAP.

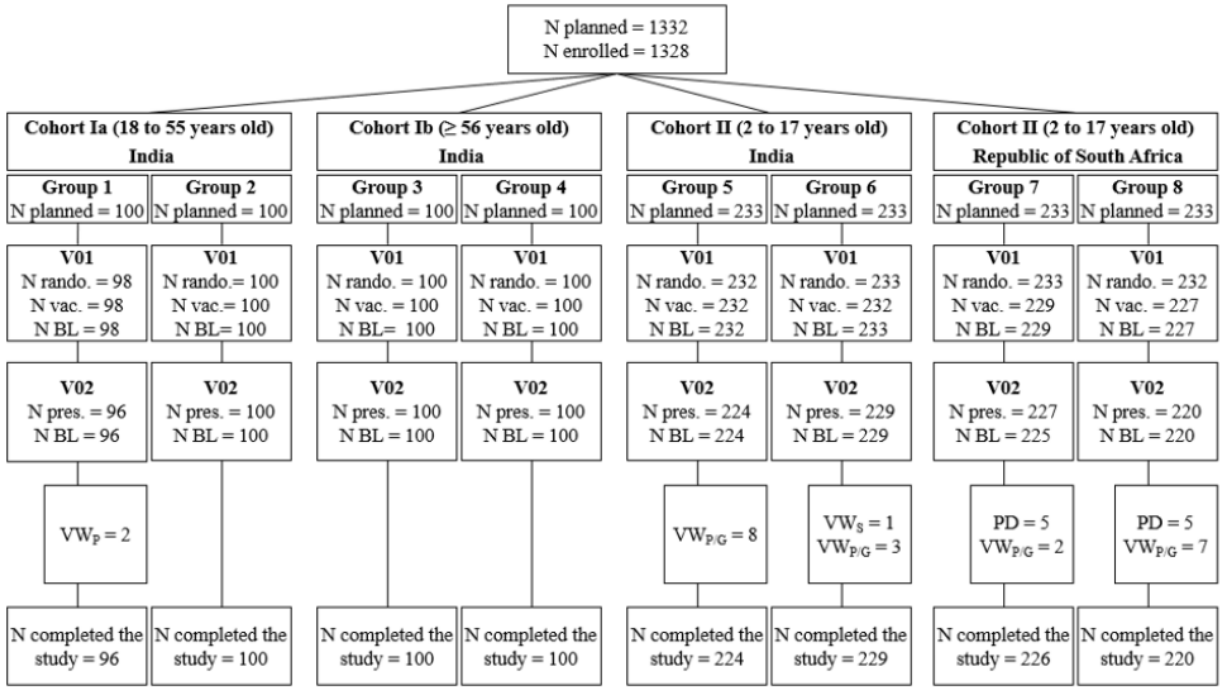
Analysis Sets

Three analysis sets will be used: the Full Analysis Set (FAS), the Per Protocol Analysis Set (PPAS), and the SafAS.

Results

Participant flow

Figure 1: Participant disposition flow chart



Abbreviations: BL, blood sample; PD, protocol deviation; pres., present; rando., randomized; vac., vaccinated; VW_P, voluntary withdrawal by participant; $VW_{P/G}$, voluntary withdrawal by parent/guardian

Recruitment

Study period: 30 December 2019 (first subject first visit) to 28 January 2023 (last subject last visit)

The analyses presented are based on a database lock date of 01 October 2024.

Table 4: Study subjects by centre *and* randomised *group in India*

Center	Investigator	Group 1 (N=98) n (%)	Group 2 (N=100) n (%)	Group 3 (N=100) n (%)	Group 4 (N=100) n (%)	Group 5 (N=232) n (%)	Group 6 (N=233) n (%)	All (N=863) n (%)
All		98 (100)	100 (100)	100 (100)	100 (100)	232 (100)	233 (100)	863 (100)
3560002	[redacted]	19 (19.4)	18 (18.0)	2 (2.0)	2 (2.0)	0	0	41 (4.8)
3560003	[redacted]	29 (29.6)	32 (32.0)	24 (24.0)	26 (26.0)	40 (17.2)	43 (18.5)	194 (22.5)
3560004	[redacted]	22 (22.4)	23 (23.0)	31 (31.0)	29 (29.0)	28 (12.1)	33 (14.2)	166 (19.2)
3560007	[redacted]	23 (23.5)	20 (20.0)	9 (9.0)	6 (6.0)	29 (12.5)	28 (12.0)	115 (13.3)
3560008	[redacted]	0	0	0	0	50 (21.6)	36 (15.5)	86 (10.0)
3560010	[redacted]	0	0	0	0	15 (6.5)	17 (7.3)	32 (3.7)
3560011	[redacted]	0	0	0	0	35 (15.1)	42 (18.0)	77 (8.9)
3560012	[redacted]	0	0	0	0	35 (15.1)	34 (14.6)	69 (8.0)
3560015	[redacted]	4 (4.1)	6 (6.0)	20 (20.0)	20 (20.0)	0	0	50 (5.8)
3560016	[redacted]	1 (1.0)	1 (1.0)	14 (14.0)	17 (17.0)	0	0	33 (3.8)

n: number of study subjects fulfilling the item listed
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.

Table 5: Study subjects by centre and randomised group in the RSA

The names of investigators are personal information and confidential information that should be redacted. (Due to the picture nature of the data, track change could not be used to hide the information)

Center	Investigator	Group 7 (N=233) n (%)	Group 8 (N=232) n (%)	All (N=465) n (%)
All		233 (100)	232 (100)	465 (100)
7100001	[redacted]	35 (15.0)	39 (16.8)	74 (15.9)
7100002	[redacted]	68 (29.2)	62 (26.7)	130 (28.0)
7100003	[redacted]	30 (12.9)	28 (12.1)	58 (12.5)
7100004	[redacted]	18 (7.7)	14 (6.0)	32 (6.9)
7100005	[redacted]	37 (15.9)	34 (14.7)	71 (15.3)
7100006	[redacted]	10 (4.3)	16 (6.9)	26 (5.6)
7100007	[redacted]	35 (15.0)	39 (16.8)	74 (15.9)

n: number of study subjects fulfilling the item listed
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA

Baseline data

Table 6: Baseline demographics by randomised group of Cohort I – Randomised study participants

	Group 1 (N=98)	Group 2 (N=100)	Group 3 (N=100)	Group 4 (N=100)	All (N=398)
Sex: n (%)					
Male	68 (69.4)	69 (69.0)	76 (76.0)	69 (69.0)	282 (70.9)
Female	30 (30.6)	31 (31.0)	24 (24.0)	31 (31.0)	116 (29.1)
Missing	0	0	0	0	0
Sex ratio: Male/Female	2.27	2.23	3.17	2.23	2.43
Age: (Years)					
M	98	100	100	100	398
Mean (SD)	36.7 (9.21)	34.8 (9.05)	61.7 (6.09)	61.1 (5.61)	48.6 (15.0)
Min; Max	19.0; 55.0	18.0; 55.0	56.0; 82.0	56.0; 87.0	18.0; 87.0
Median	36.0	36.0	60.0	59.0	56.0
Q1; Q3	31.0; 42.0	28.0; 41.0	57.0; 64.0	57.0; 63.5	36.0; 60.0
Racial Origin: n (%)					
American Indian or Alaska Native	0	0	0	0	0
Asian	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Black or African American	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
White	0	0	0	0	0
Not reported	0	0	0	0	0
Unknown	0	0	0	0	0
Multiple origin	0	0	0	0	0
Ethnicity: n (%)					
Hispanic or Latino	0	0	0	0	0
Not Hispanic or Latino	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Not reported	0	0	0	0	0
Unknown	0	0	0	0	0

N: number of participants randomized in each study group (percentages are based on N); 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 vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Table 7: Baseline demographics by randomised group of Cohort II – Randomised study participants

