25 June 2026
EMADOC-1700519818-3316805
Human Medicines Division

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

Menveo

meningococcal group a, c, w135 and y conjugate vaccine

Procedure no: EMA/PAM/0000339692

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 date	27 April 2026	27 April 2026
☐	CHMP Rapporteur AR	1 June 2026	1 June 2026
☐	CHMP comments	15 June 2026	15 June 2026
☐	Updated CHMP Rapporteur AR	18 June 2026	18 June 2026
☒	CHMP outcome	25 June 2026	25 June 2026

Table of contents

1. Introduction

On 30 March 2026, the MAH submitted a completed paediatric study for Menveo, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

The present submission includes the Clinical Study Report for study 212149 conducted with EU licensed products to assess the safety, reactogenicity, and immune responses to GVGH altSonflex1-2-3 vaccine against *Shigella sonnei* and *Shigella flexneri*, serotypes 1b, 2a, and 3a, when administered to healthy adults, children and infants (Phase II). Menveo was administered in the study as an active control vaccine along with other control vaccines such as Typhim Vi and Infanrix hexa, since it could provide potential benefit to study participants randomised to the control groups.

Study 212149 was not conducted in accordance with an agreed paediatric investigation plan for Menveo.

A short critical expert overview has also been provided.

The current indication for Menveo in EU is:

Menveo (MenACWY vaccine) is indicated for active immunisation of children (from 2 years of age), adolescents and adults at risk of exposure to *Neisseria meningitidis* groups A, C, W-135 and Y, to prevent invasive disease.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that "A staged Phase 1/2 observer-blind, randomised, controlled, multi-country study to evaluate the safety, reactogenicity, and immune responses to the GVGH altSonflex1-2-3 vaccine against S. sonnei and S. flexneri, serotypes 1b, 2a, and 3a, in adults in Europe (Stage 1) followed by age de-escalation from adults to children and infants, and dose-finding in infants in Africa (Stage 2). (study number: 212149, EudraCT number: 2021-000891-12)" is a stand alone study.

2.2. Information on the pharmaceutical formulation used in the study

Study interventions administered in the study are AltSonflex1-2-3 in 3 doses (3.75, 7.5 or 15 µg of OAg of each component), altSonflex placebo (Al(OH03 suspended in buffered saline), Menveo, Boostrix, Infanrix Hexa, Typhim VI and MR-Vac. All the interventions were administered via intramuscular injection except for MR-vac which was administered subcutaneous.

Information is provided regarding Menveo only.

- Adults: 1 dose of 0.5 mL of Menveo was administered IM.
- Children: 1 dose of 0.5 mL of Menveo was administered IM.
- Infants: 2 doses of 0.5 mL of Menveo was administered IM.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report(s) for study 212149: A staged Phase 1/2 observer-blind, randomised, controlled, multi-country study to evaluate the safety, reactogenicity, and immune responses to the GVGH altSonflex1-2-3 vaccine against *S. sonnei* and *S. flexneri*, serotypes 1b, 2a, and 3a, in adults in Europe (Stage 1) followed by age de-escalation from adults to children and infants, and dose-finding in infants in Africa (Stage 2).

Menveo (Meningococcal MenACWY Conjugate Vaccine, also referred to as MenACWY) is a quadrivalent meningococcal serogroups A, C, W-135 and Y oligosaccharide vaccine, conjugated to Corynebacterium diphtheriae cross-reacting material 197 carrier protein (a nontoxic mutant of diphtheria toxin).

Menveo was registered in the European Union (EU) through the centralised procedure on 15 March 2010 for use in adolescents and adults 11 years of age and older. The age indication was extended to children (2 to 10 years of age) in April 2012. The vaccine is approved in 58 countries including the EU, the United States (US), and the United Kingdom (UK) and it is pre-qualified by the World Health Organization.

In study 212149, Menveo was administered as an active control vaccine along with the other control vaccines such as Typhim Vi and Infanrix hexa, since it could provide potential benefit to study participants randomised to the control groups. MR-VAC was also administered as part of the National Immunisation Program (NIP). Menveo, being an active control vaccine, was not a part of the study objectives, therefore its immunogenicity was not analysed. Safety events were evaluated for both the study vaccine and the active control vaccines.

