Amsterdam, 13 November 2025
EMADOC-1700519818-2383013
Human Medicines Division

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

MenQuadfi

Meningococcal Group A, C, W and Y conjugate vaccine

Procedure no: EMA/PAM/0000293240

Note

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

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	Start of procedure	15 September 2025	15 September 2025
☐	CHMP Rapporteur AR	20 October 2025	14 October 2025
☐	CHMP comments	3 November 2025	N/A
☐	Updated CHMP Rapporteur AR	6 November 2025	N/A
☒	CHMP outcome	13 November 2025	13 November 2025

Table of contents

1. Introduction

On 22 August 2025, the MAH submitted the completed paediatric study MEQ00086 for MenQuadfi, in accordance with Article 46 of Regulation (EC) No1901/2006, 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 MEQ00086, a descriptive, Phase IV, open-label, single-arm multi-centre study to assess the immunogenicity and safety of MenQuadfi as a booster vaccine in healthy toddlers 12 to 23 months of age who had been primed with at least 1 dose of another quadrivalent meningococcal conjugate vaccine, i.e., Nimenrix (MCV4-TT) or Menveo (MCV4-CRM), in infancy is a stand-alone study.

Study MEQ00086 is not included in the MenQuadfi Paediatric Investigational Plan (PIP).

2.2. Information on the pharmaceutical formulation used in the study

The formulation of MenQuadfi (MenACYW) vaccine 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 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:

- Study MEQ00086: A descriptive, Phase IV, open-label, single-arm multi-centre study to assess the immunogenicity and safety of MenQuadfi as a booster vaccine in healthy toddlers 12 to 23 months of age who had been primed with at least 1 dose of another quadrivalent meningococcal conjugate vaccine, i.e., Nimenrix (MCV4-TT) or Menveo (MCV4-CRM), in infancy.

2.3.2. Clinical study MEQ00086

Description

Study MEQ00086 is a descriptive, Phase IV, open-label, single-arm multi-centre study to assess the immunogenicity and safety of MenQuadfi as a booster vaccine in healthy toddlers 12 to 23 months of age who had been primed with at least 1 dose of another quadrivalent meningococcal conjugate vaccine, i.e., Nimenrix (MCV4-TT) or Menveo (MCV4-CRM), in infancy.

This study was conducted at 2 study centres in Argentina.

The study was conducted between 07 September 2023 (first subject first visit) and 09 September 2024 (last subject last visit).

Methods

Study participants

Inclusion Criteria

I01: Aged 12 to 23 months on the day of inclusion.

I02: Participants who are healthy as determined by medical evaluation including medical history, physical examination, and judgment of the Investigator.

I03: Received at least one priming dose of licensed Nimenrix or Menveo vaccine during infancy before 12 months of age with an interval of at least 2 months between the last vaccination with Nimenrix or Menveo and the MenQuadfi booster dose.

I04: Informed consent form has been signed and dated by the parent(s) or other legally acceptable representative and by an independent witness, if required by local regulations.

I05: Participant and parent/legally acceptable representative(s) are able to attend all scheduled visits and to comply with all study procedures.

I06: Covered by health insurance, if required by local regulations.

Exclusion criteria

E01: Known or suspected congenital or acquired immunodeficiency; or receipt of immunosuppressive therapy, such as anti-cancer chemotherapy or radiation therapy, within the preceding 6 months; or long-term systemic corticosteroid therapy (prednisone or equivalent for more than 2 consecutive weeks within the past 3 months).

E02: History of meningococcal infection, confirmed either clinically, serologically, or microbiologically.

E03: At high risk for meningococcal infection during the study (specifically but not limited to participants with persistent complement deficiency, with anatomic or functional asplenia, or participants traveling to countries with high endemic or epidemic disease).

E04: Personal history of Guillain-Barré syndrome.

E05: Personal history of an Arthus-like reaction after vaccination with a tetanus toxoid-containing vaccine.

E06: Known systemic hypersensitivity to any of the study intervention components, or history of a life-threatening reaction to the study intervention used in the study or to a product containing any of the same substances.

E07: Laboratory-confirmed thrombocytopenia, or known suspected thrombocytopenia, as reported by the parent/legally acceptable representative, contraindicating intramuscular injection.

E08: Bleeding disorder, or receipt of anticoagulants in the 3 weeks preceding inclusion, contraindicating intramuscular injection.

E09: Chronic illness that, in the opinion of the investigator, is at a stage where it might interfere with study conduct or completion.

E10: Moderate or severe acute illness/infection (according to investigator judgment) or febrile illness (temperature ≥ 38.0°C [≥ 100.4°F]) on the day of study intervention administration. A prospective

participant should not be included in the study until the condition has resolved or the febrile event has subsided.

E11: Receipt of any vaccine (including COVID-19 vaccines) in the 4 weeks preceding the study intervention administration or planned receipt of any vaccine (including COVID-19 vaccines) in the 4 weeks following the study intervention administration except for influenza vaccination, which may be received at least 2 weeks before or 2 weeks after the study intervention. This exception includes monovalent pandemic influenza vaccines and multivalent influenza vaccines.

E12: Previous vaccination with a Meningococcal C vaccine or Meningococcal B (MenB) vaccine.

E13: Receipt of immunoglobulins, blood or blood-derived products in the past 3 months.

E14: Receipt of oral or injectable antibiotic therapy within 72 hours prior to the first blood draw.

E15: Participation at the time of study enrollment (or in the 4 weeks preceding the study intervention administration) or planned participation during the present study period in another clinical study investigating a vaccine, drug, medical device, or medical procedure.

E16: Participant is in an emergency setting, or hospitalized involuntarily.

E17: Identified as a natural or adopted child of the Investigator or employee with direct involvement in the proposed study.

Treatments

All participants were to receive a single booster dose of MenACYW conjugate vaccine at Visit 1 on Day (D) 01. MenACYW Conjugate Vaccine (MenQuadfi, manufactured by Sanofi Pasteur Inc., Swiftwater, PA, USA, was supplied as a liquid formulation (0.5 mL dose). The route of administration was intramuscular (IM).

Each dose of MenACYW conjugate vaccine contains the following components:

Meningococcal capsular polysaccharides:

• Serogroup A*: 10 μg

• Serogroup C*: 10 μg

• Serogroup Y*: 10 μg

• Serogroup W*: 10 μg

* Conjugated to tetanus toxoid protein carrier: 55 μg**

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

Batch number: VA031976

Objectives

<u>Immunogenicity objectives:</u>

1) To describe the immune response to a booster dose of MenACYW conjugate vaccine as measured by the serum bactericidal assay using human complement (hSBA) in toddlers aged

12 to 23 months, who had been primed with at least 1 dose of another MCV4 vaccine during infancy.

2) To describe the antibody responses to meningococcal serogroups A, C, W, and Y before and 1 month after a booster dose of MenACYW conjugate vaccine as measured by hSBA and serum bactericidal assay using baby rabbit complement (rSBA) in toddlers 12 to 23 months of age who had been primed with at least 1 dose of another MCV4 vaccine during infancy.

3) To describe the antibody responses to meningococcal serogroups A, C, W, and Y before and 1 month after a booster dose of MenACYW conjugate vaccine as measured by hSBA and rSBA in toddlers 12 to 23 months of age who had been primed with 2 doses of another MCV4 vaccine during infancy.