	Group 5 (N=232)	Group 6 (N=233)	Group 7 (N=233)	Group 8 (N=232)	All (N=930)
Sex: n (%)					
Male	131 (56.5)	115 (49.4)	110 (47.2)	122 (52.6)	478 (51.4)
Female	101 (43.5)	118 (50.6)	123 (52.8)	110 (47.4)	452 (48.6)
Missing	0	0	0	0	0
Sex ratio: Male/Female	1.30	0.97	0.89	1.11	1.06
Age: (Years)					
M	232	233	233	232	930
Mean (SD)	9.39 (4.19)	9.34 (4.10)	9.45 (4.01)	9.19 (4.19)	9.35 (4.12)
Min; Max	2.00; 17.0	2.00; 17.0	2.00; 17.0	2.00; 17.0	2.00; 17.0
Median	9.50	10.0	9.00	9.50	9.00
Q1; Q3	7.00; 12.5	6.00; 13.0	6.00; 13.0	6.00; 12.0	6.00; 13.0
Age: (2 to 9 Years)					
M	116	116	118	116	466
Mean (SD)	5.89 (2.41)	5.88 (2.27)	6.06 (2.06)	5.72 (2.51)	5.89 (2.32)
Min; Max	2.00; 9.00	2.00; 9.00	2.00; 9.00	2.00; 9.00	2.00; 9.00
Median	7.00	6.00	6.00	6.00	6.00
Q1; Q3	3.50; 8.00	4.00; 8.00	4.00; 8.00	3.00; 8.00	4.00; 8.00
Age: (10 to 17 Years)					
M	116	117	115	116	464
Mean (SD)	12.9 (2.17)	12.8 (2.13)	12.9 (2.04)	12.7 (2.18)	12.8 (2.13)
Min; Max	10.0; 17.0	10.0; 17.0	10.0; 17.0	10.0; 17.0	10.0; 17.0
Median	12.5	13.0	13.0	12.0	13.0
Q1; Q3	11.0; 15.0	11.0; 15.0	11.0; 15.0	11.0; 14.5	11.0; 15.0
Racial Origin: n (%)					
American Indian or Alaska Native	0	0	0	0	0
Asian	232 (100)	233 (100)	0	0	465 (50.0)
Black or African American	0	0	142 (60.9)	139 (59.9)	281 (30.2)
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
White	0	0	9 (3.9)	10 (4.3)	19 (2.0)
Not reported	0	0	6 (2.6)	3 (1.3)	9 (1.0)
Unknown	0	0	6 (2.6)	9 (3.9)	15 (1.6)
Multiple origin	0	0	70 (30.0)	71 (30.6)	141 (15.2)
Ethnicity: n (%)					
Hispanic or Latino	0	0	0	1 (0.4)	1 (0.1)
Not Hispanic or Latino	232 (100)	233 (100)	230 (98.7)	227 (97.8)	922 (99.1)
Not reported	0	0	0	1 (0.4)	1 (0.1)
Unknown	0	0	3 (1.3)	3 (1.3)	6 (0.6)

N: number of participants randomized in each study group (percentages are based on N); 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 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Source: Section 8,Modified from MET55 CSR Table 8.25

Number analysed

Table 8: Immunogenicity analysis sets by randomised group of Cohort I - Randomised study subjects

	Group 1 (N=98) n (%)	Group 2 (N=100) n (%)	Group 3 (N=100) n (%)	Group 4 (N=100) n (%)	All (N=398) n (%)
Full Analysis Set	96 (98.0)	100 (100)	100 (100)	100 (100)	396 (99.5)
Subjects with at least one criterion for exclusion from FAS	2 (2.0)	0	0	0	2 (0.5)
Not injected	0	0	0	0	0
Did not have a valid post-vaccination blood sample result	2 (2.0)	0	0	0	2 (0.5)
Per Protocol Analysis Set	95 (96.9)	99 (99.0)	97 (97.0)	96 (96.0)	387 (97.2)
Subjects with at least one criterion for exclusion from PPAS	3 (3.1)	1 (1.0)	3 (3.0)	4 (4.0)	11 (2.8)
Did not meet all protocol-specified inclusion / exclusion criteria	0	0	0	0	0
Did not receive vaccine	0	0	0	0	0
Received a vaccine other than the one that he / she was randomized to receive	0	0	0	0	0
Preparation and / or administration of vaccine was not done as per-protocol	0	0	1 (1.0)	3 (3.0)	4 (1.0)
Did not receive vaccine in the proper time window	0	0	0	0	0
Did not provide the post-dose serology sample or not in time window	3 (3.1)	1 (1.0)	2 (2.0)	1 (1.0)	7 (1.8)
Received protocol-prohibited therapy / medication / vaccine	0	0	0	0	0
V02 sample did not produce valid result	0	0	0	0	0
Other protocol deviations	0	0	0	0	0

n: number of study subjects fulfilling the item listed
Note: a study subject may be associated with more than one criterion
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08016n17.sas Datasets=ADSL ADIS Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08016_i.rtf (06NOV2024 5:04)

Table 9: Immunogenicity analysis sets by randomised group of Cohort II - Randomised study subjects

	Group 5 (N=232) n (%)	Group 6 (N=233) n (%)	Group 7 (N=233) n (%)	Group 8 (N=232) n (%)	All (N=930) n (%)
Full Analysis Set	224 (96.6)	229 (98.3)	225 (96.6)	220 (94.8)	898 (96.6)
Subjects with at least one criterion for exclusion from FAS	8 (3.4)	4 (1.7)	8 (3.4)	12 (5.2)	32 (3.4)
Not injected	0	1 (0.4)	4 (1.7)	5 (2.2)	10 (1.1)
Did not have a valid post-vaccination blood sample result	8 (3.4)	4 (1.7)	8 (3.4)	12 (5.2)	32 (3.4)
Per Protocol Analysis Set	222 (95.7)	228 (97.9)	223 (95.7)	217 (93.5)	890 (95.7)
Subjects with at least one criterion for exclusion from PPAS	10 (4.3)	5 (2.1)	10 (4.3)	15 (6.5)	40 (4.3)
Did not meet all protocol-specified inclusion / exclusion criteria	0	0	2 (0.9)	1 (0.4)	3 (0.3)
Did not receive vaccine	0	1 (0.4)	4 (1.7)	5 (2.2)	10 (1.1)
Received a vaccine other than the one that he / she was randomized to receive	0	0	0	0	0
Preparation and / or administration of vaccine was not done as per-protocol	0	0	2 (0.9)	5 (2.2)	7 (0.8)
Did not receive vaccine in the proper time window	0	0	0	0	0
Did not provide the post-dose serology sample or not in time window	10 (4.3)	5 (2.1)	10 (4.3)	14 (6.0)	39 (4.2)
Received protocol-prohibited therapy / medication / vaccine	0	0	0	1 (0.4)	1 (0.1)
V02 sample did not produce valid result	0	0	0	0	0
Other protocol deviations	0	0	0	0	0

n: number of study subjects fulfilling the item listed
Note: a study subject may be associated with more than one criterion
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Study: MET55 Program: t08016n17.sas Datasets=ADSL ADIS Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08017_i.rtf (06NOV2024 5:04)

Table 10: Safety analysis set by vaccination Group of Cohort I - Randomised study subjects

	Group 1 (N=98) n (%)	Group 2 (N=100) n (%)	Group 3 (N=100) n (%)	Group 4 (N=100) n (%)	All (N=398) n (%)
Safety Analysis Set	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Solicited injection site safety assessed	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Solicited systemic safety assessed	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)

n: number of study subjects experiencing the endpoint
Safety endpoints are considered assessed if at least one data point has been collected; unsolicited adverse events are never missing as all study subjects had a 30 minute surveillance period after injection
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08020n21.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08020_i.rtf (06NOV2024 5:04)

Table 11: Safety analysis set by vaccination Group of Cohort II - Randomised study subjects

	Group 5 (N=232) n (%)	Group 6 (N=232) n (%)	Group 7 (N=229) n (%)	Group 8 (N=227) n (%)	Randomized but not vaccinated (N=10) n (%)	All (N=930) n (%)
Safety Analysis Set	232 (100)	232 (100)	229 (100)	227 (100)	-	920 (98.9)
Solicited injection site safety assessed	227 (97.8)	229 (98.7)	227 (99.1)	222 (97.8)	-	905 (97.3)
Solicited systemic safety assessed	227 (97.8)	229 (98.7)	227 (99.1)	222 (97.8)	-	905 (97.3)

n: number of study subjects experiencing the endpoint

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

Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.

Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.

Study: MET55 Program: t08020n21.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08021_i.rtf (06NOV2024 5:04)

Efficacy results

Primary Immunogenicity Objective

The primary objective was to demonstrate the NI of hSBA antibody seroprotection (ie, percentages of participants who achieve ≥ 1:8 in hSBA titres) against meningococcal serogroups A, C, Y, and W following the administration of a single dose of MenACYW conjugate vaccine (Group 5 [India] + Group 7 [RSA]) compared to Menactra (Group 6 [India] + Group 8 [RSA]) in children and adolescents aged 2 to 17 years (Cohort II).

Table 12: Non-inferiority of hSBA vaccine seroprotection (titre >=1:8) at D30 after vaccination between (Group 5 + Group 7) versus (Group 6 + Group 8) of Cohort II – Per-Protocol Analysis Set

	Group 5 + Group 7 (N=445)			Group 6 + Group 8 (N=445)			(Group 5 + Group 7) - (Group 6 + Group 8)		
Serogroup	n/M	(%)	95% CI	n/M	(%)	95% CI	Difference (%)	95% CI	Non-inferiority
A	397/443	89.6	(86.4; 92.3)	368/443	83.1	(79.2; 86.4)	6.55	(2.03; 11.08)	Yes
C	442/445	99.3	(98.0; 99.9)	344/443	77.7	(73.5; 81.4)	21.67	(17.82; 25.80)	Yes
Y	430/445	96.6	(94.5; 98.1)	379/443	85.6	(81.9; 88.7)	11.08	(7.43; 14.89)	Yes
W	439/445	98.7	(97.1; 99.5)	390/445	87.6	(84.2; 90.6)	11.01	(7.86; 14.47)	Yes

n: Number of participants who achieved an hSBA vaccine seroprotection.