2.3.2. Clinical study

Study 212149: A staged Phase 1/2 observer-blind, randomised, controlled, multi-country study to evaluate the safety, reactogenicity, and immune responses to the GVGH altSonflex1-2-3 vaccine against S. sonnei and S. flexneri, serotypes 1b, 2a, and 3a, in adults in Europe (Stage 1) followed by age de-escalation from adults to children and infants, and dose-finding in infants in Africa (Stage 2)

Description

This was a Phase 1/2 observer-blind, controlled, self-contained, randomised, multi-country, staged, age-de-escalation study. It evaluated the safety and immunogenicity of the altSonflex1-2-3 GMMA candidate vaccine against *S. sonnei* and *S. flexneri* serotypes 1b, 2a, and 3a. The study was conducted at 2 sites in 2 different countries: Belgium (Stage 1: Adults 18 to 50 years of age Safety Cohort) and Kenya (Stage 2: Adults 18 to 50 years of age, Children 24 to 59 months of age, Infants 9 months of age Safety cohort, and Infants 9 months of age Dose-finding cohort). The candidate altSonflex1-2-3 vaccine was administered intramuscularly at 3 different doses (Dose A [low], Dose B [medium], and Dose C [high]).

The overall study design and pre-defined safety data review timepoints are presented in Figure 1.

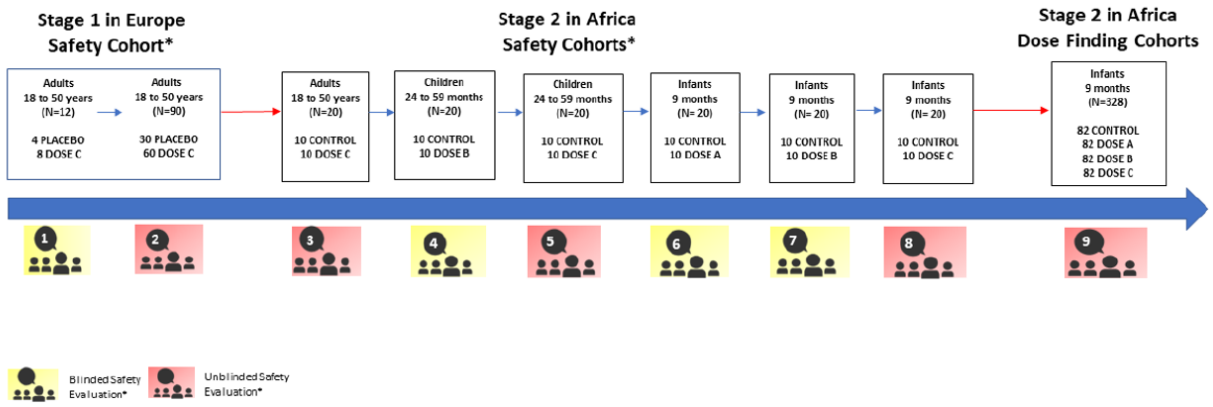


Figure 1: Study design overview

In Stage 1 of the study, participants were randomised 2:1 to receive either 2 injections of the altSonflex1-2-3 vaccine or a placebo. The study interventions were administered either with a 3-month or a 6-month interval, see Figure 2.

