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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: EMEA/H/C/001095/P46/032

Note

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

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1. Introduction

On May 19, 2015, the MAH submitted a completed paediatric study for Menveo, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

The MAH stated that the submitted paediatric study does not influence the benefit risk for Menveo and therefore no amendments to the product information have been identified.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that V59_43 is a stand alone study.

2.2. Information on the pharmaceutical formulation used in the study

Not applicable

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- V59_43

2.3.2. Clinical study

Clinical study number and title

Description

V59_43 is a phase 3, open label, single arm multicenter study designed to evaluate the safety and immunogenicity of meningococcal ACWY conjugate vaccine in healthy subjects 2 to 75 years of age in India.

Methods

Objective(s)

Immunogenicity objectives (all at day 29 postvaccination):

Primary

- To assess the immunogenicity of a single injection of MenACWY-CRM as measured by the percentage of subjects with Human Serum Bactericidal Assay (hSBA) seroresponse, directed against N meningitidis serogroups A, C, W and Y.

- Seroresponse is defined as: for subjects with a prevaccination hSBA titer <1:4, a postvaccination hSBA titer ≥1:8, for subjects with a prevaccination hSBA titer ≥1:4, an increase in hSBA titer of at least four times the prevaccination titer.

Secondary

- To assess the immunogenicity of a single injection of MenACWY-CRM as measured by hSBA Geometric Mean Titer (GMTs) and by the percentage of subjects with hSBA titer ≥1:8, directed against N meningitidis serogroups A, C, W and Y.

Safety objectives:

To assess the safety profile following MenACWY-CRM vaccination in terms of percentage and number of subjects with:

- Solicited local and systemic adverse events (AEs) reported from day 1 (day of vaccination) through day 7 postvaccination.
- All other AEs reported from day 1 through day 7 postvaccination.
- Serious AEs (SAEs) and medically attended AEs from day 1 through day 29.

Study design

Phase 3, multi-center, single arm, open-label study

Assessor's comments

The lack of a comparator arm limits the ability to make inferences from this study. The study will describe the immunogenicity and safety of Menveo in Indian children and adults between the age of 2 and 75 years.

Study population /Sample size

In total 180 healthy subjects were enrolled in this study, 60 per each age group (2 to 10 years, 11 to 18 years, and 19 to 75 years).

Main inclusion criteria:

1. 2 - 75 years of age inclusive who have given their written assent and whose parent or legal guardian has given written informed consent at the time of enrollment.
2. In good health as determined by the outcome of medical history, physical examination and clinical judgment of the investigator;
3. With a negative urine pregnancy test (for female subjects only).

Main exclusion criteria:

1. History of any meningococcal vaccine administration;
2. Current or previous, confirmed or suspected disease caused by N meningitidis;

Treatments

Subjects received a single dose (0.5 ml) of Meningococcal ACWY-CRM conjugated vaccine (MenACWY).

Outcomes/endpoints

Immunogenicity Endpoints

The measure of immunogenicity used in this study was a serum bactericidal assay using hSBA for serogroup A, serogroup C, serogroup W, and serogroup Y performed at Novartis Vaccines and Diagnostics, Klinische Serologie, Marburg (Germany).

Primary Response Variables

- Percentage of subjects with hSBA seroresponse to N meningitidis serogroups A, C, W and Y at day 29.

Secondary Response Variables

For the secondary immunogenicity endpoints the following measures were to be evaluated:

- hSBA Geometric Mean Titer(GMTs) to N meningitidis serogroups A, C, W and Y at day 1 and day 29.
- hSBA Geometric Mean Ratio (GMR) to N meningitidis serogroups A, C, W and Y.
- Percentage of subjects with hSBA titer $\geq$1:8 to N meningitidis serogroups A, C, W and Y at day 1 and day 29.

Safety Endpoints

Solicited local and systemic AEs and other unsolicited AEs were collected from day 1 through day 7 of the study. SAEs, AEs resulting in premature withdrawal and other medically attended events were collected from day 1 through day 29. An unexpected adverse event was one that was not listed in the current Summary of Product Characteristics or the Investigator's Brochure or an event that was by nature more specific or more severe than a listed event.

Statistical Methods

Definition of populations analysed:

1) All Enrolled Population: All subjects who had signed an informed consent, underwent screening procedure(s), and had a subject number assigned.

2) All Exposed Population: All subjects in the all enrolled population who received a study vaccination.