4) To describe the antibody responses to meningococcal serogroups A, C, W, and Y before and 1 month after a booster dose of MenACYW conjugate vaccine as measured by hSBA and rSBA in toddlers 12 to 23 months of age who had been primed with 1 dose of another MCV4 vaccine during infancy.

5) To describe the antibody responses to tetanus toxoid before and 1 month after a booster dose of MenACYW conjugate vaccine in toddlers 12 to 23 months of age who had been primed with at least 1 dose of another MCV4 vaccine during infancy.

Safety objectives:

To describe the safety profile of a booster dose of MenACYW conjugate vaccine administered to toddlers 12 to 23 months of age who had been primed with at least 1 dose of another MCV4 vaccine during infancy.

Outcomes/endpoints

Immunogenicity:

1) hSBA antibody titres ≥ 1:8 (seroprotection) against meningococcal serogroups A, C, W and Y at Day (D) 31 (+14 days) after booster vaccination with MenACYW conjugate vaccine.

2) At D01 (baseline) before vaccination and at D31 [+14 days] after the administration of a booster dose of MenACYW conjugate vaccine the following was to be assessed for meningococcal serogroups A, C, W and Y as measured by **hSBA**:

   - Antibody titres against meningococcal serogroups A, C, W, and Y.
   - Antibody titres ≥ 1:4 and ≥ 1:8.
   - ≥ 4-fold rise from pre-vaccination to postvaccination.
   - Vaccine seroresponse, defined as follows:
     - o For a participant with a pre-vaccination titre < 1:8, a post-vaccination titre ≥ 1:16.
     - o For a participant with a pre-vaccination titre ≥ 1:8, a post-vaccination titre at least 4-fold greater than the pre-vaccination titre.

   At D01 (baseline) before vaccination and at D31 [+14 days] after the administration of a booster dose of MenACYW conjugate vaccine the following was to be assessed for meningococcal serogroups A, C, W and Y as measured by rSBA:

- Antibody titres against meningococcal serogroups A, C, W, and Y.
- Antibody titres ≥ 1:8 and ≥ 1:128.
- ≥ 4-fold rise from pre-vaccination to postvaccination.
- Vaccine seroresponse defined as follows:
    - For a participant with a prevaccination titre < 1:8, a post-vaccination titre ≥ 1:32.
    - For a participant with a prevaccination titre ≥ 1:8, a post-vaccination titre at least 4-fold greater that the pre-vaccination titre.

3) Same endpoints as described for endpoint #2.
4) Same endpoints as described for endpoint #2.
5) Antibody concentrations against tetanus toxoid at D01 (baseline) and at D31 (+14 days) after the administration of a booster dose of MenACYW conjugate vaccine.

Safety

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

Sample size

There were no statistically powered hypotheses in this study, thus no formal sample size computation was performed. All analyses were descriptive. The target sample size was set to approximatively 180 participants (minimum of 30 evaluable participants from the lower enrolling of the 2 vaccine groups) to have at least 150 evaluable participants assuming a drop-out rate of approximatively 15%.

Randomisation and blinding (masking)

Participants were not randomised.

This was a single-arm open-label study.

Statistical Methods

All immunogenicity analyses were performed on the Per-Protocol Analysis Set (PPAS) and presented overall and by priming vaccine. Additional immunogenicity analyses were performed on the Full Analysis Set (FAS).

All analyses were descriptive; no hypotheses were tested.

In general, categorical variables were summarized and presented as frequency counts and proportions/percentages, along with 95% confidence intervals (CIs). The 95% CIs of point estimates were calculated using the normal approximation for quantitative data and the Exact binomial distribution (Clopper-Pearson method) for percentages. For geometric mean titres (GMTs), 95% CIs of point estimates were calculated using normal approximation assuming they were log-normally distributed.

For immunogenicity data, assuming that log10 transformation of the titres/concentrations followed a normal distribution, first, the mean and 95% CIs were calculated on log10 (titres/concentrations) using the usual calculation for normal distribution, then antilog transformations were applied to the results of calculations, to compute GMT/geometric mean concentrations (GMCs) and their 95% CIs.

Reverse cumulative distribution curve (RCDC) figures were provided for the antibody titres against meningococcal serogroups and the antibody concentrations against tetanus toxoid contained in MenACYW conjugate vaccine.

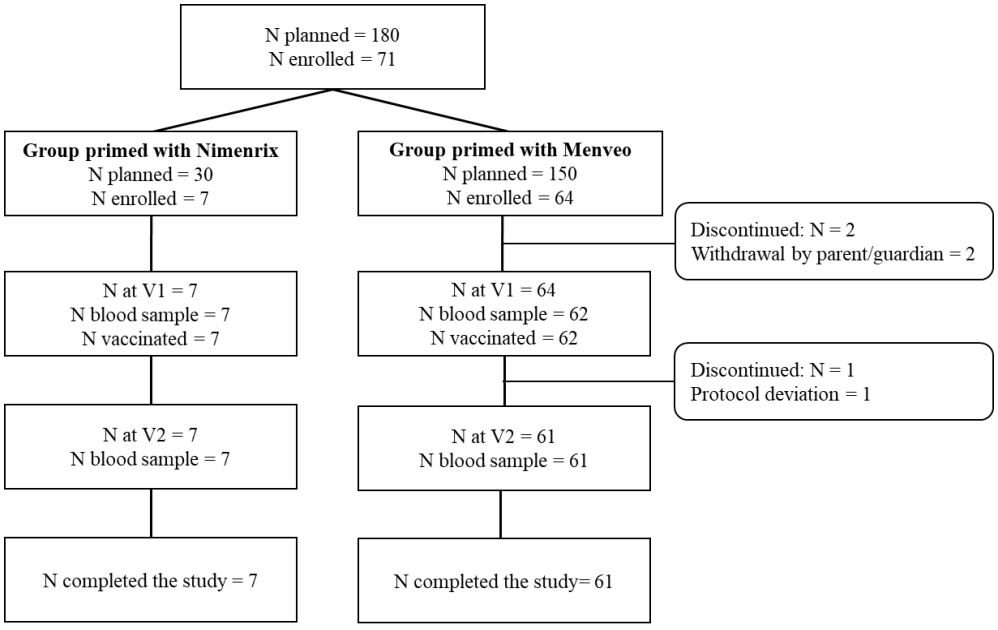
Safety analyses were performed on the Safety Analysis Set (SafAS) and presented for the entire study population receiving MenACYW conjugate vaccine. The main parameters for the safety endpoints were described by 95% CIs using the Exact binomial method (Clopper-Pearson method).

Results

Participant flow

The participant flow is depicted in the figure below.

Figure 1 - Participant Disposition Flow Chart



Abbreviation: V, visit; Source: Modified from MEQ00086 CSR Table 8.2 and Table 8.9 and Appendix 16.1 Listing 1.1, Appendix 16.3 Listing 3.1, and Appendix 16.4 Listing 4.1

Protocol deviations

A total of 13 participants (18.3%) had at least one major protocol deviation: 1 participant (14.3%) and 12 participants (18.8%) in the group previously primed with Nimenrix and in the group previously primed with Menveo, respectively. Most protocol deviations were due to "Sample (blood) handled incorrectly during collection, processing, storage or shipment" and occurred exclusively in the group previously primed with Menveo (11 participants out of 64 [17.2%]). Only 1 participant (1.4%) in the overall study population had at least 1 critical protocol deviation; this participant was in the group previously primed with Menveo. The critical deviation was that the participant received their last vaccination with Menveo less than 2 months before enrollment for the MenACYW conjugate vaccine booster dose.