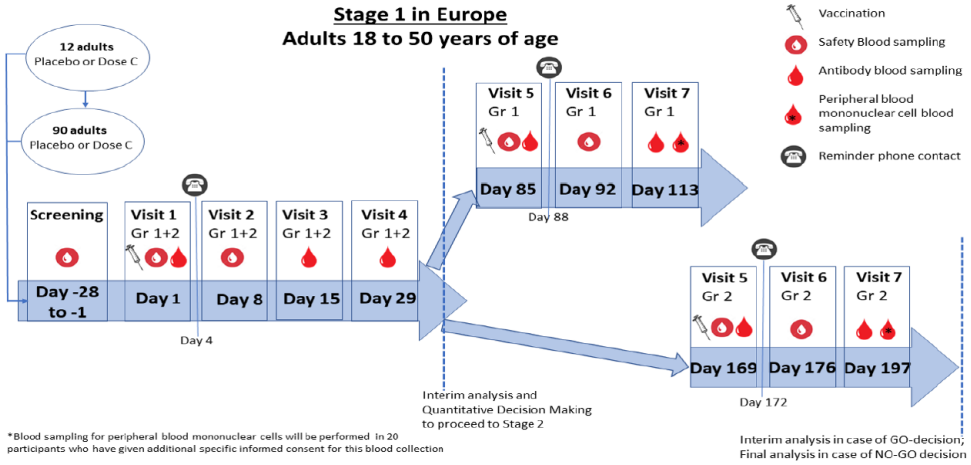


Figure 2: Stage 1 in Europe study design

In Stage 2, 20 adults received 2 vaccinations of either Dose C (dose previously administered to adults in Europe in Stage 1) of altSonflex1-2-3 or a control vaccine (1:1 randomisation ratio); 2 groups of 20 children received 2 vaccinations of either Dose B or C of altSonflex1-2- 3 or a control vaccine (1:1 randomisation ratio); 3 groups of 20 infants received 3 primary vaccinations of either Dose A, B or C of altSonflex1-2-3 or a control vaccine (1:1 randomisation ratio). Infants also received an expanded program on immunisation (EPI) vaccination with measles and rubella vaccine (MR-VAC) at 28 days after first vaccination and at 28 days after the third vaccination. See Figure 3.

In the dose-finding step of the study, a total of 328 infants were vaccinated with either Dose A, Dose B, or Dose C of the altSonflex1-2-3 candidate vaccine, or with a control vaccine (1:1:1:1 randomisation ratio). The vaccination schedule was the same as in the infant safety cohort. However, in this cohort, the EPI vaccination with MR-VAC was given concomitantly with the first vaccination and with the third vaccination. See Figure 3.

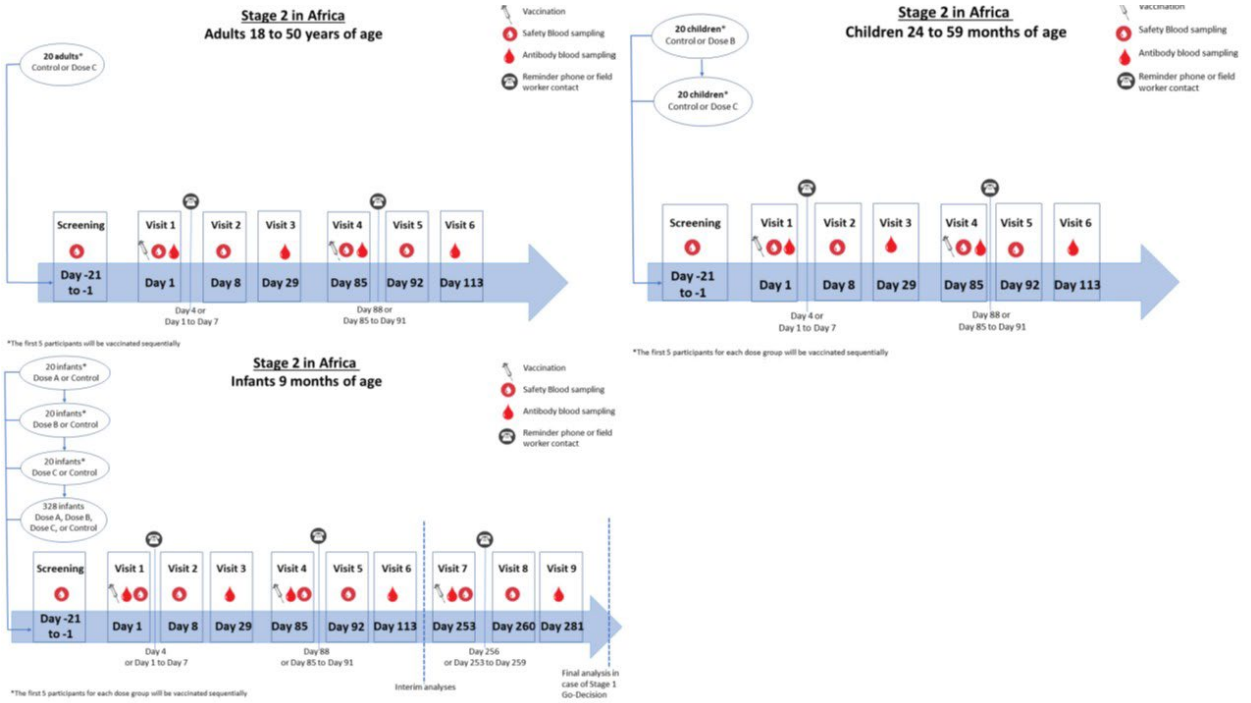


Figure 3: Stage 2 in Africa study design

Assessor´s comment:

Menveo was used as an active control vaccine in Stage 2, to provide benefit for the participants included in the placebo arm. The current report will only focus on this part.