3) Full Analysis Set (FAS)/Modified Intention-to-Treat (MITT) Immunogenicity Population: All subjects in the exposed population who provided at least one evaluable serum sample whose assay result was available for at least one serogroup.

4) Per Protocol (PP) Population, Immunogenicity: All subjects in the FAS who:

- Provided evaluable serum samples at day 1 and day 29, and
- Had no major protocol violations.

5) Safety Population: All subjects in the exposed population who provided any post-baseline safety data.

Analysis of Demographic and Baseline Characteristics

Descriptive statistics (mean, standard deviation, median, minimum and maximum) for age, height and weight at enrolment were to be calculated overall and for each age group. Distributions of subjects by

sex, ethnic origin, and previous vaccination were to be summarized overall and for each age group. Demographic data were to be tabulated for the Enrolled, FAS, PPS, and Safety populations.

For this study there was no hypothesis statistically tested. Endpoints were to be reported descriptively.

Primary analysis

The number and percentage of subjects with hSBA seroresponse (as previously defined) and associated 2-sided 95% Clopper-Pearson CIs were to be computed for each *N meningitidis* serogroups A, C, W and Y at day 29, overall.

Due to the descriptive nature of analyses, there were no considerations with regard to type I or II errors or to multiplicity.

The primary immunogenicity analysis was based on the Per Protocol (PP) population.

Secondary Endpoints:

- hSBA GMTs: The hSBA titers at each visit (day 1 and day 29) were logarithmically transformed (base10) (to fulfill normal distribution assumption) and summarized by serogroup. GMTs and associated 2-sided 95% confidence interval (CIs) were calculated at each time point by exponentiating the corresponding log-transformed means and 95% CIs. Titers below the limit of detection would be set to half that limit for the purposes of analysis. GMTs were to be reported for each N meningitidis serogroups A, C, W and Y;
- hSBA GMR was defined as the geometric mean of the subject's titer at day 29 divided by the subject's titer at day 1. Its associated 2-sided 95% CIs were also to be computed for each N meningitidis serogroups A, C, W and Y;
- The number and percentage of subjects with hSBA titer $\geq$1:8 to N meningitidis serogroups A, C, W and Y were to be computed for each serogroup at day 1 and day 29 along with their associated 2-sided 95% Clopper-Pearson CIs.

Additional exploratory analyses

The statistical analysis for immunogenicity (including primary and secondary endpoints listed above) was to be performed also stratified according to the age at enrolment (2 through 10 years of age, 11 through 18 years of age, and 19 through 75 years of age).

Interim analyses

One interim analysis of safety data from this trial was initially planned. For all adult subjects' (aged 19 through 75 years) day 1 through day 29 safety data were analysed and submitted to the Competent Authority for their review and acceptance before subjects from 2 years through 18 years of age were enrolled into the study.

On request of local health authorities an unplanned second interim analysis was introduced. Safety data from day 1 through day 29 of the adolescent (aged 11 through 18 years) age group were analysed and submitted to the Competent Authority for their review and acceptance before subjects from 2 years through 10 years of age were enrolled into the study.

Assessor's comments

The (unplanned, commissioned) interim analysis is not expected to have impacted the results in the last age cohort, considering the nature of the trial (single armed, descriptive study).

Results

Recruitment/ Number analysed

In total 180 subjects were enrolled in this study, 60 per each age group (2 through 10 years, 11 through 18 years and 19 through 75 years). All enrolled subjects were exposed to the single dose of MenACWY vaccine and completed the study without any premature withdrawals.

In total, 5 subjects reported 6 protocol deviations; 3 subjects in 11 through 18 years group and 2 subjects in 19 through 75 years group. The reasons for protocol deviations were subjects received excluded concomitant medication (n=1) , subjects did not satisfy the entry criteria but were randomized in the study (n=2) and no serological results available at visit 1 (n=1) or visit 2 (n=2). Therefore 175 persons were included in the PPS.

Table 1 Overview of datasets

	2 - 10 Years N=60	11 - 18 Years N=60	19 - 75 Years N=60	Total N=180
Enrolled set	60 (100%)	60 (100%)	60 (100%)	180 (100%)
Exposed set:	60 (100%)	60 (100%)	60 (100%)	180 (100%)
FAS	60 (100%)	60 (100%)	60 (100%)	180 (100%)
PPS	60 (100%)	57 (95%)	58 (96.7%)	175 (97.2%)

Source: Table 14.1.1.1. Abbreviations: FAS =Full analysis set, PPS = Per protocol set. Categorical parameters: N (%), number and % of subjects.