M: Number of participants with available data for the endpoint.

N: number of participants in Per-Protocol Analysis Set

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.

The overall non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all 4 serogroups.

Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.

Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.

Secondary Immunogenicity Objectives

For all secondary immunogenicity objectives, only data from the PPAS are presented. As the differences between each PPAS and each full analysis set (FAS) were not greater than 10% for any secondary immunogenicity objective, the analyses were not produced in the FAS. Described below are the results from hSBA analyses. For secondary objectives 1 through 5, a subset of participants with blood samples available were also tested for meningococcal antibody responses as measured by rSBA.

Secondary Objective #1: To describe the antibody titres to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in adults aged 18 to 55 years in India (Cohort I).

Geometric mean titres

Table 13: Summary of geometric means of hSBA titres at D0 before and at D30 after vaccination of Cohort I – Per-Protocol Analysis Set

		Group 1 (N=95)			Group 2 (N=99)			Group 3 (N=97)			Group 4 (N=96)		
Serogroup	Time Point	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)
A	D0	95	7.28	(6.03; 8.78)	99	9.60	(7.68; 12.0)	97	15.3	(12.2; 19.3)	96	12.5	(10.2; 15.4)
	D30	94	52.8	(34.7; 80.3)	99	39.2	(27.8; 55.3)	96	56.6	(38.2; 83.9)	96	36.2	(26.8; 48.8)
C	D0	95	6.20	(4.99; 7.70)	99	7.05	(5.53; 8.99)	97	8.00	(6.18; 10.4)	96	8.00	(6.13; 10.4)
	D30	95	551	(365; 831)	99	107	(68.8; 165)	97	393	(255; 606)	96	159	(102; 248)
Y	D0	95	5.24	(3.86; 7.11)	99	4.03	(3.09; 5.25)	97	6.36	(4.57; 8.86)	96	6.97	(5.03; 9.68)
	D30	95	119	(80.2; 177)	99	47.4	(30.7; 73.1)	97	197	(127; 303)	96	55.4	(35.5; 86.4)
W	D0	95	4.18	(3.39; 5.15)	99	4.17	(3.39; 5.14)	97	4.42	(3.53; 5.54)	96	5.66	(4.40; 7.27)
	D30	94	106	(72.8; 153)	99	63.1	(44.7; 89.1)	97	90.8	(60.4; 137)	96	34.6	(23.5; 51.2)

M: number of participants with available data for the relevant endpoint.
N: number of participants in Per-Protocol Analysis Set
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Titres ≥1:8

Table 14: Number and percentage of participants with hSBA titre >=1:8 at D0 before and at D30 after vaccination of Cohort I – Per-Protocol Analysis Set

			Group 1 (N=95)			Group 2 (N=99)			Group 3 (N=97)			Group 4 (N=96)		
Serogroup	Time Point	hSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D0	>=1:8	58/95	61.1	(50.5; 70.9)	72/99	72.7	(62.9; 81.2)	80/97	82.5	(73.4; 89.4)	74/96	77.1	(67.4; 85.0)
	D30	>=1:8	72/94	76.6	(66.7; 84.7)	87/99	87.9	(79.8; 93.6)	79/96	82.3	(73.2; 89.3)	83/96	86.5	(78.0; 92.6)
C	D0	>=1:8	45/95	47.4	(37.0; 57.9)	50/99	50.5	(40.3; 60.7)	52/97	53.6	(43.2; 63.8)	48/96	50.0	(39.6; 60.4)
	D30	>=1:8	92/95	96.8	(91.0; 99.3)	88/99	88.9	(81.0; 94.3)	93/97	95.9	(89.8; 98.9)	86/96	89.6	(81.7; 94.9)
Y	D0	>=1:8	28/95	29.5	(20.6; 39.7)	24/99	24.2	(16.2; 33.9)	35/97	36.1	(26.6; 46.5)	39/96	40.6	(30.7; 51.1)
	D30	>=1:8	88/95	92.6	(85.4; 97.0)	76/99	76.8	(67.2; 84.7)	91/97	93.8	(87.0; 97.7)	76/96	79.2	(69.7; 86.8)
W	D0	>=1:8	28/95	29.5	(20.6; 39.7)	29/99	29.3	(20.6; 39.3)	30/97	30.9	(21.9; 41.1)	37/96	38.5	(28.8; 49.0)
	D30	>=1:8	88/94	93.6	(86.6; 97.6)	90/99	90.9	(83.4; 95.8)	87/97	89.7	(81.9; 94.9)	76/96	79.2	(69.7; 86.8)

n: number of participants experiencing the endpoint listed in the first 3 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 vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Vaccine Seroresponse

Table 15: Number and percentage of participants with hSBA vaccine seroresponse from D0 before to D30 after vaccination of Cohort I – Per-Protocol Analysis Set

		Group 1 (N=95)			Group 2 (N=99)			Group 3 (N=97)			Group 4 (N=96)		
Serogroup	Baseline Status	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	Any	58/94	61.7	(51.1; 71.5)	48/99	48.5	(38.3; 58.7)	52/96	54.2	(43.7; 64.4)	42/96	43.8	(33.6; 54.3)
	S-	24/37	64.9	(47.5; 79.8)	18/27	66.7	(46.0; 83.5)	14/17	82.4	(56.6; 96.2)	12/22	54.5	(32.2; 75.6)
	S+	34/57	59.6	(45.8; 72.4)	30/72	41.7	(30.2; 53.9)	38/79	48.1	(36.7; 59.6)	30/74	40.5	(29.3; 52.6)
C	Any	89/95	93.7	(86.8; 97.6)	67/99	67.7	(57.5; 76.7)	82/97	84.5	(75.8; 91.1)	76/96	79.2	(69.7; 86.8)
	S-	47/50	94.0	(83.5; 98.7)	33/49	67.3	(52.5; 80.1)	40/45	88.9	(75.9; 96.3)	38/48	79.2	(65.0; 89.5)
	S+	42/45	93.3	(81.7; 98.6)	34/50	68.0	(53.3; 80.5)	42/52	80.8	(67.5; 90.4)	38/48	79.2	(65.0; 89.5)
Y	Any	74/95	77.9	(68.2; 85.8)	63/99	63.6	(53.4; 73.1)	78/97	80.4	(71.1; 87.8)	59/96	61.5	(51.0; 71.2)
	S-	57/67	85.1	(74.3; 92.6)	48/75	64.0	(52.1; 74.8)	53/62	85.5	(74.2; 93.1)	35/57	61.4	(47.6; 74.0)
	S+	17/28	60.7	(40.6; 78.5)	15/24	62.5	(40.6; 81.2)	25/35	71.4	(53.7; 85.4)	24/39	61.5	(44.6; 76.6)
W	Any	77/94	81.9	(72.6; 89.1)	69/99	69.7	(59.6; 78.5)	77/97	79.4	(70.0; 86.9)	53/96	55.2	(44.7; 65.4)
	S-	58/67	86.6	(76.0; 93.7)	59/70	84.3	(73.6; 91.9)	56/67	83.6	(72.5; 91.5)	35/59	59.3	(45.7; 71.9)
	S+	19/27	70.4	(49.8; 86.2)	10/29	34.5	(17.9; 54.3)	21/30	70.0	(50.6; 85.3)	18/37	48.6	(31.9; 65.6)

n: number of participants with titers that meet the hSBA vaccine seroresponse criteria; hSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:16; for a participant with a pre-vaccination titer >= 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer.
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.
S-: Pre-vaccination baseline titer is < 1:8; S+: Pre-vaccination baseline titer is >= 1:8
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Secondary Objective #2: To describe the antibody titres to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Quadri Meningo (or any locally available licensed meningococcal vaccine) in adults aged ≥ 56 years in India (Cohort Ib)

See data presented for Secondary Objective #1.