No immunogenicity data was collected for Menveo. As only safety data was collected in a limited population, limited new information can be expected from this study for the already authorised vaccine Menveo.

Methods

Assessor´s comment:

For ease of reference, methods relevant to the assessment of the information regarding Menveo will be included in the current report. No comments on total study design will be provided as assessment of the investigational drug is outside the scope of this report. Comments will only be provided when relevant to the assessment of Menveo.

Study participants

Inclusion Criteria: The study enrolled male or female healthy participants who are seronegative for HIV. For adults, age at time of vaccination should be between, and including, 18 and 50 years at time of the first study intervention. Child participants should be between, and including, 24 and 59 months of age at time of first vaccination. Infant participants should be 9 months of age at time of first vaccination. In addition, child and infant participants should have normal nutritional Z score (-2SD or greater), previously completed routine childhood vaccinations and born after gestation period of ≥37 weeks.

Exclusion Criteria: The main exclusion criteria included known exposure to *Shigella* during the lifetime of the participant or prior receipt of an experimental *Shigella* vaccine or live *Shigella* challenge. Pregnant or lactating female participants or female participants planning to become pregnant or planning to discontinue contraceptive precautions were also excluded from the study.

Assessor´s comment:

Of note, in the EU Menveo is indicated for use in children from 2 years of age, adolescents and adults. In several non-European countries the indication does cover individuals as young as 2 months of age.

Treatments

In Stage 2 of the study, the Control groups received the following vaccines:

- Adults 18 to 50 years of age: a single dose of 0.5 mL Menveo vaccine intramuscularly (IM) administered on Day 1 and Boostrix on Day 85.
- Children 24 to 59 months of age: a single dose of 0.5 mL Menveo vaccine IM administered on Day 1 and Typhim Vi on Day 85.
- Infants 9 months of age Safety cohort: 2 doses of 0.5 mL Menveo vaccine via IM on Day 1 and Day 85, single dose of Infanrix hexa via IM on Day 253, and 2 doses of MR-VAC subcutaneously (SC) on Day 29 and Day 281.
- Infants 9 months of age Dose-finding cohort: 2 doses of 0.5 mL Menveo vaccine IM on Day 1 and Day 85, single dose of Infanrix hexa IM on Day 253, and 2 doses of MR-VAC SC on Day 1 and Day 253.

Assessor´s comment:

Administration of Menveo is in line with the posology included in the SmPC for adults and children 24 to 59 months. No posology is included in the EU SmPC for infants 9 months of age as this is outside of the approved indication in the EU.

Objective(s)

There were no study objectives directly related to Menveo. Only the safety data obtained related to Menveo are reported in this document.

Outcomes/endpoints

The data on solicited events (up to 7 days post vaccination) and unsolicited adverse events (AEs) (up to 28 days post vaccination) are presented following a single vaccine administration (Day 1) in adults (18-50 years of age) and children (24 to 59 months of age) and following 2 doses (Day 1 and Day 85) in infants (9 months of age). All solicited and unsolicited events of Grade 1 or above were considered for reporting. The solicited administration-site events, collected in the study as per protocol, were erythema, pain, and swelling. The solicited systemic event collected in the study as per protocol was fever (defined as temperature ≥38.0°C) which was assessed for relatedness by the investigator. Serious adverse event (SAE) data were collected throughout the study period in all groups.

Assessor´s comment:

Safety assessments seem appropriate, although the list of solicited systemic events, i.e. only fever, is considered limited.

Sample size

The sample size calculation is not relevant to the assessment of Menveo.

Randomisation and blinding (masking)

Allocation of the participant to a study group at the investigator site will be performed using a randomisation system on internet.