Baseline data

The population consisted of Asian in each group. The average age of the subjects at study entry was 17.49 (±13.432) years and among all enrolled female subjects, 24.4% had childbearing potential.

Table 2 Summary of Demography of Subjects by Age Group and Overall - Enrolled Set

	2 - 10 Years N=60	11 - 18 Years N=60	19 - 75 Years N=60	Total N=180
Age (years):	5.77±2.5	14.03±1.931	32.67±12.297	17.49±13.432
Sex:				
Male	27 (45%)	27 (45%)	39 (65%)	93 (51.7%)
Female	33 (55%)	33 (55%)	21 (35%)	87 (48.3%)
Race				
Asian	60 (100%)	60 (100%)	60 (100%)	180 (100%)
American Indian or Alaska Native	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Black or African American	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)
White	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Weight (kg):	18.87±5.807	41.08±11.845	61.25±10.641	40.4±19.9
Height (cm):	112.47±15.654	152.73±11.622	164.6±9.243	143.27±25.574
Met entry criteria				
Yes	60 (100%)	58 (96.7%)	60 (100%)	178 (98.9%)
Childbearing potential				
No	33 (55%)	7 (11.7%)	3 (5%)	43 (23.9%)
Yes	0	26 (43.3%)	18 (30%)	44 (24.4%)

Source: Table 14.1.1.3. Categorical parameters: N (%); non-categorical parameters: Mean±SD.

Assessor's comments

The study population is relatively young. The oldest cohort consisted of more males than the youngest two cohorts. This is unlikely to have influenced study outcome.

Efficacy results

Analysis of Immunogenicity

Seroresponse

Overall in 2 through 75 years group, at day 29 postvaccination, the seroresponse rate to a single dose of MenACWY was 72%, 88%, 55%, and 71%, respectively, for serogroups A, C, W, and Y. Among the subjects with baseline hSBA <1:4, the seroresponse rate at day 29 postvaccination was 72%, 93%, 88%, and 84%, respectively, for serogroups A, C, W and Y. For subjects with baseline hSBA ≥1:4, the seroresponse rate were 100%, 77%, 33% and 57%, respectively, for serogroups A, C, W, and Y.

The hSBA response overall and per age strata is presented in table 3.

Table 3. Number and Percentage of Subjects (95% CIs) with Seroresponse Against N meningitidis Serogroups A, C, W, and Y at Day 29 Postvaccination (PPS)

Serogroup	Baseline	2 - 10 Years	11 - 18 Years	19 - 75 Years	Overall
		N=60	N=59	N=58	N=177
A	hSBA <1:4	43 (74%) (61%-85%) N=58	44 (76%) (63%-86%) N=58	37 (65%) (51%-77%) N=57	124 (72%) (64%-78%) N=173
	hSBA ≥1:4	2 (100%) (16%-100%) N=2	1 (100%) (3%-100%) N=1	1 (100%) (3%-100%) N=1	4 (100%) (40%-100%) N=4
	Overall	45 (75%) (62%-85%)	45 (76%) (63%-86%)	38 (66%) (52%-78%)	128 (72%) (65%-79%)
		N=60	N=59	N=58	N=177
C	hSBA <1:4	43 (90%) (77%-97%) N=48	36 (95%) (82%-99%) N=38	34 (94%) (81%-99%) N=36	113 (93%) (86%-97%) N=122
	hSBA ≥1:4	6 (60%) (26%-88%) N=10	17 (81%) (58%-95%) N=21	18 (82%) (60%-95%) N=22	41 (77%) (64%-88%) N=53
	Overall	49 (84%) (73%-93%) N=58	53 (90%) (79%-96%)	52 (90%) (79%-96%)	154 (88%) (82%-92%) N=175
		N=60	N=59	N=58	N=177
W	hSBA <1:4	22 (88%) (69%-97%) N=25	19 (90%) (70%-99%) N=21	19 (86%) (65%-97%) N=22	60 (88%) (78%-95%) N=68
	hSBA ≥1:4	13 (37%) (21%-55%) N=35	11 (29%) (15%-46%) N=38	12 (34%) (19%-52%) N=35	36 (33%) (25%-43%) N=108
	Overall	35 (58%) (45%-71%)	30 (51%) (37%-64%)	31 (54%) (41%-68%) N=57	96 (55%) (47%-62%) N=176
		N=60	N=59	N=58	N=177
Y	hSBA <1:4	32 (76%) (61%-88%) N=42	24 (89%) (71%-98%) N=27	22 (92%) (73%-99%) N=24	78 (84%) (75%-91%) N=93
	hSBA ≥1:4	8 (50%) (25%-75%) N=16	17 (53%) (35%-71%) N=32	21 (64%) (45%-80%) N=33	46 (57%) (45%-68%) N=81
	Overall	40 (69%) (55%-80%) N=58	41 (69%) (56%-81%)	43 (75%) (62%-86%) N=57	124 (71%) (64%-78%) N=174