Recruitment

Study MEQ00086 was conducted between 07 September 2023 (first participant first visit) and 09 September 2024 (last participant last visit).

This study was conducted at 2 centres that enrolled participants in Argentina.

Baseline data

Table 1 - Baseline Demographic – Study Participants with Data in Case Report Form (CRF)

	Primed with Nimenrix (N=7)	Primed with Menveo (N=64)	All (N=71)
Sex: n (%)			
Male	3 (42.9)	34 (53.1)	37 (52.1)
Female	4 (57.1)	30 (46.9)	34 (47.9)
Missing	0	0	0
Sex ratio: Male/Female	0.75	1.13	1.09
Age (months)			
M	7	64	71
Mean (SD)	12.9 (1.07)	14.5 (1.46)	14.3 (1.50)
Min ; Max	12.0 ; 15.0	12.0 ; 18.0	12.0 ; 18.0
Median	13.0	14.0	14.0
Q1 ; Q3	12.0 ; 13.0	13.0 ; 15.0	13.0 ; 15.0

N: number of participants with data in CRF
n: number of participants fulfilling the item listed
M: number of participants with available data for the relevant endpoint
Q1; Q3: first quartile; third quartile
SD : Standard Deviation
Percentages are based on N.
Source: Reproduced from MEQ00086 CSR table 8.13

Number analysed

A total of approximately 180 participants (with a minimum of 30 evaluable participants in a vaccine group) were expected to be enrolled with the aim to obtain a total of 150 evaluable participants.

Because of a low recruitment rate, despite mitigation efforts that included extending the enrollment period, it was decided, in agreement with the Investigator, to end recruitment for this solely descriptive study before reaching the target of 180 participants in total (and the minimum of 30 evaluable participants from the lower enrolling of the 2 vaccine groups). Therefore, the actual number of enrolled participants was 71. An overview of participants per analysis set is depicted in the table below.

Table 2 - Study MEQ000086 analysis sets

	Group previously primed with Nimenrix	Group previously primed with Menveo	Group previously primed with either Nimenrix or Menveo (Overall)
Planned	Minimum of 30	Minimum of 150	180
Actual	7	64	71
FAS	7	61	68
SafAS	7	62	69
PPAS	6	59	65

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

Immunogenicity results

Immunogenicity Objective 1: hSBA Antibody Titres ≥ 1: 8 (Seroprotection) Against Meningococcal Serogroups A, C, W and Y at D31 After Booster Vaccination with MenACYW Conjugate Vaccine

The seroprotection rates (hSBA titres ≥ 1:8) at D31 post-booster dose with MenACYW conjugate vaccine in the PPAS are presented in the table below.

Table 3 - Summary of hSBA Seroprotection Rate (≥ 1:8) 30 Days after MenACYW Conjugate Vaccine Dose Received at V01 - PPAS

		Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	**hSBA Titers**	**n/M**	**%**	**(95% CI)***	**n/M**	**%**	**(95% CI)***	**n/M**	**%**	**(95% CI)***
A	≥ 1:8	6/6	100	(54.1 ; 100)	52/52	100	(93.2 ; 100)	58/58	100	(93.8 ; 100)
C	≥ 1:8	5/5	100	(47.8 ; 100)	56/56	100	(93.6 ; 100)	61/61	100	(94.1 ; 100)
Y	≥ 1:8	5/5	100	(47.8 ; 100)	47/47	100	(92.5 ; 100)	52/52	100	(93.2 ; 100)
W	≥ 1:8	5/5	100	(47.8 ; 100)	53/53	100	(93.3 ; 100)	58/58	100	(93.8 ; 100)

N: number of participants in Per-Protocol Analysis Set;
n: number of participants experiencing the endpoint listed in the first column;
M: number of participants with available data for the relevant endpoint
percentages are based on M
*95% CI of the single proportion calculated from the exact binomial method
Source: Modified from MEQ00086 CSR Table 8.61

Immunogenicity Objective 2: Antibody Response Before and After Booster Vaccination in Toddlers Previously Primed with at Least 1 Dose

hSBA Antibody Titres ≥ 1:8

The number and percentage of participants in the PPAS with hSBA titres ≥ 1:8 before (D01) and 30 days after (D31) the booster vaccination with MenACYW conjugate vaccine are presented for serogroups A, C, Y, and W in the table below.

Table 4 - Number and Percentage of Participants with hSBA Titres ≥ 1:8 Before and 30 Days After MenACYW Conjugate Vaccine Dose – PPAS

			Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	**Timepoint**	**hSBA Titers**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
A	Pre-Dose (D01)	≥ 1:8	4/6	66.7	(22.3 ; 95.7)	40/55	72.7	(59.0 ; 83.9)	44/61	72.1	(59.2 ; 82.9)
	Post-Dose (D31)	≥ 1:8	6/6	100	(54.1 ; 100)	52/52	100	(93.2 ; 100)	58/58	100	(93.8 ; 100)
C	Pre-Dose (D01)	≥ 1:8	6/6	100	(54.1 ; 100)	32/57	56.1	(42.4 ; 69.3)	38/63	60.3	(47.2 ; 72.4)
	Post-Dose (D31)	≥ 1:8	5/5	100	(47.8 ; 100)	56/56	100	(93.6 ; 100)	61/61	100	(94.1 ; 100)
Y	Pre-Dose (D01)	≥ 1:8	6/6	100	(54.1 ; 100)	36/56	64.3	(50.4 ; 76.6)	42/62	67.7	(54.7 ; 79.1)
	Post-Dose (D31)	≥ 1:8	5/5	100	(47.8 ; 100)	47/47	100	(92.5 ; 100)	52/52	100	(93.2 ; 100)
W	Pre-Dose (D01)	≥ 1:8	6/6	100	(54.1 ; 100)	41/58	70.7	(57.3 ; 81.9)	47/64	73.4	(60.9 ; 83.7)
	Post-Dose (D31)	≥ 1:8	5/5	100	(47.8 ; 100)	53/53	100	(93.3 ; 100)	58/58	100	(93.8 ; 100)

N: number of participants in Per-Protocol Analysis Set
n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint ; percentages are based on M
Source: Modified from MEQ00086 CSR Table 8.67

Vaccine Seroresponse (based on hSBA)

The summary of hSBA vaccine seroresponse rates 30 days after post-booster dose of MenACYW conjugate vaccine in the PPAS is presented in the table below.

Table 5 - Summary of hSBA Vaccine Seroresponse 30 Days after MenACYW Conjugate Vaccine Dose Received at Visit 1 – PPAS

	Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	**n/M**	**%**	**(95% CI)***	**n/M**	**%**	**(95% CI)***	**n/M**	**%**	**(95% CI)***
A	5/6	83.3	(35.9 ; 99.6)	46/50	92.0	(80.8 ; 97.8)	51/56	91.1	(80.4 ; 97.0)
C	5/5	100	(47.8 ; 100)	54/54	100	(93.4 ; 100)	59/59	100	(93.9 ; 100)
Y	5/5	100	(47.8 ; 100)	44/46	95.7	(85.2 ; 99.5)	49/51	96.1	(86.5 ; 99.5)
W	5/5	100	(47.8 ; 100)	52/52	100	(93.2 ; 100)	57/57	100	(93.7 ; 100)

n: number of participants with titers that meet the hSBA vaccine seroresponse criteria
M: number of participants with valid serology results for the particular serogroup
N: number of participants in Per-Protocol Analysis Set; percentages are based on M
hSBA vaccine seroresponse is defined as:
For a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:16
For a participant with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer
*95% CI of the single proportion calculated using the exact binomial method
Source: Modified from MEQ00086 CSR Table 8.63

hSBA Geometric Mean Titres

The hSBA GMTs at D01 pre-booster dose and at D31 post-booster dose with MenACYW conjugate vaccine in the PPAS are presented for serogroups A, C, Y and W in the table below.