The randomisation algorithm will use a stratification procedure accounting for Stage (Stage 1 or Stage 2), age (adults, children, or infants), and cohort (safety or dose-finding) and a minimisation procedure accounting for study. Minimisation factors will have equal weight in the minimisation algorithm.

Data will be collected in an observer-blind manner. To do so, study interventions will be prepared and administered by qualified unblinded staff who will not participate in data collection, evaluation, review, or the entry of any study endpoint (i.e., reactogenicity, safety, efficacy).

Statistical Methods

Not relevant for the current submission.

Results

Assessor´s comment:

Assessment will only focus on Stage 2, during which Menveo was administered as an active control vaccine.

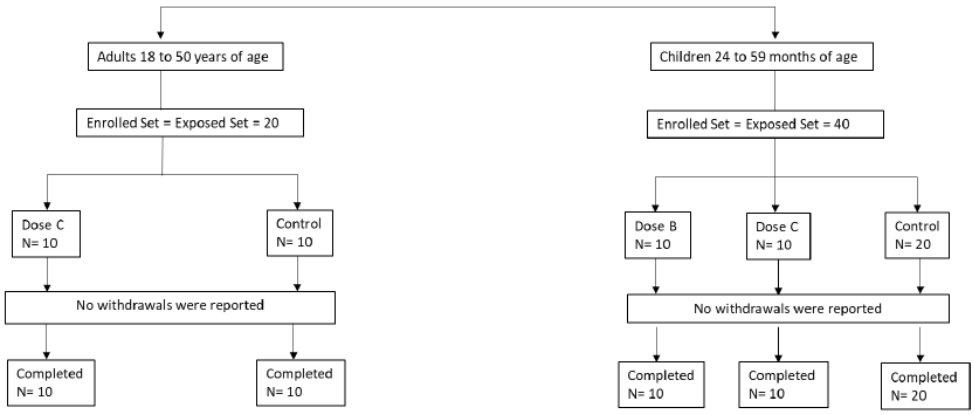
Participant flow

Adults 18 to 50 years of age

A total of 20 participants were enrolled and received the study intervention. There were no withdrawals/discontinuations reported, and all the 20 participants completed the study.

Children 24 to 59 months of age

A total of 40 participants were enrolled and received the study intervention. There were no withdrawals/discontinuations reported, and all the 40 participants completed the study.



Source: Tables 14.1.1.1b, 14.1.1.1c, 14.1.2.1b, and 14.1.2.1c

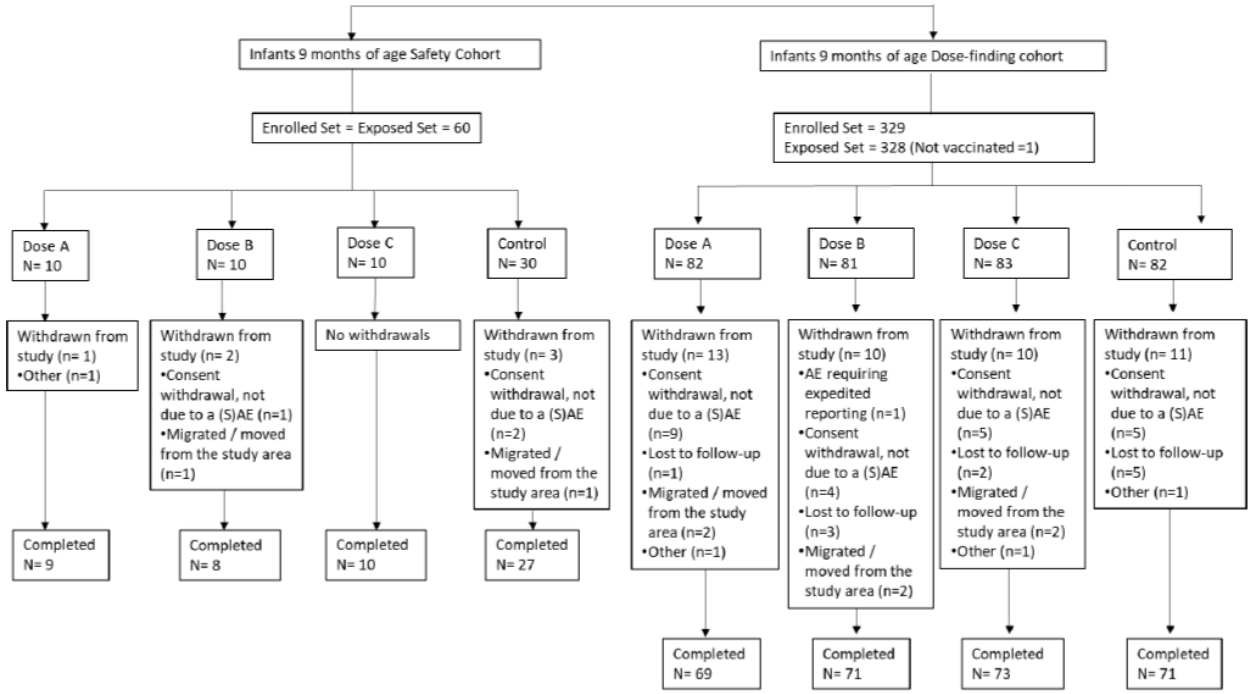
Figure 4: Disposition of Participants - Africa Stage 2: Adults 18 to 50 years of age and Children 24 to 59 months of age