Secondary Objective #3: To describe the antibody titres to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India and RSA (Cohort II)

Geometric mean titres

Table 16: Summary of geometric means of hSBA titres at D0 before and at D30 after vaccination of Cohort II – Per-Protocol Analysis Set

		India						RSA						India and RSA					
		Group 5 (N=222)			Group 6 (N=228)			Group 7 (N=223)			Group 8 (N=217)			Group 5 + Group 7 (N=445)			Group 6 + Group 8 (N=445)		
Serogroup	Time Point	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)	M	GMT	(95% CI)
A	D0	222	7.33	(6.50; 8.26)	228	7.71	(6.94; 8.58)	223	7.47	(6.59; 8.47)	217	6.71	(5.97; 7.55)	445	7.40	(6.79; 8.07)	445	7.21	(6.66; 7.80)
	D30	220	70.3	(56.5; 87.6)	228	40.9	(32.8; 51.1)	223	44.9	(37.1; 54.4)	215	31.9	(25.5; 40.0)	443	56.1	(48.5; 65.0)	443	36.3	(31.0; 42.5)
C	D0	222	3.36	(3.00; 3.76)	228	3.17	(2.84; 3.55)	223	4.69	(4.10; 5.36)	217	4.55	(3.97; 5.20)	445	3.97	(3.63; 4.34)	445	3.78	(3.46; 4.13)
	D30	222	595	(494; 716)	228	38.3	(28.4; 51.6)	223	606	(488; 751)	215	59.2	(44.0; 79.7)	445	600	(521; 692)	443	47.3	(38.3; 58.4)
Y	D0	222	3.32	(2.84; 3.88)	228	3.12	(2.70; 3.60)	221	3.69	(3.13; 4.34)	217	3.96	(3.35; 4.69)	443	3.50	(3.13; 3.91)	445	3.50	(3.14; 3.91)
	D30	222	119	(97.4; 145)	228	27.1	(21.7; 33.8)	223	233	(195; 279)	215	81.5	(66.0; 101)	445	167	(145; 191)	443	46.2	(39.3; 54.3)
W	D0	222	3.23	(2.86; 3.65)	228	2.85	(2.56; 3.17)	223	5.74	(4.89; 6.74)	217	5.85	(4.97; 6.88)	445	4.31	(3.88; 4.78)	445	4.04	(3.65; 4.48)
	D30	222	92.8	(78.7; 109)	228	24.3	(19.8; 29.7)	223	157	(129; 191)	217	52.5	(42.3; 65.2)	445	121	(106; 137)	445	35.4	(30.4; 41.1)

M: number of participants with available data for the relevant endpoint.
N: number of participants in Per-Protocol Analysis Set
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.

Titres ≥1:8

Table 17: Number and percentage of participants with hSBA titre >=1:8 at D0 before and at D30 after vaccination of Cohort II – Per-Protocol Analysis Set

			India						RSA					
			Group 5 (N=222)			Group 6 (N=228)			Group 7 (N=223)			Group 8 (N=217)		
Serogroup	Time Point	hSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D0	>=1:8	135/222	60.8	(54.1; 67.3)	145/228	63.6	(57.0; 69.8)	136/223	61.0	(54.2; 67.4)	125/217	57.6	(50.7; 64.3)
	D30	>=1:8	197/220	89.5	(84.7; 93.3)	191/228	83.8	(78.3; 88.3)	200/223	89.7	(84.9; 93.3)	177/215	82.3	(76.6; 87.2)
C	D0	>=1:8	44/222	19.8	(14.8; 25.7)	42/228	18.4	(13.6; 24.1)	72/223	32.3	(26.2; 38.9)	66/217	30.4	(24.4; 37.0)
	D30	>=1:8	221/222	99.5	(97.5; 100)	166/228	72.8	(66.5; 78.5)	221/223	99.1	(96.8; 99.9)	178/215	82.8	(77.1; 87.6)
Y	D0	>=1:8	36/222	16.2	(11.6; 21.7)	31/228	13.6	(9.4; 18.7)	47/221	21.3	(16.1; 27.3)	55/217	25.3	(19.7; 31.7)
	D30	>=1:8	208/222	93.7	(89.6; 96.5)	175/228	76.8	(70.7; 82.1)	222/223	99.6	(97.5; 100)	204/215	94.9	(91.0; 97.4)
W	D0	>=1:8	42/222	18.9	(14.0; 24.7)	31/228	13.6	(9.4; 18.7)	94/223	42.2	(35.6; 48.9)	89/217	41.0	(34.4; 47.9)
	D30	>=1:8	218/222	98.2	(95.5; 99.5)	187/228	82.0	(76.4; 86.8)	221/223	99.1	(96.8; 99.9)	203/217	93.5	(89.4; 96.4)

			India and RSA					
			Group 5 + Group 7 (N=445)			Group 6 + Group 8 (N=445)		
Serogroup	Time Point	hSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)
A	D0	>=1:8	271/445	60.9	(56.2; 65.5)	270/445	60.7	(56.0; 65.2)
	D30	>=1:8	397/443	89.6	(86.4; 92.3)	368/443	83.1	(79.2; 86.4)
C	D0	>=1:8	116/445	26.1	(22.0; 30.4)	108/445	24.3	(20.4; 28.5)
	D30	>=1:8	442/445	99.3	(98.0; 99.9)	344/443	77.7	(73.5; 81.4)
Y	D0	>=1:8	83/443	18.7	(15.2; 22.7)	86/445	19.3	(15.8; 23.3)
	D30	>=1:8	430/445	96.6	(94.5; 98.1)	379/443	85.6	(81.9; 88.7)
W	D0	>=1:8	136/445	30.6	(26.3; 35.1)	120/445	27.0	(22.9; 31.3)
	D30	>=1:8	439/445	98.7	(97.1; 99.5)	390/445	87.6	(84.2; 90.6)

n: number of participants experiencing the endpoint listed in the first 3 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 vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA. Source: Modified from MET55 CSR Table 8.144

Vaccine Seroresponse

For participants with any pre-vaccination titres, the vaccine seroresponse rates correspond to the percentages of participants with a ≥ 4-fold rise in hSBA titres from D0 to D30. For participants with pre-vaccination titre < 1:8, the percentages of participants with a vaccine seroresponse (ie, with post-vaccination titre ≥ 1:16) were higher in Groups 5 + 7 than in Groups 6 + 8, respectively, for each serogroup, except serogroup A for which there was no significant difference between pooled groups.

Table 18: Number and percentage of participants with hSBA vaccine seroresponse from D0 before to D30 after vaccination of Cohort II – Per-Protocol Analysis Set

		India						RSA					
		Group 5 (N=222)			Group 6 (N=228)			Group 7 (N=223)			Group 8 (N=217)		
Serogroup	Baseline Status	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	Any	166/220	75.5	(69.2; 81.0)	140/228	61.4	(54.8; 67.8)	151/223	67.7	(61.1; 73.8)	120/215	55.8	(48.9; 62.6)
	S-	74/86	86.0	(76.9; 92.6)	58/83	69.9	(58.8; 79.5)	63/87	72.4	(61.8; 81.5)	58/91	63.7	(53.0; 73.6)
	S+	92/134	68.7	(60.1; 76.4)	82/145	56.6	(48.1; 64.8)	88/136	64.7	(56.1; 72.7)	62/124	50.0	(40.9; 59.1)
C	Any	218/222	98.2	(95.5; 99.5)	141/228	61.8	(55.2; 68.2)	218/223	97.8	(94.8; 99.3)	140/215	65.1	(58.3; 71.5)
	S-	177/178	99.4	(96.9; 100)	113/186	60.8	(53.3; 67.8)	148/151	98.0	(94.3; 99.6)	97/150	64.7	(56.5; 72.3)
	S+	41/44	93.2	(81.3; 98.6)	28/42	66.7	(50.5; 80.4)	70/72	97.2	(90.3; 99.7)	43/65	66.2	(53.4; 77.4)
Y	Any	201/222	90.5	(85.9; 94.0)	155/228	68.0	(61.5; 74.0)	210/221	95.0	(91.3; 97.5)	179/215	83.3	(77.6; 88.0)
	S-	176/186	94.6	(90.3; 97.4)	152/197	77.2	(70.7; 82.8)	172/174	98.9	(95.9; 99.9)	139/160	86.9	(80.6; 91.7)
	S+	25/36	69.4	(51.9; 83.7)	3/31	9.7	(2.0; 25.8)	38/47	80.9	(66.7; 90.9)	40/55	72.7	(59.0; 83.9)
W	Any	204/222	91.9	(87.5; 95.1)	138/228	60.5	(53.9; 66.9)	201/223	90.1	(85.4; 93.7)	148/217	68.2	(61.6; 74.3)
	S-	172/180	95.6	(91.4; 98.1)	125/197	63.5	(56.3; 70.2)	126/129	97.7	(93.4; 99.5)	101/128	78.9	(70.8; 85.6)
	S+	32/42	76.2	(60.5; 87.9)	13/31	41.9	(24.5; 60.9)	75/94	79.8	(70.2; 87.4)	47/89	52.8	(41.9; 63.5)

		India and RSA					
		Group 5 + Group 7 (N=445)			Group 6 + Group 8 (N=445)		
Serogroup	Baseline Status	n/M	%	(95% CI)	n/M	%	(95% CI)
A	Any	317/443	71.6	(67.1; 75.7)	260/443	58.7	(53.9; 63.3)
	S-	137/173	79.2	(72.4; 85.0)	116/174	66.7	(59.1; 73.6)
	S+	180/270	66.7	(60.7; 72.3)	144/269	53.5	(47.4; 59.6)
C	Any	436/445	98.0	(96.2; 99.1)	281/443	63.4	(58.8; 67.9)
	S-	325/329	98.8	(96.9; 99.7)	210/336	62.5	(57.1; 67.7)
	S+	111/116	95.7	(90.2; 98.6)	71/107	66.4	(56.6; 75.2)
Y	Any	411/443	92.8	(90.0; 95.0)	334/443	75.4	(71.1; 79.3)
	S-	348/360	96.7	(94.2; 98.3)	291/357	81.5	(77.1; 85.4)
	S+	63/83	75.9	(65.3; 84.6)	43/86	50.0	(39.0; 61.0)
W	Any	405/445	91.0	(88.0; 93.5)	286/445	64.3	(59.6; 68.7)
	S-	298/309	96.4	(93.7; 98.2)	226/325	69.5	(64.2; 74.5)
	S+	107/136	78.7	(70.8; 85.2)	60/120	50.0	(40.7; 59.3)

n: number of participants with titers that meet the hSBA vaccine seroresponse criteria; hSBA vaccine seroresponse: for a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be >= 1:16; for a participant with a pre-vaccination titer >= 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer.
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.
S-: Pre-vaccination baseline titer is < 1:8; S+: Pre-vaccination baseline titer is >= 1:8
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Source: Modified from MET55 CSR Table 8.148

Secondary Objective #4: To describe the antibody titres to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in India (Cohort II)

See data presented for Secondary Objective #3.