GMTs and GMRs

At baseline before MenACWY-CRM vaccination, the hSBA GMTs against serogroups A, C, W and Y in overall 2 through 75 years group were 2.07, 3.63, 11 and 6.26, respectively. In 2 through 10 years, the baseline hSBA GMTs against serogroup A, C, W and Y were 2.08, 2.88, 9.27 and 3.59, respectively. In 11 through 18 years group, the baseline GMTs were 2.05, 4.01, 14 and 7.87, respectively, against serogroup A, C, W and Y. Similarly for subjects in 19 through 75 years group, the baseline GMTs were 2.07, 4.14, 12 and 8.69, respectively, against serogroups A, C, W and Y.

At day 29 postvaccination, the GMTs in overall 2 through 75 years group were 35, 153, 80 and 93 against serogroup A, C W and Y respectively. At day 29 postvaccination, the GMTs in among 2 through 10 years, 11 through 18 years and 19 through 75 years groups were 30, 50 and 29 against serogroup A, 67, 191 and 287 against serogroup C, 60, 75 and 116 against serogroup W and 45, 105 and 173 against serogroup Y, respectively.

Overall in 2 through 75 years group, at day 29 postvaccination, the GMTs increased 17 fold (GMR) over the baseline against serogroup A, 42-fold against serogroup C, 7.09-fold against serogroup W and 15-fold against serogroup Y.

The GMTs and GMRs overall and per age strata are presented in table 4.

Table 4. Geometric Mean hSBA Titers (95% Confidence Intervals) and Geometric Mean Ratios Against N meningitidis Serogroups A, C, W, and Y at Day 1 and Day 29 by Age Group and Overall – Per Protocol Set

Serogroups		GMTs and GMRs (95% CIs)			
		2 - 10 Years	11 - 18 Years	19 - 75 Years	Overall
A		N=60	N=60	N=60	N=180
	Day 1	2.08 (1.97-2.20)	2.05 (1.95-2.16) N=59	2.07 (1.93-2.21)	2.07 (2.00-2.14) N=179
	Day 29	30 (19-47)	50 (30-84)	29 (16-51) N=58	35 (26-47) N=178
	Day 29/Day 1	14 (9.11-22)	24 (14-40) N=59	14 (7.92-24) N=58	17 (13-23) N=177
C		N=60	N=60	N=60	N=180
	Day 1	2.88 (2.26-3.65) N=58	4.01 (3.00-5.35) N=59	4.14 (3.12-5.49)	3.63 (3.11-4.25) N=177
	Day 29	67 (44-101)	191 (117-310)	287 (191-431) N=58	153 (117-199) N=178
	Day 29/Day 1	22 (14-34) N=58	49 (30-80) N=59	70 (43-112) N=58	42 (32-56) N=175
W		N=60	N=60	N=60	N=180
	Day 1	9.27 (6.33-14)	14 (9.13-20) N=59	12 (7.70-17) N=59	11 (9.05-14) N=178
	Day 29	60 (44-81)	75 (54-105)	116 (71-187) N=58	80 (64-100) N=178
	Day 29/Day 1	6.42 (4.22-9.76)	5.60 (3.51-8.91) N=59	10 (5.44-19) N=57	7.09 (5.32-9.46) N=176
Y		N=60	N=60	N=60	N=180
	Day 1	3.59 (2.75-4.70) N=59	7.87 (5.48-11) N=59	8.69 (5.98-13) N=59	6.26 (5.13-7.65) N=177
	Day 29	45 (29-69) N=59	105 (72-155)	173 (97-309) N=58	93 (70-123) N=177
	Day 29/Day 1	12 (7.84-19) N=58	14 (8.48-22) N=59	18 (9.59-35) N=57	15 (11-20) N=174

Source: Table 14.2.1.3.1. Abbreviations: hSBA = Human serum bactericidal assay; CI = Confidence intervals; GMTs = Geometric mean titers; GMRs = Geometric mean ratios.