Table 6- hSBA geometric mean titres against meningococcal serogroups A, C, Y, and W before and 30 days after MenACYW conjugate vaccine dose received at V01 - Per-Protocol Analysis Set

		Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	Timepoint	M	GMT	95% CI	M	GMT	95% CI	M	GMT	95% CI
A	D01	6	28.5	(3.75 ; 216)	55	12.9	(9.36 ; 17.8)	61	14.0	(10.1 ; 19.4)
C	D01	6	64.0	(25.5 ; 161)	57	10.3	(6.90 ; 15.5)	63	12.3	(8.29 ; 18.2)
Y	D01	6	50.8	(18.8 ; 137)	56	12.2	(8.33 ; 17.8)	62	14.0	(9.70 ; 20.2)
W	D01	6	90.5	(42.2 ; 194)	58	14.2	(9.87 ; 20.4)	64	16.9	(11.8 ; 24.2)
A	D31	6	813	(558 ; 1183)	52	212	(137 ; 328)	58	244	(163 ; 366)
C	D31	5	3566	(1736 ; 7326)	56	963	(718 ; 1290)	61	1072	(805 ; 1426)
Y	D31	5	1783	(341 ; 9335)	47	884	(631 ; 1237)	52	945	(683 ; 1309)
W	D31	5	2353	(449 ; 12317)	53	875	(654 ; 1172)	58	953	(712 ; 1275)

N: number of participants in Per-Protocol Analysis Set
M: number of participants with available data for the relevant endpoint
GMT: geometric mean titers

Source: Modified from Section 8, Table 8.69, Table 8.71, Table 8.73 and Table 8.75

rSBA antibody titres ≥ 1:8 and ≥ 1:128

The number and percentage of participants with rSBA titres ≥ 1:8 and ≥ 1:128 before (D01) and after (D31) the booster vaccination with MenACYW conjugate vaccine in the PPAS are presented for serogroups A, C, Y, and W in the table below.

Table 7- Number and percentage of participants with rSBA titres >=1:8 and >=1:128 before and 30 days after MenACYW conjugate vaccine dose received at V01 - Per-Protocol Analysis Set

			Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	Timepoint	rSBA Titers	n/M	%	(95% CI)	n/M	%	(95% CI)	n/M	%	(95% CI)
A	Pre-Dose (D01)	>=1:8	3/5	60.0	(14.7 ; 94.7)	28/50	56.0	(41.3 ; 70.0)	31/55	56.4	(42.3 ; 69.7)
		>=1:128	3/5	60.0	(14.7 ; 94.7)	27/50	54.0	(39.3 ; 68.2)	30/55	54.5	(40.6 ; 68.0)
	Post-Dose (D31)	>=1:8	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
		>=1:128	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
C	Pre-Dose (D01)	>=1:8	6/6	100	(54.1 ; 100)	18/55	32.7	(20.7 ; 46.7)	24/61	39.3	(27.1 ; 52.7)
		>=1:128	4/6	66.7	(22.3 ; 95.7)	11/55	20.0	(10.4 ; 33.0)	15/61	24.6	(14.5 ; 37.3)
	Post-Dose (D31)	>=1:8	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
		>=1:128	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
Y	Pre-Dose (D01)	>=1:8	5/5	100	(47.8 ; 100)	28/54	51.9	(37.8 ; 65.7)	33/59	55.9	(42.4 ; 68.8)
		>=1:128	3/5	60.0	(14.7 ; 94.7)	23/54	42.6	(29.2 ; 56.8)	26/59	44.1	(31.2 ; 57.6)
	Post-Dose (D31)	>=1:8	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
		>=1:128	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
W	Pre-Dose (D01)	>=1:8	6/6	100	(54.1 ; 100)	33/57	57.9	(44.1 ; 70.9)	39/63	61.9	(48.8 ; 73.9)
		>=1:128	4/6	66.7	(22.3 ; 95.7)	22/57	38.6	(26.0 ; 52.4)	26/63	41.3	(29.0 ; 54.4)
	Post-Dose (D31)	>=1:8	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
		>=1:128	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)

N: number of participants in Per-Protocol Analysis Set
n: number of participants experiencing the endpoint listed in the first three columns
M: number of participants with available data for the relevant endpoint ; percentages are based on M
Study: MEQ00086 Program: T08085.sas Dataset=ADIS Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08085_i.rtf (09JUN2025 9:19)

Source: Section 8, Table 8.85

Vaccine Seroresponse (based on rSBA)

The summary of rSBA seroresponse rate at D31 post-booster dose MenACYW conjugate vaccine in the PPAS is provided in the table below.

Table 8- Summary of rSBA Vaccine Seroresponse 30 days after MenACYW conjugate vaccine dose received at V01 - Per-Protocol Analysis Set

	Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	n/M	%	(95% CI)*	n/M	%	(95% CI)*	n/M	%	(95% CI)*
A	5/5	100	(47.8 ; 100)	40/49	81.6	(68.0 ; 91.2)	45/54	83.3	(70.7 ; 92.1)
C	6/6	100	(54.1 ; 100)	53/54	98.1	(90.1 ; 100)	59/60	98.3	(91.1 ; 100)
Y	5/5	100	(47.8 ; 100)	52/53	98.1	(89.9 ; 100)	57/58	98.3	(90.8 ; 100)
W	6/6	100	(54.1 ; 100)	56/56	100	(93.6 ; 100)	62/62	100	(94.2 ; 100)

N: number of participants in Per-Protocol Analysis Set;
n: number of participants with titers that meet the rSBA vaccine seroresponse criteria
M: number of participants with valid serology results for the particular serogroup
percentages are based on M
rSBA vaccine seroresponse is defined as:
For a participant with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:32
For a participant with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be at least 4-fold greater than the pre-vaccination titer
*95% CI of the single proportion calculated using the exact binomial method
Study: MEQ00086 Program: T08081.sas Dataset=ADIS Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08081_i.rtf (09JUN2025 9:19)

Source: Section 8, Table 8.81

rSBA Geometric Mean Titres

The rSBA GMTs at D01 pre-booster dose and at D31 post-booster dose with MenACYW conjugate vaccine in the PPAS are presented for serogroups A, C, Y and W in the table below.