Secondary Objective #5: To describe the antibody titres to the meningococcal serogroups A, C, Y, and W before and at D30 (+14 days) after vaccination with MenACYW conjugate vaccine or Menactra in children and adolescents aged 2 to 17 years in RSA (Cohort II)

See data presented for Secondary Objective #3.

Safety results

Extent of Exposure

Table 19: Safety analysis by vaccination Group of Cohort I – Randomised study participants

	Group 1 (N=98) n (%)	Group 2 (N=100) n (%)	Group 3 (N=100) n (%)	Group 4 (N=100) n (%)	All (N=398) n (%)
Safety Analysis Set	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Solicited injection site safety assessed	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)
Solicited systemic safety assessed	98 (100)	100 (100)	100 (100)	100 (100)	398 (100)

n: number of study participants experiencing the endpoint
Safety endpoints are considered assessed if at least one data point has been collected; unsolicited AEs are never missing as all study participants had a 30-minute surveillance period after injection
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Table 20: Safety Analysis Set by vaccination Group of Cohort II – Randomised study participants

	Group 5 (N=232) n (%)	Group 6 (N=232) n (%)	Group 7 (N=229) n (%)	Group 8 (N=227) n (%)	Randomized but not vaccinated (N=10) n (%)	All (N=930) n (%)
Safety Analysis Set	232 (100)	232 (100)	229 (100)	227 (100)	-	920 (98.9)
Solicited injection site safety assessed	227 (97.8)	229 (98.7)	227 (99.1)	222 (97.8)	-	905 (97.3)
Solicited systemic safety assessed	227 (97.8)	229 (98.7)	227 (99.1)	222 (97.8)	-	905 (97.3)

n: number of study participants experiencing the endpoint
Safety endpoints are considered assessed if at least one data point has been collected; unsolicited AEs are never missing as all study participants had a 30-minute surveillance period after injection
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.

Safety Summary after Study Vaccine Dose – SafAS

Table 21: Safety overview after vaccine injection of Cohort I – Safety Analysis Set

	Group 1 (N=98)			Group 2 (N=100)			Group 3 (N=100)			Group 4 (N=100)		
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	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Immediate unsolicited AR	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Solicited reaction within solicited period after vaccine injection	32/98	32.7	(23.5; 42.9)	26/100	26.0	(17.7; 35.7)	17/100	17.0	(10.2; 25.8)	21/100	21.0	(13.5; 30.3)
Solicited injection site reaction	27/98	27.6	(19.0; 37.5)	24/100	24.0	(16.0; 33.6)	9/100	9.0	(4.2; 16.4)	16/100	16.0	(9.4; 24.7)
Solicited systemic reaction	13/98	13.3	(7.3; 21.6)	8/100	8.0	(3.5; 15.2)	8/100	8.0	(3.5; 15.2)	8/100	8.0	(3.5; 15.2)
Within 30 days after vaccine injection												
Unsolicited AE	7/98	7.1	(2.9; 14.2)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
Unsolicited AR	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Unsolicited non-serious AE	6/98	6.1	(2.3; 12.9)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
Unsolicited non-serious AR	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Unsolicited non-serious injection site AR	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Unsolicited non-serious systemic AE	6/98	6.1	(2.3; 12.9)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
Unsolicited non-serious systemic AR	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
AE leading to study discontinuation	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
SAE	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Death	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
AESI	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
During the study												
SAE	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Death	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
AESI	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)

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 Safety Analysis Set; Percentages are based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs.
"Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious.
AR: Reactions related to IMP (MenACYW/Menactra/Quadri Meningo)
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.

Table 22: Safety overview after vaccine injection of Cohort II – Safety Analysis Set

	Group 5 (N=232)			Group 6 (N=232)			Group 7 (N=229)			Group 8 (N=227)		
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	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
Immediate unsolicited AR	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
Solicited reaction within solicited period after vaccine injection	79/227	34.8	(28.6; 41.4)	41/229	17.9	(13.2; 23.5)	115/227	50.7	(44.0; 57.3)	128/222	57.7	(50.9; 64.2)
Solicited injection site reaction	52/227	22.9	(17.6; 28.9)	30/229	13.1	(9.0; 18.2)	96/227	42.3	(35.8; 49.0)	99/222	44.6	(37.9; 51.4)
Solicited systemic reaction	48/227	21.1	(16.0; 27.0)	19/229	8.3	(5.1; 12.7)	82/227	36.1	(29.9; 42.7)	92/222	41.4	(34.9; 48.2)
Within 30 days after vaccine injection												
Unsolicited AE	8/232	3.4	(1.5; 6.7)	12/232	5.2	(2.7; 8.9)	22/229	9.6	(6.1; 14.2)	30/227	13.2	(9.1; 18.3)
Unsolicited AR	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	1/229	0.4	(0; 2.4)	1/227	0.4	(0; 2.4)
Unsolicited non-serious AE	7/232	3.0	(1.2; 6.1)	12/232	5.2	(2.7; 8.9)	22/229	9.6	(6.1; 14.2)	30/227	13.2	(9.1; 18.3)
Unsolicited non-serious AR	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	1/229	0.4	(0; 2.4)	1/227	0.4	(0; 2.4)
Unsolicited non-serious injection site AR	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
Unsolicited non-serious systemic AE	7/232	3.0	(1.2; 6.1)	12/232	5.2	(2.7; 8.9)	22/229	9.6	(6.1; 14.2)	30/227	13.2	(9.1; 18.3)
Unsolicited non-serious systemic AR	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	1/229	0.4	(0; 2.4)	1/227	0.4	(0; 2.4)
AE leading to study discontinuation	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
SAE	1/232	0.4	(0; 2.4)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
Death	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
AESI	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
During the study												
SAE	1/232	0.4	(0; 2.4)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
Death	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)
AESI	0/232	0	(0; 1.6)	0/232	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)

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 Safety Analysis Set; Percentages are based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs.
"Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious.
AR: Reactions related to IMP (MenACYW/Menactra/Quadri Meningo)
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.

Adverse Events

Cohort I- Adults ≥18 Years

Table 23: Solicited injection site reactions after vaccine injection for Cohort I, by maximum intensity during the solicited period – Safety Analysis Set

		Group 1 (N=98)			Group 2 (N=100)			Group 3 (N=100)			Group 4 (N=100)		
Subjects experiencing at least one:	**Maximum intensity**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Injection site pain	Any	27/98	27.6	(19.0; 37.5)	24/100	24.0	(16.0; 33.6)	9/100	9.0	(4.2; 16.4)	14/100	14.0	(7.9; 22.4)
	Grade 1	21/98	21.4	(13.8; 30.9)	20/100	20.0	(12.7; 29.2)	9/100	9.0	(4.2; 16.4)	14/100	14.0	(7.9; 22.4)
	Grade 2	6/98	6.1	(2.3; 12.9)	4/100	4.0	(1.1; 9.9)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Injection site erythema	Any	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	1/100	1.0	(0; 5.4)
	Grade 1	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	1/100	1.0	(0; 5.4)
	Grade 2	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Injection site swelling	Any	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	2/100	2.0	(0.2; 7.0)
	Grade 1	1/98	1.0	(0; 5.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	2/100	2.0	(0.2; 7.0)
	Grade 2	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)

n: number of subjects experiencing the endpoint listed in the first two columns
M: number of subjects with available data for the relevant endpoint
N: number of subjects in safety analysis set
Percentages are based on M.
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08036to59.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08038_i.rtf (06NOV2024 5:10)

Table 24: Solicited systemic reactions after vaccine injection of Cohort I, by maximum intensity during the solicited period - Safety Analysis Set