Percentage of subjects with hSBA ≥1:8

At day 1 before MenACWY-CRM vaccination, in overall 2 through 75 years group, 1% of subjects had hSBA ≥1:8 for serogroup A, 21% for serogroup C, 58% for serogroup W and 42% for serogroup Y. At day 29 post MenACWY-CRM vaccination, the percentage of subjects with hSBA ≥1:8 were 72% for serogroup A, 95% for serogroup C, 94% for serogroup W and 90% for serogroup Y.

The % subjects with hSBA ≥1:8 overall and per age strata are presented in table 5.

Table 5. Number and Percentage (95% CI) of Subjects With hSBA ≥1:8 Against N meningitidis Serogroups A, C, W and Y at Day 1 and Day 29 – Per Protocol Set

Serogroup		Percentage of Subjects (95% CI)			
		2 - 10 Years	11 - 18 Years	19 - 75 Years	Overall
		N=60	N=60	N=60	N=180
A	Day 1	0 (0%) (0%-6%)	1 (2%) (0%-9%) N=59	1 (2%) (0%-9%)	2 (1%) (0%-4%) N=179
	Day 29	45 (75%) (62%-85%)	46 (77%) (64%-87%)	38 (66%) (52%-78%) N=58	129 (72%) (65%-79%) N=178
		N=60	N=60	N=60	N=180
C	Day 1	8 (14%) (6%-25%) N=58	14 (24%) (14%-37%) N=59	15 (25%) (15%-38%)	37 (21%) (15%-28%) N=177
	Day 29	55 (92%) (82%-97%)	58 (97%) (88%-100%)	56 (97%) (88%-100%) N=58	169 (95%) (91%-98%) N=178
		N=60	N=60	N=60	N=180
W	Day 1	31 (52%) (38%-65%)	37 (63%) (49%-75%) N=59	35 (59%) (46%-72%) N=59	103 (58%) (50%-65%) N=178
	Day 29	57 (95%) (86%-99%)	57 (95%) (86%-99%)	54 (93%) (83%-98%) N=58	168 (94%) (90%-97%) N=178
		N=60	N=60	N=60	N=180
Y	Day 1	13 (22%) (12%-35%) N=59	31 (53%) (39%-66%) N=59	31 (53%) (39%-66%) N=59	75 (42%) (35%-50%) N=177
	Day 29	49 (83%) (71%-92%) N=59	57 (95%) (86%-99%)	54 (93%) (83%-98%) N=58	160 (90%) (85%-94%) N=177

Source: Table 14.2.1.2.1.Abbreviations: hSBA = human serum bactericidal assay; CI = Confidence interval.

Assessors comments

The immune response is broadly in line with what is known from the registration trials and reported in the SmPC.

Safety results

Extent of Exposure

A total of 180 subjects were enrolled in this study, 60 subjects in each of the 3 age groups (2 through 10 years, 11 through 18 years and 19 through 75 years); all of them provided postvaccination safety data and were included in the safety set.

Adverse events

Any solicited AEs from day 1 through day 7 after MenACWY-CRM vaccination were reported by 3.3% of subjects in the 2 through 5 years age group; 20% of subjects in the 6 through 10 years, 35% of subjects in the 11 through 18 years and 18.3% of subjects in the 19 through 75 years age group reported any solicited AEs. None of the subjects in the 2 through 5 years age group reported solicited systemic AEs. 10% of subjects in 6 through 10 years, 11.7% of subjects in 11 through 18 years and 15% of subjects in 19 through 75 years of age group reported at least one solicited systemic AEs.

Solicited AEs

In the 2 through 5 years age group, the most commonly reported solicited local AE from 6 hours through day 7 after MenACWY-CRM vaccination was tenderness by 3.3% of subjects. In the age group 6 through 75 years, pain (17.3 % of subjects) of mild intensity was the most frequently reported solicited local AE; 13.3% of subjects in the 6 through 10 years, 28.3% of subjects in the 11 through 18 years and 8.3% of subjects in the 19 through 75 years age group reported pain after MenACWY-CRM vaccination. There were no severe local AEs reported. None of the subjects reported erythema or induration.