Table 9- rSBA geometric mean titres against meningococcal serogroups A, C, Y, and W before and 30 days after MenACYW conjugate vaccine dose received at V01 - Per-Protocol Analysis Set

		Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Serogroup	Timepoint	M	GMT	95% CI	M	GMT	95% CI	M	GMT	95% CI
A	D01	5	84.4	(1.67 ; 4278)	50	82.1	(31.3 ; 215)	55	82.3	(33.3 ; 203)
C	D01	6	181	(54.8 ; 598)	55	8.63	(4.84 ; 15.4)	61	11.6	(6.54 ; 20.7)
Y	D01	5	97.0	(26.3 ; 358)	54	27.8	(13.3 ; 58.1)	59	30.9	(15.6 ; 61.2)
W	D01	6	181	(32.9 ; 997)	57	23.0	(11.6 ; 45.6)	63	28.0	(14.7 ; 53.5)
A	D31	6	4598	(1313 ; 16094)	58	4728	(3499 ; 6388)	64	4715	(3547 ; 6268)
C	D31	6	11585	(5402 ; 24845)	58	3264	(2377 ; 4483)	64	3676	(2707 ; 4990)
Y	D31	6	5161	(3545 ; 7513)	58	5202	(3997 ; 6770)	64	5198	(4091 ; 6604)
W	D31	6	11585	(2393 ; 56077)	58	9122	(6368 ; 13067)	64	9329	(6627 ; 13132)

N: number of participants in Per-Protocol Analysis Set
M: number of participants with available data for the relevant endpoint
GMT: geometric mean titers

Source: Modified from Section 8, Table 8.87, Table 8.89, Table 8.91 and Table 8.93

Immunogenicity Objective 3: Antibody response before and after booster vaccination in toddlers primed with 2 doses

As all recruited participants were primed with 2 doses during infancy, the results were the same as those described for the objective above (at least 1 dose).

Immunogenicity Objective 4: Antibody response before and after booster vaccination in toddlers primed with 1 dose

The analysis was not performed as it was designed for participants who had received 1 priming dose, whereas all recruited participants were primed with 2 doses.

Immunogenicity Objective 5: Antibody Response to Tetanus Toxoid Before and After Booster Vaccination in Toddlers Previously Primed with at Least 1 Dose

The summary of geometric mean concentrations (GMCs) against tetanus toxoid at D0 pre-booster dose and at D31 post-booster dose with MenACYW conjugate vaccine in the PPAS is provided in the table below.

Table 10 - Summary of Geometric Means of Concentrations Against Tetanus Toxoid GMCs at D01 and 30 Days After Vaccination – PPAS

		Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Antigens	**Time Point**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**
Anti-tetanus	D01	6	1.14	(0.514 ; 2.53)	59	0.605	(0.446 ; 0.822)	65	0.642	(0.482 ; 0.854)
	D31	6	8.13	(4.83 ; 13.7)	58	8.61	(6.00 ; 12.4)	64	8.56	(6.17 ; 11.9)

M: Number of participants with available data for the endpoint and time point.
N: number of participants in Per-Protocol Analysis Set.
95% CI calculated using calculation for normal distribution on log10(titer) following by antilog transformation.
Source: Reproduced from MEQ00086 CSR Table 8.97

The number and percentages of participants in the PPAS with anti-tetanus antibody concentrations ≥ 0.01 IU/mL, ≥ 0.1 IU/mL, and ≥ 1.0 IU/mL are presented in the table below.

Table 11 - Summary of Response Rate Against Tetanus Toxoid at D01 and 30 Days After Vaccination – PPAS

			Primed with Nimenrix (N=6)			Primed with Menveo (N=59)			All (N=65)		
Antigens	**Criterion**	**Time Point**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Anti-Tetanus	≥ 0.01 IU/mL	D01	6/6	100	(54.1 ; 100)	59/59	100	(93.9 ; 100)	65/65	100	(94.5 ; 100)
		D31	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
	≥ 0.1 IU/mL	D01	6/6	100	(54.1 ; 100)	55/59	93.2	(83.5 ; 98.1)	61/65	93.8	(85.0 ; 98.3)
		D31	6/6	100	(54.1 ; 100)	58/58	100	(93.8 ; 100)	64/64	100	(94.4 ; 100)
	≥ 1.0 IU/mL	D01	3/6	50.0	(11.8 ; 88.2)	19/59	32.2	(20.6 ; 45.6)	22/65	33.8	(22.6 ; 46.6)
		D31	6/6	100	(54.1 ; 100)	54/58	93.1	(83.3 ; 98.1)	60/64	93.8	(84.8 ; 98.3)

n: number of participants with valid serology results for the particular antigen and who met the criterion.
M: Number of participants with available data for the endpoint and time point. Percentages are based on M.
N: number of participants in Per-Protocol Analysis Set
95% CI of the single proportion calculated from the exact binomial method.
Source: Modified from MEQ00086 CSR Table 8.99

Safety results

Extent of exposure

The number and percentage of participants included in the SafAS are presented by vaccine group in the table below.

Table 12 - Safety analysis set – study participants who received at least one administration

	Primed with Nimenrix (N=7) n (%)	Primed with Menveo (N=64) n (%)	All (N=71) n (%)
Safety Analysis Set	7 (100)	62 (96.9)	69 (97.2)

N: number of participants with data in CRF
n: number of participants experiencing the endpoint,
Safety Analysis Set is defined as "participants who received at least one dose of study vaccines".
Source: Modified from MEQ00086 CSR Table 8.11

Safety Summary

The safety overview post-vaccination is presented in the table below.

Table 13 - Safety overview after MenACYW conjugate vaccine dose received at V01 - SafAS

	Primed with Nimenrix (N=7)			Primed with Menveo (N=62)			All (N=69)		
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 minutes after vaccine injection									
Immediate unsolicited AE	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
Immediate unsolicited AR	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
Solicited reaction within solicited period after vaccine injection									
Solicited injection site reaction	4/7	57.1	(18.4 ; 90.1)	20/62	32.3	(20.9 ; 45.3)	24/69	34.8	(23.7 ; 47.2)
Solicited systemic reaction	3/7	42.9	(9.9 ; 81.6)	32/62	51.6	(38.6 ; 64.5)	35/69	50.7	(38.4 ; 63.0)
Within 30 days after vaccine injection									
Unsolicited AE	2/7	28.6	(3.7 ; 71.0)	21/62	33.9	(22.3 ; 47.0)	23/69	33.3	(22.4 ; 45.7)
Unsolicited AR	0/7	0	(0 ; 41.0)	2/62	3.2	(0.4 ; 11.2)	2/69	2.9	(0.4 ; 10.1)
Unsolicited non-serious AE	2/7	28.6	(3.7 ; 71.0)	21/62	33.9	(22.3 ; 47.0)	23/69	33.3	(22.4 ; 45.7)
Unsolicited non-serious AR	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)
Unsolicited non-serious injection site AE	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
Unsolicited non-serious injection site AR	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
Unsolicited non-serious systemic AE	2/7	28.6	(3.7 ; 71.0)	21/62	33.9	(22.3 ; 47.0)	23/69	33.3	(22.4 ; 45.7)
Unsolicited non-serious systemic AR	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)
AE leading to study discontinuation	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
SAE	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)
Death	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
AESI	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)
During the Study									
SAE	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)
Death	0/7	0	(0 ; 41.0)	0/62	0	(0 ; 5.8)	0/69	0	(0 ; 5.2)
AESI	0/7	0	(0 ; 41.0)	1/62	1.6	(0 ; 8.7)	1/69	1.4	(0 ; 7.8)

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
Percentages are based on M
AESI: Adverse event of special interest; AR: Reactions related to the study vaccine; SAE: Serious adverse event;
Study: MEQ00086 Program: T08018.sas Datasets=ADSL ADAE ADRC Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08018_i.rtf (09JUN2025 9:11)
Source: Section 8. Table 8.18

Solicited reactions

Solicited reactions within 7 days of vaccination are presented for overall group in the SafAS in the table below.