Infants 9 months of age in Africa, safety cohort

A total of 60 participants were enrolled and received the study intervention. Of the total participants, 54 participants completed the study, while 6 participants withdrew from the study (Figure 5).

Infants 9 months of age in Africa, dose-finding cohort

A total of 329 participants were enrolled in the study. A total of 328 participants received the study intervention, of which, 284 participants completed the study, while 44 participants in the Exposed Set withdrew from the study (Figure 5). One participant was randomised to altSonflex1-2-3 Dose A but did not receive the study intervention due to ongoing medical condition starting during the visit before vaccination.



Abbreviations: AE= Adverse event, (S)AE= (Serious) adverse event
Source: Tables 14.1.1.1d, 14.1.1.1e, 14.1.2.1d, and 14.1.2.1e

Figure 5: Disposition of Participants - Africa Stage 2: Infants 9 months of age

Assessor´s comment:

In total 10 adults and 20 children aged 24-59 months were exposed to Menveo. This population will only provide limited information regarding Menveo.

In total 112 infants were exposed to Menveo. It should be noted that Menveo and MR-VAC both were administered on Day 1 in 82 of these participants (included in the dose-finding part).

All adults and children completed the study. Approximately 10% of infants withdrew from the study, none of which were due to an (S)AE.

Recruitment

Study period: First patient first visit occurred on 06 October 2021 and last patient last visit occurred on 24 June 2025.

Stage 2 was conducted in Kenya.

Baseline data

Demographic and baseline characteristics were similar across the different intervention groups.

Adults 18 to 50 years of age: Most participants were female (12 [60.0%]). The mean (SD) age was 30.7 (6.2) years and mean (SD) BMI was 21.0 (3.0) kg/m2. All participants were Black or African American (20 [100.0%]).

Children 24 to 59 months of age: The sex distribution among children from Africa was balanced (21 [52.5%] males and 19 [47.5%] females). The mean (SD) age was 37.5 (9.1) months, and the mean (SD) BMI was 15.2 (1.3) kg/m2. All participants were Black or African American (40 [100.0%]).

Infants 9 months of age, safety cohort: The sex distribution among infants from Africa was balanced (28 [46.7%] males and 32 [53.3%] females). The mean (SD) age was 9.0 (0.2*) months. All participants were Black or African American (60 [100.0%]).

*Some infants were vaccinated on the day they turned 9 months old. Due to a discrepancy between real-life and programmatic calculations of age these participants were considered as 8 months old resulting in the 0.2 SD, however in real-life all infants were at least 9 months of age at the time of vaccination.

Infants 9 months of age, dose-finding cohort: The sex distribution among infants from Africa was balanced (163 [49.7%] males and 165 [50.3%] females) and the mean (SD) age was 9.0 (0.0) months. All participants were Black or African American (328 [100.0%]).

Number analysed

All participants receiving Menveo were included in the exposed and safety sets.

Efficacy results

Not applicable for the current submission. No immunogenicity data was collected for Menveo.