In the 2 through 5 years age group, there were no solicited systemic AEs reported. In 6 through 10 years of age group, the most commonly reported solicited systemic AE from 6 hours through day 7 were malaise (6.7% of subjects), and headache (6.7% of subjects), followed by arthralgia (3.3% of subjects) and myalgia (3.3% of subjects). Body temperature of ≥38.0° C was reported by 3.3% of subjects. None of the subjects reported body temperature of ≥40° C. The use of analgesics and antipyretics were reported by 6.7% of subjects. In the 11 through 18 years age group the most commonly reported solicited systemic AE from 6 hours through day 7 were headache (8.3% of subjects) and chills (6.7% of subjects), followed by malaise (3.3% of subjects). Body temperature of ≥38.0° C was reported by 1.7% of subjects. The use of analgesics and antipyretics were reported by 8.3% of subjects. In the 19 through 75 years age group the most commonly reported solicited systemic AE from 6 hours through day 7 was headache (11.7% of subjects) followed by chills, malaise and myalgia (3.3% of subjects). Body temperature of ≥38.0° C was reported by 1.7% of subjects. The use of analgesics and antipyretics were reported by 3.3% of subjects in the 19 through 75 years of age group.

One subject in 11 through 18 years of age reported severe headache on day 4 after vaccination.

Unsolicited AEs

In the overall age group (2 through 75 years), 10.6% of the subjects reported unsolicited AEs; 15% of subjects in the 2 through 10 years, 10% of subjects in the 11 through 18 years and 6.7% of subjects in the 19 through 75 years age group reported unsolicited AEs.

In 2 through 10 years age group, the most commonly affected SOC was infections and infestations (10% of subjects). For 11 through 18 years age group, the most commonly affected SOC was infections and infestations and gastrointestinal disorders (3.3% of subjects), whereas for 19 through 75 years age group, general disorders and administration site conditions (3.3% of subjects) were commonly affected SOC.

Possibly related unsolicited AEs were reported by 1.7% of subjects in the 2 through 10 years of age group, 3.3% of subjects in the 11 through 18 years and 2.8% in the 19 through 75 years of age groups.

<u>Deaths, withdrawals and SAEs</u>

No deaths were reported during the entire course of the study.

No subject was prematurely withdrawn from the study due to AE.

One (1.7%) subject (subject no: 05002) in the 19 through 75 years age group reported SAE (pyrexia) which was considered to be possibly or probably related to the study vaccines as per the investigator.

The subject was hospitalized on day 2 after vaccination because the investigator suspected Malaria (which was finally ruled out after laboratory investigation).

Other significant events

There was one pregnancy during the course of the study. The subject (01004) was followed up until the outcome of the pregnancy is known. The subject delivered a live born baby with no congenital abnormalities.

Assessor's comments

The rates of AEs seems lower than what is known from registration studies. According to the MAH this reflects the overall lower rates of AEs reported from studies in India. The MAH refers to two publications (Bravo, 2014 and Bermal, 2011) to substantiate this, both reporting on vaccine trials in India. It is possible that differences in attitudes and access to health care would explain the lower rates of AEs. Importantly, no unexpected safety signals emerged and the findings are in line with the known safety profile of Menveo, which is overall well tolerated.

2.3.3. Discussion on clinical aspects

Study V59_43 was a single armed, open label study conducted in India which aimed to evaluate the immunogenicity and safety of MenACWY in children and adults aged between 2 and 75 years. The immunogenicity is broadly in line with what is reported in the SmPC for the different age groups. Overall, the seroresponse rate was 72%, 88%, 55%, and 71%, respectively, for serogroups A, C, W, and Y. The percentage of subjects with hSBA ≥1:8 were 72% for serogroup A, 95% for serogroup C, 94% for serogroup W, and 90% for serogroup Y.

The reported AEs were slightly lower than the known safety profile for Menveo, which could potentially be related to differences in reporting AEs in India. There were no unexpected observations and overall they confirm the tolerability and favourable safety profile of Menveo.

In conclusion, the trial demonstrated that a single dose of Menveo is well-tolerated and immunogenic in healthy Indian subjects 2 through 75 years of age.

Consequently, no further regulatory action considering Menveo is required, based on the presented results.

3. Rapporteur's overall conclusion and recommendation

Overall conclusion

The commitment is regarded as fulfilled, through the submission of the full clinical study report.

☒ **Fulfilled:**

No regulatory action required.

4. Additional clarification requested

N/A