Table 14 - Solicited reactions within 7 days after MenACYW conjugate vaccine dose received at V01 - Safety Analysis Set

		All (N=69)	
Participants experiencing at least one:	**n/M**	**%**	**(95% CI)**
Solicited reaction	40/69	58.0	(45.5 ; 69.8)
Injection site reaction	24/69	34.8	(23.7 ; 47.2)
Injection site Tenderness	21/69	30.4	(19.9 ; 42.7)
Injection site Erythema	4/69	5.8	(1.6 ; 14.2)
Injection site Swelling	4/69	5.8	(1.6 ; 14.2)
Systemic reaction	35/69	50.7	(38.4 ; 63.0)
Fever	11/68	16.2	(8.4 ; 27.1)
Vomiting	12/69	17.4	(9.3 ; 28.4)
Crying abnormal	14/69	20.3	(11.6 ; 31.7)
Drowsiness	13/69	18.8	(10.4 ; 30.1)
Appetite lost	14/69	20.3	(11.6 ; 31.7)
Irritability	22/69	31.9	(21.2 ; 44.2)

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
Percentages are based on M.
Study: MEQ00086 Program: T08020.sas Datasets=ADSL ADRC Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08020_i.rtf (09JUN2025 9:11)

Source: Section 8. Table 8.20

Tenderness was the most frequently reported solicited injection site reaction within 7 days following vaccination (30.4% of participants), followed by erythema (5.8% of participants) and swelling (5.8% of participants).

Most solicited injection site reactions were of Grade 1 or 2 intensity, started within D01-D04, and resolved after 1-3 days. No solicited injection site reactions were ongoing at D09. A total of 2 participants (2.9%) reported at least 1 Grade 3 solicited injection site reaction within 7 days of vaccination. Grade 3 solicited injection site reactions consisted of tenderness, reported by the 2 participants, see table below.

Table 15 - Solicited injection site reactions after MenACYW conjugate vaccine dose received at V01, by maximum intensity during the solicited period - Safety Analysis Set

Participants experiencing at least one:	Maximum intensity:	n/M	All (N=69) %	(95% CI)
Injection site Tenderness	Any	21/69	30.4	(19.9 ; 42.7)
	Grade 1	15/69	21.7	(12.7 ; 33.3)
	Grade 2	4/69	5.8	(1.6 ; 14.2)
	Grade 3	2/69	2.9	(0.4 ; 10.1)
Injection site Erythema	Any	4/69	5.8	(1.6 ; 14.2)
	Grade 1	3/69	4.3	(0.9 ; 12.2)
	Grade 2	1/69	1.4	(0 ; 7.8)
	Grade 3	0/69	0	(0 ; 5.2)
Injection site Swelling	Any	4/69	5.8	(1.6 ; 14.2)
	Grade 1	4/69	5.8	(1.6 ; 14.2)
	Grade 2	0/69	0	(0 ; 5.2)
	Grade 3	0/69	0	(0 ; 5.2)

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first two columns
M: number of participants with available data for the relevant endpoint;
Percentages are based on M
Study: MEQ00086 Program: T08022.sas Datasets=ADSL ADRC Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08022_i.rtf (09JUN2025 9:12)

Source: Section 8. Table 8.22

Irritability was the most frequently reported solicited systemic reaction within 7 days following vaccination (31.9% of participants), followed by crying abnormal (20.3% of participants), appetite lost (20.3% of participants), drowsiness (18.8% of participants), vomiting (17.4% of participants), and fever (16.2% of participants)).

Most systemic reactions were of Grade 1 or Grade 2 intensity, started within D01-D04, and resolved after 1-3 days. A total of 5 participants (7.2%) experienced at least 1 Grade 3 solicited systemic reaction within 7 days of vaccination. Grade 3 solicited systemic reactions consisted predominantly of vomiting (2.9%) followed by crying abnormally (1.4%), drowsiness (1.4%), and irritability (1.4%), see table below.

Table 16 - Solicited systemic reactions after MenACYW conjugate vaccine dose received at V01, by maximum intensity during the solicited period - Safety Analysis Set

Participants experiencing at least one:	Maximum intensity:	n/M	All (N=69) %	(95% CI)
Fever	Any	11/68	16.2	(8.4 ; 27.1)
	Grade 1	7/68	10.3	(4.2 ; 20.1)
	Grade 2	4/68	5.9	(1.6 ; 14.4)
	Grade 3	0/68	0	(0 ; 5.3)
Vomiting	Any	12/69	17.4	(9.3 ; 28.4)
	Grade 1	6/69	8.7	(3.3 ; 18.0)
	Grade 2	4/69	5.8	(1.6 ; 14.2)
	Grade 3	2/69	2.9	(0.4 ; 10.1)
Crying abnormal	Any	14/69	20.3	(11.6 ; 31.7)
	Grade 1	10/69	14.5	(7.2 ; 25.0)
	Grade 2	3/69	4.3	(0.9 ; 12.2)
	Grade 3	1/69	1.4	(0 ; 7.8)
Drowsiness	Any	13/69	18.8	(10.4 ; 30.1)
	Grade 1	10/69	14.5	(7.2 ; 25.0)
	Grade 2	2/69	2.9	(0.4 ; 10.1)
	Grade 3	1/69	1.4	(0 ; 7.8)
Appetite lost	Any	14/69	20.3	(11.6 ; 31.7)
	Grade 1	10/69	14.5	(7.2 ; 25.0)
	Grade 2	4/69	5.8	(1.6 ; 14.2)
	Grade 3	0/69	0	(0 ; 5.2)
Irritability	Any	22/69	31.9	(21.2 ; 44.2)
	Grade 1	13/69	18.8	(10.4 ; 30.1)
	Grade 2	8/69	11.6	(5.1 ; 21.6)
	Grade 3	1/69	1.4	(0 ; 7.8)

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first two columns
M: number of participants with available data for the relevant endpoint;
Percentages are based on M
Study: MEQ00086 Program: T08027.sas Datasets=ADSL ADRC Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08027_i.rtf (09JUN2025 9:12)
Source: Section 8, Table 8.27

Unsolicited AEs

The summary of unsolicited AEs within 30 days after vaccination in the SafAS is provided in the table below.

Table 17 - Summary of unsolicited AEs within 30 days after MenACYW conjugate vaccine dose received at V01 - Safety Analysis Set

	Primed with Nimenrix (N=7)				Primed with Menveo (N=62)				All (N=69)			
Participants experiencing at least one:	n	%	(95% CI)	n AEs	n	%	(95% CI)	n AEs	n	%	(95% CI)	n AEs
Immediate unsolicited AE	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Grade 3 immediate unsolicited AE	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Immediate unsolicited AR	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Grade 3 immediate unsolicited AR	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Unsolicited AE	2	28.6	(3.7 ; 71.0)	4	21	33.9	(22.3 ; 47.0)	27	23	33.3	(22.4 ; 45.7)	31
Grade 3 unsolicited AE	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
Unsolicited AR	0	0	(0 ; 41.0)	0	2	3.2	(0.4 ; 11.2)	2	2	2.9	(0.4 ; 10.1)	2
Grade 3 unsolicited AR	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
Unsolicited injection site AR	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Grade 3 unsolicited injection site AR	0	0	(0 ; 41.0)	0	0	0	(0 ; 5.8)	0	0	0	(0 ; 5.2)	0
Unsolicited systemic AE	2	28.6	(3.7 ; 71.0)	4	21	33.9	(22.3 ; 47.0)	27	23	33.3	(22.4 ; 45.7)	31
Grade 3 unsolicited systemic AE	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
Unsolicited systemic AR	0	0	(0 ; 41.0)	0	2	3.2	(0.4 ; 11.2)	2	2	2.9	(0.4 ; 10.1)	2
Grade 3 unsolicited systemic AR	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
SAE	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
Grade 3 SAE	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
AESI	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1
Grade 3 AESI	0	0	(0 ; 41.0)	0	1	1.6	(0 ; 8.7)	1	1	1.4	(0 ; 7.8)	1

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first column
Percentages are based on N
n AEs: number of AEs
AR: Reactions related to the study vaccine
'Immediate unsolicited AE' is collected only for immediate unsolicited systemic AE.
'Unsolicited AE' also includes immediate and serious unsolicited AEs.
Study: MEQ00086 Program: T08031.sas Datasets=ADSL ADAE Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08031_x.pdf (09JUN2025 9:13)

No immediate unsolicited AEs were reported within 30 minutes of vaccination.