Safety results

Exposure

Adults 18 to 50 years of age: All 10 (100%) participants in the Control group received 1 dose each of BOOSTRIX (DTPA) and MENVEO vaccines.

Children 24 to 59 months of age: All participants in the Control group received 1 dose each of TYPHIM VI and MENVEO vaccine.

Infants 9 months of age in Africa, safety cohort: In the Control group, a total of 30 participants received MENVEO vaccine, of which, 1 (3.3%) participant received 1 dose and 29 (96.7%) participants received 2 doses. A total of 27 (90%) participants received 1 vaccine dose of INFANRIX HEXA

Infants 9 months of age in Africa, dose-finding cohort: In the Control group, a total of 82 participants received MENVEO vaccine, of which, 8 (9.8%) participants received 1 dose and 74 (90.2%) participants received 2 vaccine doses. A total of 71 (86.6%) participants received 1 dose of INFANRIX HEXA vaccine

Adverse events

Adults 18 to 50 years of age

Following single dose Menveo administration (Day 1), solicited events were reported in 2 (20.0%) participants. All events were administration-site events of pain; no systemic events were reported

One (10%) participant had 1 unsolicited AE of headache within 28 days post vaccination. There were no Grade 3 unsolicited AEs reported.

Children 24 to 59 months of age

Following single dose Menveo administration (Day 1), at least 1 solicited administration-site event of pain (Grade 1 intensity) was reported in 3 (15%) participants. No other administration site events or solicited systemic events (fever, ≥38.0°C) were reported.

Eight (40%) participants had at least 1 unsolicited AE within 28 days post vaccination. There were no Grade 3 unsolicited AEs reported. The most commonly reported unsolicited AE by preferred term (PT) was neutropenia (2 [10%] participants); same events (PTs) were also considered related to study vaccination by the investigator.

Infants 9 months of age in Africa, safety cohort

Following first dose of Menveo administration (Day 1), at least 1 solicited event was reported in 7 (23.3%) participants including 4 (13.3%) participants with at least 1 solicited administration-site event and 4 (13.3%) participants with at least 1 solicited systemic event (fever, ≥38.0°C). At least 1 solicited administration-site event of pain was reported in 3 (10%) participants, at least 1 event of swelling in 2 (6.7%) participants, and erythema in 1 (3.3%) participant. At least 1 solicited systemic event of fever were reported in 4 (13.3%) participants. None of the solicited events were of Grade 3 intensity.

A total of 17 (56.7%) participants had at least 1 unsolicited AE within 28 days post vaccination. The most commonly reported unsolicited AE by PT include upper respiratory tract infection (URTI) (7 [23.3%] participants), rhinitis (4 [13.3%] participants), and diarrhoea (2 [6.7%] participants). There were no Grade 3 unsolicited AEs reported, and 1 (3.3%) participant had an unsolicited AE of vomiting considered related to vaccination by the investigator.

Following second dose Menveo administration (Day 85), at least 1 solicited event was reported by 4 (13.8%) participants including 3 (10.3%) participants with at least 1 solicited administration-site events and 1 (3.4%) participant with at least 1 solicited systemic event. At least 1 solicited

administration-site event of Grade 1 pain was reported in 3 (10.3%) participants and Grade 1 swelling in 1 (3.4%) participant. At least 1 solicited systemic event of Grade 1 fever was reported in 1 (3.4%) participant. None of the solicited events were of Grade 3 intensity.

A total of 10 (34.5%) participants had at least 1 unsolicited AE within 28 days post vaccination. The most commonly reported unsolicited AE by PT include rhinitis, conjunctivitis, and nasopharyngitis (2 [6.9%] participants each). There were no Grade 3 unsolicited AEs reported, and none of the unsolicited AEs were considered related to vaccination by the investigator.

Infants 9 months of age in Africa, dose-finding cohort

Following first dose of Menveo and MR-VAC administration (Day 1), at least 1 solicited event was reported in 25 (30.9%) participants, including 20 (24.7%) participants with at least 1 solicited administration-site event and 7 (8.6%) participants with at least 1 solicited systemic event. At least 1 solicited administration-site event of pain was reported in 14 (17.3%) participants, swelling and erythema in 9 (11.1%) participants each. At least 1 solicited systemic event of fever was reported in 7 (8.6%) participants. None of the solicited events were of Grade 3 intensity.