		Group 1 (N=98)			Group 2 (N=100)			Group 3 (N=100)			Group 4 (N=100)		
Subjects experiencing at least one:	**Maximum intensity**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Fever	Any	5/98	5.1	(1.7; 11.5)	2/100	2.0	(0.2; 7.0)	3/100	3.0	(0.6; 8.5)	4/100	4.0	(1.1; 9.9)
	Grade 1	5/98	5.1	(1.7; 11.5)	2/100	2.0	(0.2; 7.0)	2/100	2.0	(0.2; 7.0)	3/100	3.0	(0.6; 8.5)
	Grade 2	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
	Grade 3	0/98	0	(0; 3.7)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Headache	Any	6/98	6.1	(2.3; 12.9)	6/100	6.0	(2.2; 12.6)	3/100	3.0	(0.6; 8.5)	3/100	3.0	(0.6; 8.5)
	Grade 1	5/98	5.1	(1.7; 11.5)	2/100	2.0	(0.2; 7.0)	3/100	3.0	(0.6; 8.5)	3/100	3.0	(0.6; 8.5)
	Grade 2	1/98	1.0	(0; 5.6)	3/100	3.0	(0.6; 8.5)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	0/98	0	(0; 3.7)	1/100	1.0	(0; 5.4)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Malaise	Any	6/98	6.1	(2.3; 12.9)	5/100	5.0	(1.6; 11.3)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
	Grade 1	4/98	4.1	(1.1; 10.1)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)	1/100	1.0	(0; 5.4)
	Grade 2	2/98	2.0	(0.2; 7.2)	3/100	3.0	(0.6; 8.5)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	0/98	0	(0; 3.7)	1/100	1.0	(0; 5.4)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
Myalgia	Any	5/98	5.1	(1.7; 11.5)	6/100	6.0	(2.2; 12.6)	2/100	2.0	(0.2; 7.0)	0/100	0	(0; 3.6)
	Grade 1	2/98	2.0	(0.2; 7.2)	3/100	3.0	(0.6; 8.5)	2/100	2.0	(0.2; 7.0)	0/100	0	(0; 3.6)
	Grade 2	2/98	2.0	(0.2; 7.2)	2/100	2.0	(0.2; 7.0)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)
	Grade 3	1/98	1.0	(0; 5.6)	1/100	1.0	(0; 5.4)	0/100	0	(0; 3.6)	0/100	0	(0; 3.6)

n: number of subjects experiencing the endpoint listed in the first two columns
M: number of subjects with available data for the relevant endpoint
N: number of subjects in safety analysis set
Percentages are based on M.
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08036to59.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08050_i.rtf (06NOV2024 5:12)

Table 25: Unsolicited AEs within 30 days after vaccine injection of Cohort I, by system organ class and preferred term - Safety Analysis Set

	Group 1 (N=98)				Group 2 (N=100)				Group 3 (N=100)				Group 4 (N=100)			
Subjects experiencing at least one:	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**
Unsolicited AE	7	7.1	(2.9; 14.2)	7	1	1.0	(0; 5.4)	1	1	1.0	(0; 5.4)	1	1	1.0	(0; 5.4)	1
Gastrointestinal disorders	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Vomiting	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
General disorders and administration site conditions	2	2.0	(0.2; 7.2)	2	0	0	(0; 3.6)	0	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Non-cardiac chest pain	2	2.0	(0.2; 7.2)	2	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Pyrexia	0	0	(0; 3.7)	0	0	0	(0; 3.6)	0	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Infections and infestations	2	2.0	(0.2; 7.2)	2	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	1	1.0	(0; 5.4)	1
COVID-19	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	1	1.0	(0; 5.4)	1
Nasopharyngitis	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Nervous system disorders	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Dizziness postural	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Respiratory, thoracic and mediastinal disorders	1	1.0	(0; 5.6)	1	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Cough	1	1.0	(0; 5.6)	1	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0

n: number of subjects experiencing the endpoint listed in the first column
n AEs: number of AEs
N: number of subjects in safety analysis set
Percentages are based on N.
MedDRA Version: 26.0
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08060n61n68to75.sas Datasets=ADSL ADAE Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08068_i.rtf (06NOV2024 5:14)

Table 26: Unsolicited ARs within 30 days after vaccine injection of Cohort I, by system organ class and preferred term - Safety Analysis Set

	Group 1 (N=98)				Group 2 (N=100)				Group 3 (N=100)				Group 4 (N=100)			
Subjects experiencing at least one:	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**
Unsolicited AR	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Gastrointestinal disorders	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0
Vomiting	1	1.0	(0; 5.6)	1	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0	0	0	(0; 3.6)	0

n: number of subjects experiencing the endpoint listed in the first column
n ARs: number of ARs
N: number of subjects in safety analysis set
Percentages are based on N.
AR: reactions related to IMP (MENACYW/Menactra/Quadri Meningo)
MedDRA Version: 26.0
Group 1: MenACYW conjugate vaccine at aged 18 to 55 years in India. Group 2: Menactra at aged 18 to 55 years in India.
Group 3: MenACYW conjugate vaccine at aged >= 56 years in India. Group 4: Quadri Meningo at aged >= 56 years in India.
Study: MET55 Program: t08060n61n68to75.sas Datasets=ADSL ADAE Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08070_i.rtf (06NOV2024 5:14)

Cohort II - Children and Adolescents Aged 2 to 17 Years

Table 27: Solicited injection site reactions after vaccine injection for Cohort II, by maximum intensity during the solicited period – Safety Analysis Set

		Group 5 (N=232)			Group 6 (N=232)			Group 7 (N=229)			Group 8 (N=227)		
Subjects experiencing at least one:	**Maximum intensity**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Injection site pain	Any	52/227	22.9	(17.6; 28.9)	29/229	12.7	(8.6; 17.7)	85/227	37.4	(31.1; 44.1)	82/222	36.9	(30.6; 43.7)
	Grade 1	47/227	20.7	(15.6; 26.6)	27/229	11.8	(7.9; 16.7)	59/227	26.0	(20.4; 32.2)	63/222	28.4	(22.5; 34.8)
	Grade 2	5/227	2.2	(0.7; 5.1)	2/229	0.9	(0.1; 3.1)	24/227	10.6	(6.9; 15.3)	15/222	6.8	(3.8; 10.9)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	2/227	0.9	(0.1; 3.1)	4/222	1.8	(0.5; 4.5)
Injection site erythema	Any	1/227	0.4	(0; 2.4)	0/229	0	(0; 1.6)	28/227	12.3	(8.4; 17.3)	27/222	12.2	(8.2; 17.2)
	Grade 1	1/227	0.4	(0; 2.4)	0/229	0	(0; 1.6)	26/227	11.5	(7.6; 16.3)	16/222	7.2	(4.2; 11.4)
	Grade 2	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	2/227	0.9	(0.1; 3.1)	7/222	3.2	(1.3; 6.4)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	0/227	0	(0; 1.6)	4/222	1.8	(0.5; 4.5)
Injection site swelling	Any	1/227	0.4	(0; 2.4)	1/229	0.4	(0; 2.4)	25/227	11.0	(7.3; 15.8)	37/222	16.7	(12.0; 22.2)
	Grade 1	1/227	0.4	(0; 2.4)	1/229	0.4	(0; 2.4)	19/227	8.4	(5.1; 12.8)	24/222	10.8	(7.1; 15.7)
	Grade 2	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	3/227	1.3	(0.3; 3.8)	10/222	4.5	(2.2; 8.1)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	3/227	1.3	(0.3; 3.8)	3/222	1.4	(0.3; 3.9)

n: number of subjects experiencing the endpoint listed in the first two columns
M: number of subjects with available data for the relevant endpoint
N: number of subjects in safety analysis set
Percentages are based on M.
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Study: MET55 Program: t08036to59.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08039_i.rtf (06NOV2024 5:10)

Table 28: Solicited systemic reactions after vaccine injection of Cohort II, by maximum intensity during the solicited period - Safety Analysis Set