There were 33.3% of participants who experienced at least 1 unsolicited AE within 30 days of vaccination.

Most unsolicited AEs were of grade 1 intensity, started during D05-D08 and ≥ D16 and resolved after 1-3 days. One Grade 3 unsolicited AE (febrile convulsion) was reported in 1 participant (1.4%) and was assessed as related to the vaccine by the Investigator and unrelated by the Sponsor.

Unsolicited ARs

The frequency of participants experiencing at least 1 unsolicited AR within 30 days of vaccination is presented per system organ class (SOC) and preferred term (PT) in the SafAS in the table below.

Table 18 - Unsolicited AEs within 30 days after MenACYW conjugate vaccine dose received at V01, by system organ class and preferred term - Safety Analysis Set

	All (N=69)			
Participants experiencing at least one:	n	%	(95% CI)	n AEs
Unsolicited AE	23	33.3	(22.4 ; 45.7)	31
Gastrointestinal disorders	7	10.1	(4.2 ; 19.8)	8
Diarrhoea	5	7.2	(2.4 ; 16.1)	5
Teething	2	2.9	(0.4 ; 10.1)	2
Vomiting	1	1.4	(0 ; 7.8)	1
General disorders and administration site conditions	4	5.8	(1.6 ; 14.2)	4
Pyrexia	4	5.8	(1.6 ; 14.2)	4
Infections and infestations	11	15.9	(8.2 ; 26.7)	12
Bronchitis	1	1.4	(0 ; 7.8)	1
Gastroenteritis	1	1.4	(0 ; 7.8)	1
Hand-foot-and-mouth disease	1	1.4	(0 ; 7.8)	1
Laryngitis	1	1.4	(0 ; 7.8)	1
Nasopharyngitis	4	5.8	(1.6 ; 14.2)	4
Otitis media acute	2	2.9	(0.4 ; 10.1)	2
Pharyngitis	1	1.4	(0 ; 7.8)	1
Tuberculosis	1	1.4	(0 ; 7.8)	1
Nervous system disorders	1	1.4	(0 ; 7.8)	1
Febrile convulsion	1	1.4	(0 ; 7.8)	1
Respiratory, thoracic and mediastinal disorders	4	5.8	(1.6 ; 14.2)	4
Catarrh	2	2.9	(0.4 ; 10.1)	2
Rhinorrhoea	2	2.9	(0.4 ; 10.1)	2
Skin and subcutaneous tissue disorders	1	1.4	(0 ; 7.8)	2
Papule	1	1.4	(0 ; 7.8)	2

N: number of participants in Safety Analysis Set
n: number of participants experiencing the endpoint listed in the first column
n AEs: number of AEs
Percentages are based on N
MedDRA Version: 28.0.
Study: MEQ00086 Program: t08034to08039.sas Datasets=ADSL ADAE Output: PRODOPS/PLC16012/MEQ00086/CSR_01/REPORT/OUTPUT/T08034_x.pdf (09JUN2025 9:13)

The unsolicited ARs were of Grade 1 (1.4% of participants) or Grade 3 (1.4% of participants) intensity. Most unsolicited ARs started during D01-D08 and resolved after 1-3 days.

There were no unsolicited ARs that occurred at the injection site within 30 days of vaccination.

At least 1 unsolicited systemic AR was reported in 2.9% of participants within 30 days of vaccination.

Serious Adverse Events Including Deaths

There was 1 participant who experienced 1 SAE within 30 days of vaccination. This participant was in the group previously primed with Menveo and experienced febrile convulsion. This SAE was assessed as related to the vaccine by the Investigator due to temporal association but was assessed as not related by the Sponsor as the participant had a confirmed parainfluenza virus 3 infection. This SAE was also an AESI.

No deaths were reported during the study.

Adverse Events of Special Interest

There was 1 participant who experienced 1 AESI (also considered as an SAE) within 30 days of vaccination. See section above for details.

2.3.3. Discussion on clinical aspects

MenQuadfi has been approved in the EU on 18 November 2020 (EMEA/H/C/005084/0000) and is indicated for the active immunization of individuals from the age of 12 months and older against invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, W, and Y. A variation to extend the indication to include individuals from 6 weeks of age and older in the EU was submitted to EMA on 25 June 2025, with the procedure currently ongoing.

Study MEQ00086 was a descriptive, Phase IV, open-label, single-arm multi-centre study to assess the immunogenicity and safety of MenQuadfi as a booster vaccine in healthy toddlers 12 to 23 months of age who had been primed with at least 1 dose of another quadrivalent meningococcal conjugate vaccine, ie, Nimenrix (MCV4-TT) or Menveo (MCV4-CRM), in infancy. The study was conducted at two study centres in Argentina. It is critically noted that no hypotheses testing was planned for the study and it was an open-label, single arm study, which limits the conclusions that can be drawn from the study. However, as results of this study are not used to inform the SmPC, no further issue is made in this regard.

Study design and methods

The study inclusion and exclusion criteria intended to recruit a population of healthy toddlers aged 12 to 23 months who received at least one dose of Nimenrix or Menveo vaccine during infancy before 12 months of age. The interval between the last dose of Nimenrix or Menveo and the MenQuadfi booster had to be at least 2 months. Subjects with a history of meningococcal infection were excluded from the study. The inclusion and exclusion criteria are considered adequate for the intended purpose.

On day 1, all study participants received one dose of MenACYW conjugate vaccine, which was administered intramuscularly. The route of administration is in line with the recommendations in the MenQuadfi SmPC and therefore appropriate. There was no comparator vaccine administered, which hampers the interpretation of the study results.

The study investigated the immune response after a booster dose of MenACYW conjugate vaccine. The immunogenicity objectives included the evaluation of immune response by hSBA and rSBA, which is regarded acceptable. The immunogenicity endpoints included the investigation of antibody titres, seroprotection rate and seroresponse rate against meningococcal serogroups A, C, W, and Y. Additionally, the antibody concentrations against tetanus toxoid were investigated. These endpoints are considered appropriate for describing the immune response of a booster dose of MenACYW conjugate vaccine. The safety endpoints are also considered acceptable.