A total of 41 (50%) participants had at least 1 unsolicited AE within 28 days post vaccination. The most commonly reported unsolicited AE by PT include URTI (12 [14.6%] participants), diarrhoea (9 [11%] participants), rhinitis and cough (7 [8.5%] participants each). All other AEs were reported in ≤4.9% participants. There were 2 (2.4%) participants with Grade 3 unsolicited AEs reported including neutropenia (PT) and neutrophil count decreased (PT). None of the unsolicited AEs were considered related to vaccination by the investigator.

Following second dose Menveo administration (Day 85), at least 1 solicited event was reported by 27 (36.5%) participants including 21 (28.4%) participants with at least 1 solicited administration-site event and 10 (13.5%) participants with at least 1 solicited systemic event. At least 1 solicited administration-site event of pain was reported in 20 (27%) participants, erythema in 4 (5.4%) participants, and swelling in 2 (2.7%) participants. At least 1 solicited systemic event of fever (Grade 1 or above) were reported in 10 (13.5%) participants. None of the solicited events were of Grade 3 intensity.

A total of 28 (37.8%) participants had at least 1 unsolicited AE within 28 days post vaccination. The most commonly reported unsolicited AE by PT regardless of causality include URTI, gastroenteritis, diarrhoea, and vomiting (3 [4.1%] participants each). There were no Grade 3 unsolicited AEs reported, and none of the unsolicited AEs were considered related to vaccination by the investigator.

Deaths and Serious adverse events

No deaths occurred in any of the control groups.

No SAEs were reported in the control groups of adults or children. For the safety cohort of infants, 2 SAEs of pneumonia were reported in 1 (3.3%) participant, with onset on Day 35 and on Day 65, respectively. For the dose-finding cohort of infants, 1 SAE of infantile spasm was reported in 1 participant (on study Day 181, 97 days after second dose of Menveo). These SAEs resolved and were not related to study vaccination as assessed by the investigator.

Discontinuations due to an adverse event

No AEs leading to vaccine discontinuation/withdrawal were reported in the control groups.

2.3.3. Discussion on clinical aspects

The present submission includes the Clinical Study Report for study 212149; a staged Phase 1/2 observer-blind, randomised, controlled, multi-country study to evaluate the safety, reactogenicity, and immune responses to the GVGH altSonflex1-2-3 vaccine against *S. sonnei* and *S. flexneri*, serotypes 1b, 2a, and 3a, in adults in Europe (Stage 1) followed by age de-escalation from adults to children and infants, and dose-finding in infants in Africa (Stage 2). EU authorised MenACWY vaccine Menveo was administered in the study as an active control vaccine in Stage 2 of the study, since it could provide potential benefit to study participants randomised to the control groups.

Only safety data was collected for Menveo.

In the study, Menveo was administered IM to adults (n=10), children 24 to 59 months of age (n=20) and infants 9 months of age (n=182). Menveo is not approved for use in children <2 years of age in the EU.

The safety data set was extremely limited for adults and children in this study. Based on these small numbers, no clear conclusions can be drawn. The safety results were in line with the known safety profile of Menveo. No deaths, SAEs or grade 3 unsolicited AEs considered related to Menveo were observed. No safety signal was observed.

In total 112 infants 9 months of age were exposed to at least 1 dose of Menveo. Overall Menveo was well tolerated. It should be noted that for 82 infants in the dose-finding cohort, the first dose of Menveo was administered concomitantly with MR-VAC. Solicited AEs were reported more frequently in infants compared to children, however, none of these solicited AEs were of Grade 3 intensity. Only 1 unsolicited AE of vomiting was considered related to Menveo. SAEs were experienced by 2 participants: 1 participant experienced 2 SAEs of pneumonia and 1 participant experienced an SAE of infantile spasm. None of the SAEs was considered related to Menveo, which can be supported. Based on this information no new safety signal was observed.

Overall, based on the information presented, there is no need to update the Menveo SmPC, as no new efficacy/immunogenicity data was obtained or safety signal detected.

3. CHMP overall conclusion and recommendation

The results from study 212149 do not change the benefit-risk profile of Menveo. The results of this study indicate no new safety concern.

☒ **Fulfilled:**

No regulatory action required.