		Group 5 (N=232)			Group 6 (N=232)			Group 7 (N=229)			Group 8 (N=227)		
Subjects experiencing at least one:	**Maximum intensity**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Fever	Any	35/226	15.5	(11.0; 20.9)	13/229	5.7	(3.1; 9.5)	8/226	3.5	(1.5; 6.9)	6/221	2.7	(1.0; 5.8)
	Grade 1	29/226	12.8	(8.8; 17.9)	10/229	4.4	(2.1; 7.9)	3/226	1.3	(0.3; 3.8)	3/221	1.4	(0.3; 3.9)
	Grade 2	5/226	2.2	(0.7; 5.1)	3/229	1.3	(0.3; 3.8)	3/226	1.3	(0.3; 3.8)	3/221	1.4	(0.3; 3.9)
	Grade 3	1/226	0.4	(0; 2.4)	0/229	0	(0; 1.6)	2/226	0.9	(0.1; 3.2)	0/221	0	(0; 1.7)
Headache	Any	13/227	5.7	(3.1; 9.6)	3/229	1.3	(0.3; 3.8)	56/227	24.7	(19.2; 30.8)	57/222	25.7	(20.1; 31.9)
	Grade 1	10/227	4.4	(2.1; 8.0)	3/229	1.3	(0.3; 3.8)	38/227	16.7	(12.1; 22.2)	40/222	18.0	(13.2; 23.7)
	Grade 2	3/227	1.3	(0.3; 3.8)	0/229	0	(0; 1.6)	13/227	5.7	(3.1; 9.6)	13/222	5.9	(3.2; 9.8)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	5/227	2.2	(0.7; 5.1)	4/222	1.8	(0.5; 4.5)
Malaise	Any	11/227	4.8	(2.4; 8.5)	4/229	1.7	(0.5; 4.4)	45/227	19.8	(14.8; 25.6)	44/222	19.8	(14.8; 25.7)
	Grade 1	7/227	3.1	(1.2; 6.3)	3/229	1.3	(0.3; 3.8)	34/227	15.0	(10.6; 20.3)	34/222	15.3	(10.8; 20.7)
	Grade 2	4/227	1.8	(0.5; 4.5)	1/229	0.4	(0; 2.4)	10/227	4.4	(2.1; 8.0)	7/222	3.2	(1.3; 6.4)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	1/227	0.4	(0; 2.4)	3/222	1.4	(0.3; 3.9)
Myalgia	Any	7/227	3.1	(1.2; 6.3)	3/229	1.3	(0.3; 3.8)	46/227	20.3	(15.2; 26.1)	49/222	22.1	(16.8; 28.1)
	Grade 1	5/227	2.2	(0.7; 5.1)	3/229	1.3	(0.3; 3.8)	36/227	15.9	(11.4; 21.3)	37/222	16.7	(12.0; 22.2)
	Grade 2	2/227	0.9	(0.1; 3.1)	0/229	0	(0; 1.6)	9/227	4.0	(1.8; 7.4)	8/222	3.6	(1.6; 7.0)
	Grade 3	0/227	0	(0; 1.6)	0/229	0	(0; 1.6)	1/227	0.4	(0; 2.4)	4/222	1.8	(0.5; 4.5)

n: number of subjects experiencing the endpoint listed in the first two columns
M: number of subjects with available data for the relevant endpoint
N: number of subjects in safety analysis set
Percentages are based on M.
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Study: MET55 Program: t08036to59.sas Datasets=ADSL ADRC Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08051_i.rtf (06NOV2024 5:12)

Table 29: Unsolicited AEs within 30 days after vaccine injection of Cohort II, by system organ class and preferred term - Safety Analysis Set

	Group 5 (N=232)				Group 6 (N=232)				Group 7 (N=229)				Group 8 (N=227)			
Subjects experiencing at least one:	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**	**n**	**%**	**(95% CI)**	**n AEs**
Unsolicited AE	8	3.4	(1.5; 6.7)	9	12	5.2	(2.7; 8.9)	15	22	9.6	(6.1; 14.2)	32	30	13.2	(9.1; 18.3)	38
Gastrointestinal disorders	2	0.9	(0.1; 3.1)	2	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	3	9	4.0	(1.8; 7.4)	10
Abdominal pain	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Abdominal pain upper	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Constipation	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Diarrhoea	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	3	1.3	(0.3; 3.8)	3
Oral pain	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Toothache	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2
Vomiting	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	2	0.9	(0.1; 3.1)	2
General disorders and administration site conditions	2	0.9	(0.1; 3.1)	2	3	1.3	(0.3; 3.7)	3	4	1.7	(0.5; 4.4)	4	2	0.9	(0.1; 3.1)	2
Axillary pain	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	0	0	(0; 1.6)	0
Peripheral swelling	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	0	0	(0; 1.6)	0
Pyrexia	2	0.9	(0.1; 3.1)	2	3	1.3	(0.3; 3.7)	3	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2
Infections and infestations	5	2.2	(0.7; 5.0)	5	3	1.3	(0.3; 3.7)	3	6	2.6	(1.0; 5.6)	6	7	3.1	(1.2; 6.3)	10
Dengue fever	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0
Ear infection	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	2
Influenza	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	3	1.3	(0.3; 3.8)	3
Nasopharyngitis	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1
Pharyngitis	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	2
Pneumonia	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0
Soft tissue infection	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Tonsillitis	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Upper respiratory tract infection	3	1.3	(0.3; 3.7)	3	2	0.9	(0.1; 3.1)	2	2	0.9	(0.1; 3.1)	2	1	0.4	(0; 2.4)	1
Injury, poisoning and procedural complications	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Joint injury	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0
Musculoskeletal injury	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Investigations	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Cardiac murmur	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Musculoskeletal and connective tissue disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	1	0.4	(0; 2.4)	1
Back pain	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Musculoskeletal stiffness	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Pain in extremity	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Nervous system disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	3	1.3	(0.3; 3.8)	3	3	1.3	(0.3; 3.8)	4
Dizziness	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Headache	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	3	1.3	(0.3; 3.8)	4
Paraesthesia	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Psychiatric disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Enuresis	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Reproductive system and breast disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Dysmenorrhoea	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Respiratory, thoracic and mediastinal disorders	0	0	(0; 1.6)	0	5	2.2	(0.7; 5.0)	7	7	3.1	(1.2; 6.2)	8	8	3.5	(1.5; 6.8)	8
Cough	0	0	(0; 1.6)	0	5	2.2	(0.7; 5.0)	5	4	1.7	(0.5; 4.4)	4	4	1.8	(0.5; 4.5)	4
Epistaxis	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1
Nasal congestion	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Oropharyngeal pain	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	2	0.9	(0.1; 3.1)	2
Rhinorrhoea	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1
Skin and subcutaneous tissue disorders	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	3	1.3	(0.3; 3.8)	3	2	0.9	(0.1; 3.1)	2
Dry skin	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Pruritus	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Rash	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	2	0.9	(0.1; 3.1)	2	1	0.4	(0; 2.4)	1
Rash maculo-papular	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0

n: number of subjects experiencing the endpoint listed in the first column
n AEs: number of AEs
N: number of subjects in safety analysis set
Percentages are based on N.
MedDRA Version: 26.0
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Study: MET55 Program: t08060n61n68to75.sas Datasets=ADSL ADAE Output: PRODOPS/SP0047/MET55/CSR_01/REPORT/OUTPUT/T08069_i.rtf (06NOV2024 5:14)

Table 30: Unsolicited ARs within 30 days after vaccine injection of Cohort II, by system organ class and preferred term - Safety Analysis Set

	Group 5 (N=232)				Group 6 (N=232)				Group 7 (N=229)				Group 8 (N=227)			
Subjects experiencing at least one:	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**	**n**	**%**	**(95% CI)**	**n ARs**
Unsolicited AR	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	1	0.4	(0; 2.4)	1
Gastrointestinal disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Vomiting	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1
Skin and subcutaneous tissue disorders	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0
Pruritus	0	0	(0; 1.6)	0	0	0	(0; 1.6)	0	1	0.4	(0; 2.4)	1	0	0	(0; 1.6)	0

n: number of subjects experiencing the endpoint listed in the first column
n ARs: number of ARs
N: number of subjects in safety analysis set
Percentages are based on N.
AR: reactions related to IMP (MENACYW/Menactra/Quadri Meningo)
MedDRA Version: 26.0
Group 5: MenACYW conjugate vaccine at aged 2 to 17 years in India. Group 6: Menactra at aged 2 to 17 years in India.
Group 7: MenACYW conjugate vaccine at aged 2 to 17 years in RSA. Group 8: Menactra at aged 2 to 17 years in RSA.
Study: MET55 Program: t08060n61n68to75.sas Datasets=ADSL ADAE Output: PRODOPS/SP0047/MET55/CSR 01/REPORT/OUTPUT/T08071 i.rtf (06NOV2024 5:14)

Discontinuations due to Adverse Events

There were no discontinuation from the study due to AEs in any group.

Serious Adverse Events (SAE) Including Deaths

No deaths were reported during the study in any group of Cohort I (India).

During the study, 1 participant (1.0% [1/98]) in Group 1 (India) experienced an SAE that occurred within 30 days of vaccination. There were no SAEs reported in Group 2 (India), Group 3 (India), and Group 4 (India). The SAE reported in Group 1 was COVID-19. The event was considered as not related to the vaccine by the Investigator and the Sponsor. The participant was hospitalised and recovered with medication.

No deaths were reported during the study in any group of Cohort II (India and RSA).

During the study, 1 participant (0.4% [1/232]) in Group 5 (India) experienced an SAE that occurred within 30 days of vaccination. There were no SAEs reported in Group 6 (India), Group 7 (RSA), and Group 8 (RSA). The SAE reported in Group 5 was dengue fever. The event was not considered as related to the vaccine by the Investigator and the Sponsor. The participant was hospitalised and recovered with medication.