Study conduct

The Applicant provided a comprehensive participant flow. Of the planned 180 subjects, only 71 subjects were recruited due to low recruitment rate. From the 71 subjects, 7 participants have been primed with Nimenrix and 64 participants have been primed with Menveo. In the Nimenrix primed group, all subjects completed the study. In the Menveo primed group, 3 participants discontinued the study. Two participants discontinued due to withdrawals by parent/guardian and 1 discontinuation was due to a protocol deviation, as the participant had received their last vaccination with Menveo less than 2 months before enrolment. It is not regarded optimal that the recruitment had been stopped before reaching the planned enrolment target, as the low number of participants further reduce the interpretability of the study results. Nevertheless, it is regarded acceptable, as it was solely a descriptive study and results are not used to inform the SmPC.

Three participants were excluded from the FAS (2 withdrawals and 1 protocol deviation). Six participants were excluded from the PPAS due to protocol deviations, with the most common protocol deviation being "post-dose serology sample was not drawn" and "not receiving study vaccination". All participants receiving the study vaccine were included in the SafAS. The numbers analysed by analysis set are comprehensible.

Overall, there were 52.1% male and 47.9% female participants in the study. The mean age in the study was 14.3 months. The comparison of baseline characteristics between groups is hampered by the low number of subjects (especially in the Nimenrix primed group with N=7), but male/female ratio and age is grossly comparable between the groups. Race and ethnicity were not collected which is regarded acceptable for this descriptive study. The baseline characteristics were also presented by analysis set (FAS, PPAS, SafAS) and were similar across these analysis sets.

Immunogenicity results

In both groups, the seroprotection rates (defined as hSBA titres ≥ 1:8) for serogroups A, C, Y, and W at D31 post-booster dose with the MenACYW conjugate vaccine were 100%. At day1, the percentages of participants with hSBA titres ≥ 1:8 was higher for Nimenrix primed participants compared to Menveo primed participants for most serogroups. At day 31, the percentages of participants with hSBA titres ≥ 1:8 were 100% for all serogroups, independent of prime vaccine. The hSBA vaccine seroresponse rate (defined as post-vaccination titre ≥ 1:16 for a participant with a pre-vaccination titre < 1:8 or a post-vaccination titre at least 4-fold greater than the pre-vaccination titre for a participant with a pre-vaccination titre ≥ 1:8) 30 days after vaccination was high (at least 80%) in both groups and for all serogroups. The hSBA GMTs increased from D01 pre-booster dose to D31 post-booster dose for all serogroups. The GMTs were generally higher in the Nimenrix primed group compared to the Menveo primed group (both on day 1 and day 31). The booster dose with MenACYW conjugate vaccine induced a strong increase in hSBA GMTs against all serogroups irrespective of previous vaccine received. For all these endpoints, similar results were observed for analyses based on the PPAS and FAS set, which is reassuring.

Similar results as described above for the hSBA assay were observed when performing analyses based on the rSBA assay. At day1, the percentages of participants with rSBA titres ≥ 1:8 or ≥ 1:128 was higher for Nimenrix primed participants compared to Menveo primed participants for most serogroups. At day 31, the percentages of participants with rSBA titres ≥ 1:8 or ≥ 1:128 were 100% for all serogroups, independent of prime vaccine. The rSBA vaccine seroresponse rate (defined as post-vaccination titre ≥ 1:32 for a participant with a pre-vaccination titre < 1:8 or a post-vaccination titre at least 4-fold greater than the pre-vaccination titre for a participant with a pre-vaccination titre ≥ 1:8) 30 days after vaccination was high (at least 80%) in both groups and for all serogroups. The rSBA GMTs increased from D01 pre-booster dose to D31 post-booster dose for all serogroups. The booster dose with MenACYW conjugate vaccine induced a strong increase in rSBA GMTs against all serogroups irrespective of previous vaccine received. Again, similar results were observed for analyses based on the PPAS and FAS set, which is reassuring.

As all recruited participants had received two priming doses during infancy, the results for the immunogenicity objective 3 (2 priming doses) were the same as those for the immunogenicity objective 2 (at least 1 priming dose). Additionally, for the same reason, the immunogenicity objective 4 investigating the antibody response in subjects primed with 1 dose could not be performed.

The GMCs against tetanus toxoid increased from D01 to D31 both for the previously primed Nimenrix and previously primed Menveo group. A similar increase was observed for both groups. Additionally,

the response rate against tetanus vaccine at day 31 was high (at least 90%) for both groups and for all applied criteria (≥ 0.01 IU/mL, ≥ 0.1 IU/mL and ≥ 1.0 IU/mL).

Thus, overall, the immunogenicity results suggest that a booster dose of MenQuadfi vaccine is able to induce an immune response against meningococcal serogroups A, C, W and Y thirty days after administration in toddlers 12 to 23 months of age irrespective of previous vaccine received (Nimenrix or Menveo). It is agreed to the Applicant that based on the limited results of study MEQ00086, no update of the SmPC is regarded necessary.

Safety results

The safety analysis set included 7 participants in the group primed with Nimenrix and 62 participants in the group primed with Menveo. Within 30 minutes after booster dose, there were no immediate unsolicited AEs reported. The percentage of participants experiencing a solicited injection site reaction within 7 days was 34.8%, with the most frequent solicited injection site reaction being tenderness followed by erythema and swelling. The percentage of participants with a solicited systemic reaction within 7 days was 50.7%, with the most frequent solicited systemic reaction being irritability followed by crying abnormal and appetite lost. The proportion of subjects with an unsolicited AE within 30 days after vaccination was 33.3%. All of the unsolicited AE were systemic and most of them resolved within 1-3 days. Two participants experienced an unsolicited AR within 30 days, with one being of Grade 1 (diarrhoea) and one being of Grade 3 intensity (febrile convulsion, further discussed below). The most frequent unsolicited AEs were reported in the SOC "Infections and infestations", followed by "Gastrointestinal disorders" and "General disorders and administration site conditions".

None of the AE led to study discontinuation within 30 days after vaccination and there were no deaths during the study. One of the participants experienced an AESI, which was also considered an SAE. The participant experienced febrile convulsion six days after vaccination, which led to hospitalization. Diagnostic and laboratory tests were normal. The next day, the subject was discharged from the hospital. Two days later, a nasal swab was performed at the study centre which positive for parainfluenza 3 virus. Due to its temporal relatedness, the febrile seizure was considered to be related to the study vaccine by the investigator. The Sponsor considers the febrile seizure to be unrelated, as the participant had a confirmed parainfluenza virus 3 infection. For a definite decision whether the febrile convulsion could be considered as related or unrelated, more information might be necessary. However, as section 4.8 of the MenQuadfi SmPC already lists febrile convulsion as an adverse reaction following administration of MenQuadfi in subjects 12 months through 23 months, no further issue is made.

Overall, the observed safety profile is comparable to what has been described for subjects 12 to 24 months of age in the MenQuadfi SmPC. No new safety signals came up during the study. Therefore, it is agreed that based on the results of study MEQ00086 there is no need to update section 4.8 of the MenQuadfi SmPC.

3. CHMP's overall conclusion and recommendation

In study MEQ00086 it was demonstrated that a booster dose of MenQuadfi vaccine is able to induce an immune response against meningococcal serogroups A, C, W and Y thirty days after administration in toddlers 12 to 23 months of age irrespective of previous vaccine received (Nimenrix or Menveo). The observed safety profile is comparable to what has been described for subjects 12 to 24 months of age in the MenQuadfi SmPC. No new safety signals came up during the study.

There were several limitations in the study design. These limitations hamper a proper interpretation of the study results. It is agreed to the Applicant that based on the results of this study, no update to the SmPC is regarded necessary.

The B/R of MenQuadfi remains positive.

Fulfilled:

No regulatory action required.