London, 22 February 2018
EMA/CHMP/5875/2018
Committee for Medicinal Products for Human Use (CHMP)

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

Nimenrix

meningococcal group a, c, w135 and y conjugate vaccine

Procedure no: EMEA/H/C/002226/P46/051

Note

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

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1. Introduction

On 7 December 2017, the MAH submitted a paediatric clinical study report in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. MEN-ACWY-TT-106 was an open-label, multi-centre study to evaluate the immunogenicity, reactogenicity and safety of a single dose of MenACWY-TT vaccine (Nimenrix) administered at 6 years after vaccination at ~12-18 month of age with either Hib-MenC-TT vaccine (*Menitorix*) or *Hiberix* (PRP-T) and *Meningitec* (MenC-CRM_{197}). The study included follow-up to evaluate antibody persistence at 2 years.

The MAH (now Pfizer Limited) has reviewed the immunogenicity and safety results from MEN-ACWY-TT-106 and has concluded that the data do not change the benefit-risk profile of Nimenrix. The immunogenicity and safety outcomes are in line with the approved Summary of Product Characteristics (SmPC) for Nimenrix and therefore no updates to the SmPC are proposed.

A short critical expert overview has been provided.

2. Scientific discussion

2.1. Information on the development program

This submission provides the final CSR for the study.

2.2. Information on the pharmaceutical formulation used in the studies

Nimenrix was developed specifically for use in children and adults. The same formulation and dose is used across the full age range approved but the regimen (number of doses) differs by age (see SmPC).

2.3. Clinical aspects

2.3.1. Introduction

The study was conducted at 7-8 centres in Australia between 2013 and 2017.

2.3.2. Clinical studies

MenACWY-TT-106

The primary objective of the study was:
To evaluate the immunogenicity of MenACWY-TT vaccine at one month post-dose in terms of the percentages with a vaccine response (see definition below) based on rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titres.

Secondary immunogenicity objectives were:
At one month post-dose:
To evaluate the immunogenicity of a dose of Nimenrix based on percentages with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titres ≥ 1:8 and ≥ 1:128 and on the GMTs;

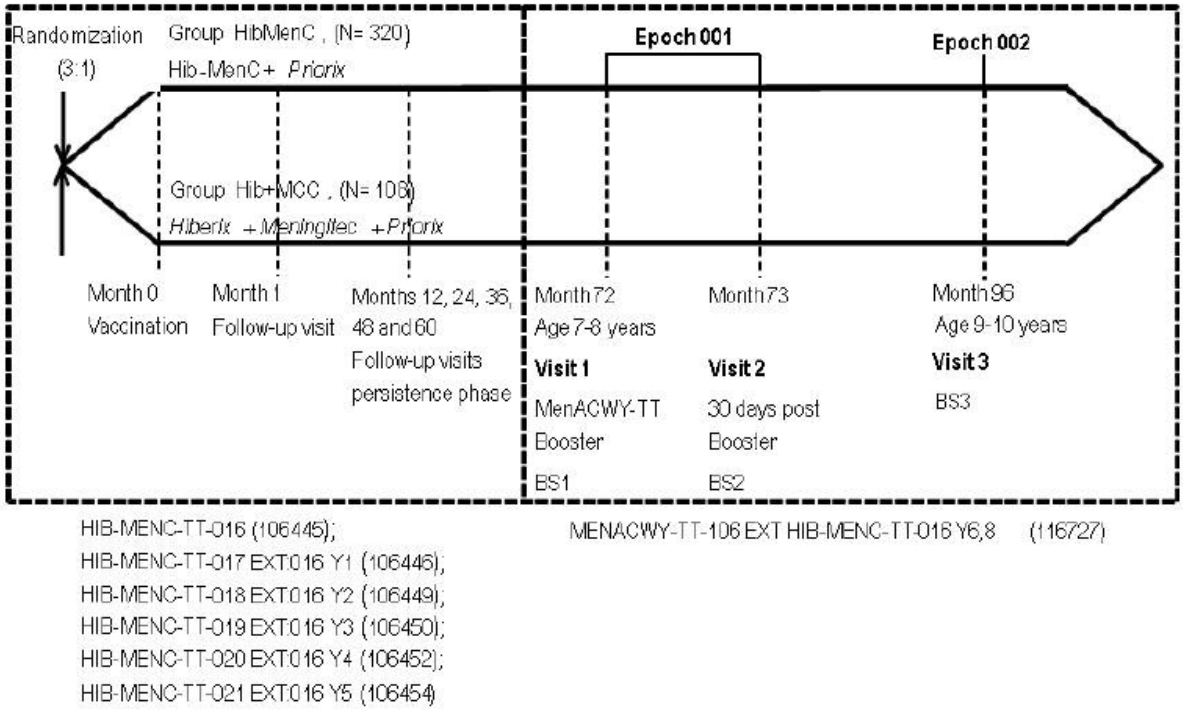
To evaluate the percentages with anti-TT concentrations ≥ 0.1 IU/mL and GMCs.