Adverse Events of Special Interest

No AESIs were reported during the study in any group of either Cohort I or Cohort II.

2.3.3. Discussion on clinical aspects

The MAH has completed a double-blind, randomised, parallel-group clinical phase 3 study in healthy adults from India (Cohort I) and children and adolescents from India and the RSA (Cohort II). The adult Cohort I was further divided in participants aged 18-55 years vaccinated either with Menquadfi (Group 1) or with Menactra (Group 2) and participants aged ≥56 years vaccinated either with Menquadfi (Group 3) or Quadri Meningo (Group 4; each group planned with n=100 subjects). The paediatric Cohort II was aged 2 to 17 years and vaccinated either with Menquadfi (Group 5 from India and Group 7 from the RSA) or Menactra (Group 6 from India and Group 8 from the RSA; each group planned with n=233 subjects). This subdivision in paediatric and adult participants as well as the

stratification of paediatric subjects in 2 subgroups 2 to 9 years and 10 to 17 years in both countries is acknowledged. The focus of this P46 procedure is the paediatric population, but the adult population will also be discussed briefly. The primary objective to demonstrate non-inferiority of the hSBA antibody titres ≥1:8 for serogroups A, C, Y and W in paediatric subjects after vaccination with Menquadfi compared to vaccination with Menactra is considered not ideal, as baseline titre levels are not taken into account for this measure. Still, the objective can be acceptable as it is complemented by data on seroresponse (i.e. for a pre-vaccination titre < 1:8, the post-vaccination titre must be ≥ 1:16, for a pre-vaccination titre ≥ 1:8, the post-vaccination titre must be at least 4-fold greater than the pre-vaccination titre) and GMTs as secondary objectives. It is critically noted that the primary as well as all secondary endpoints do not specify any success criterion for the comparison of hSBA titres ≥1:8 between vaccination. The intention to demonstrate non-inferiority for the primary measure can be taken only from the primary objective, secondary objectives and endpoints seem target a more descriptive role without clear comparison and success criterion. Considering the rather positive results on immunogenicity as described below, no concern is raised in this regard. In any case, also for the adult population the presentation of seroresponse is considered the most informative measure regarding the effect of vaccination, complemented by seroprotection and GMTs.

The number of randomised subjects fits to the planned number (only Group 1 with n=98 as well as Groups 5 and 8 with n=232 have very slightly less subjects randomised) and the vast majority of participants completed the study after the final Day 30 visit (99.5% for the combined Cohort I and 96.7% for the combined Cohort II). Protocol deviations seem to have occurred a bit more frequently in the RSA compared to India (in >12% and ~5% of participants, respectively), but seem mostly independent of treatment and not based on a specific concern. No pattern of concern is evident form the reported baseline demographics of either Cohort. Notably, in Cohort I the male/female ratio was >2, but comparable in all groups of that Cohort.

Less than 5% of subjects were HIV-positive in the RSA, which objects a reasonable interpretation of results on immunogenicity and safety. Thus, the decision by the MAH not to produce results for this subgroup can be followed.

Immunogenicity

The primary endpoint (or better the comparison/success criterion as specified in the primary objective, i.e. non-inferiority in the proportion of participants with titres ≥1:8 compared to Menactra) was met as in the two paediatric study groups vaccinated with Menquadfi (Groups 5 and 7) had a numerically higher proportion of subjects with seroprotection levels (hSBA titre levels ≥1:8) compared to the study groups vaccinated with Menquadfi for all serogroups and within both geographical locations (i.e. Groups 5 vs. 6 and 7 vs. 8). Results were comparable in both geographical regions. The numerically higher antibody titres 30 days after vaccination with Menquadfi compared to Menactra was also shown with GMTs and also seroresponse was shown to be higher after vaccination with Menquadfi for all serogroups and in both regions. No critical difference was observed for the immunoresponse in paediatric participants from India and the RSA and the pattern between vaccination groups were comparable in the two subpopulations of paediatric patients 2-9 years and 10-17 years of age.

GMTs of all serogroups were also numerically higher for the adult population when vaccinated with Menquadfi compared to Menactra (aged 18-55 years, Groups 1 vs. 2) or Quadri Meningo (≥56 years, Groups 3 vs. 4). The same trend was also demonstrated for the proportion of subjects with seroresponse 30 days after vaccination. However, the proportion of subjects with titres ≥1:8 was higher after Menquadfi vaccination for serogroups C, Y and W, whereas for serogroup A the proportion was numerically slightly higher after the comparator vaccines (overlapping CIs).

Results on immunogenicity presented based on rSBA titres showed a comparable pattern between study groups as the results presented for hSBA titres.

Safety

Only one subject of the study had an immediate AE reported in Cohort I (dizziness postural in Group 1), no paediatric subject reported an immediate reaction with 30 minutes after vaccination.

Solicited local reactions were reported substantially more frequently in paediatric patients from the RSA compared to India. Injection site erythema and swelling were reported by 11-17% of participants in the RSA, but <0.5% of those in India. No critical differences are evident between study groups of the same location (Groups 5 vs. 6 and 7 vs. 8). Injection site pain was reported in India by around 10% more subjects after vaccination with Menquadfi (22.9%) compared to Menactra (12.7%), but by a generally higher proportion in the RSA without evident differences between vaccination groups (37.4% and 36.9% of subjects vaccinated with Menquadfi and Menactra, respectively). Of note, different reporting habits across geographical regions are not uncommon. Injection site pain is a recognised very common adverse reaction upon vaccination with Menquadfi (see SmPC).

A comparable pattern (substantially higher proportions of subjects reporting events in the RSA compared to India, without critical differences between treatment groups, and slightly higher proportions with event in India after vaccination with Menquadfi compared to Menactra) is also seen for **solicited systemic reactions** headache, malaise and myalgia. However, the pattern appears different for fever, which was reported as solicited reaction most frequently by Indian adolescents after vaccination with Menquadfi (15.5% vs. 5.7% after Menactra (non-overlapping CIs) and 3.5% after Menquadfi and 2.7% after Menactra in the RSA, respectively). Fever was also reported as **grade 3** event only after vaccination with Menquadfi (0.4% in India and 0.9% in the RSA, in total 3 paediatric participants), but in all cases the event has resolved, either spontaneously or with medication. Fever is a recognised common adverse reaction upon vaccination with Menquadfi (see SmPC). Other grade 3 reactions were reported only in the RSA, without concerning imbalance between groups (headache in 2.2% and 1.8% as well as myalgia in 0.4% and 1.8% of subjects in Groups 7 and 8, respectively).

Unsolicited AEs within 30 days after vaccination were reported slightly more frequently after Menactra compared to Menquadfi, but CIs are largely overlapping within each geographical location (i.e. between Groups 5 vs. 6 and 7 vs. 8). Again, subjects in the RSA appear to have a higher reporting frequency compared to India (around factor 2-3). However, no SOC or PT stands out as specific risk in the RSA and no unexpected and/or concerning pattern of events seems evident.

One **serious AE** of dengue fever was reported for a paediatric subject in group 5, but no other serious event was reported for paediatric participants in India or the RSA. A relation to study treatment seems not evident for the event. No **death**, AESI or **discontinuation due to an AE** were reported.

No major imbalances are evident between study groups vaccinated with Menquadfi or the comparator vaccine in the **adult** Cohort 1 (Groups 1 vs. 2 and 3 vs. 4). Solicited reactions (local and systemic) seem more frequent in the adult population <55 years compared to the population >55 years of age after administration of Menquadfi (Groups 1 with 32.7% vs. 3 with 17% of participants with event). Notably, within this study Cohort unsolicited events within 30 days were most frequent for participants <55 years of age after administration of Menquadfi (Group 1, 7.1% of subjects) compared to all other treatment groups in the Cohort (1% in all other Groups). However, no specific SOC or PT stands out, that would raise concern. One serious event of Covid-19 was reported for one subject in Group 1. The proposed evaluation that this event is not directly related to the study vaccine can be followed. No discontinuation, no AESI and no death was reported for the adult population of the study.

3. CHMP's overall conclusion and recommendation

The primary immunogenicity endpoint was met and the general pattern on immunogenicity results indicates numerically higher titre levels upon vaccination with Menquadfi compared to the respective comparator vaccines in paediatric and adult study participants. Substantial differences in the reporting of safety events are evident between the two geographical locations of the paediatric investigation. In general, a higher proportion of participants in the RSA have reported safety events compared to participants in India, but independent of study vaccine. Different reporting habits across geographical regions are not uncommon. Only fever, as known common adverse reaction of Menquadfi, was most frequently reported by children in India after vaccination with Menquadfi compared to all other vaccination groups of the paediatric Cohort II. However, no critical safety finding stands out for the adult (Cohort I) or paediatric (Cohort II) study population after vaccination with Menquadfi.

☒ **Fulfilled:**

No regulatory action required.