At 2 years post-dose:
To evaluate antibody persistence based on percentages with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titres ≥ 1:8 and ≥ 1:128 and on the GMTs.

Eligible subjects were to be aged 84 to 95 months at Visit 1 (see figure below) and had to have completed initial vaccination in study HIB-MENC-TT-016 as per protocol. Excluded were subjects with any history of meningococcal disease and previous administration of any non-study meningococcal vaccine. There were 320 and 108 subjects in the HibMenC and Hib+MenCC groups, respectively, in the primary study and this open-label study planned to enrol ~240 subjects who were to be derived in a 3:1 ratio from the two treatment groups in HIB-MENC-TT-016 as follows:
HibMenC group: subjects vaccinated with Hib-MenC-TT + *Priorix* in study HIB-MENC-TT-016 and MenACWY-TT in study MENACWY-TT-106;
Hib+MCC group: subjects vaccinated with *Meningitec* + *Hiberix* + *Priorix* in study Hib-MenC-TT-016 and MenACWY-TT in study MENACWY-TT-106.

The overall design is summarised in the figure.

Figure 1 Study design overview



All subjects received one dose of Nimenrix. Blood samples were taken before vaccination and at one and 24 months after vaccination. The intervals allowed between study visits at which vaccination and sampling were performed are shown below.

Table 1 Intervals between study visits

Interval	Optimal length of interval [1]	Allowed interval[2]
Date of birth →Visit 1	7 years	84-95 months
Visit 1 →Visit 2	30 days	21-48 days[3]
Visit 1 →Visit 3	2 years	2 years ± 9 weeks

[1] Whenever possible the investigator was to arrange study visits within this interval.
[2] Subjects were not eligible for inclusion in the ATP cohort for immunogenicity if they made the study visit outside this interval.
[3] For the safety evaluation an interval of 30 days was needed. If the subject had returned for Visit 2 prior to Day 30, their parents/LAR(s) had to take home the diary card, continue to record unsolicited safety information until Day 30 and then provide the card to the study site.

A summary of the laboratory assays performed to assess the humoral immune response is provided below. For meningococcal responses rSBA titres were measured at the UK PHE laboratory.

Table 2 Humoral Immunity (Antibody determination)

Component	Scale	Assay method	Test kit/Manufacturer	Assay unit	Assay cut-off	Laboratory
Neisseria meningitidis Serogroup A L10 3125 Ab	Quantitative	Bactericidal assay using rabbit complement	in-house kit	Dilution for at least 50% killing	8	PHE*
Neisseria meningitidis Serogroup C L3v C11 Ab	Quantitative	Bactericidal assay using rabbit complement	in-house kit	Dilution for at least 50% killing	8	PHE*
Neisseria meningitidis Serogroup W L3v MP01240070 Ab	Quantitative	Bactericidal assay using rabbit complement	in-house kit	Dilution for at least 50% killing	8	PHE*
Neisseria meningitidis Serogroup Y L3v S1975 Ab	Quantitative	Bactericidal assay using rabbit complement	in-house kit	Dilution for at least 50% killing	8	PHE*
Clostridium tetani.Tetanus Toxoid Ab.IgG	Quantitative	Enzyme Linked Immuno Sorbent Assay	in-house kit	IU/mL	0.043	GSK Biologicals**

* Public Health England (PHE), Vaccine Evaluation Unit, Oxford Road, Manchester, England M13 9WZ
** GSK Biologicals Clinical Laboratory Science (CLS), Rue de l'Institut 89, 1330 Rixensart, Belgium

Primary endpoint

The rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY vaccine response rates at one month after Nimenrix, with vaccine response defined as:

- For initially seronegative subjects (pre-vaccination rSBA titre < 1:8), rSBA antibody titre ≥ 1:32 one month after vaccination;
- For initially seropositive subjects (pre-vaccination rSBA titre ≥ 1:8), at least 4-fold increase in rSBA titres from pre-vaccination to one month after vaccination.

Secondary endpoints

- rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titres ≥ 1:8, ≥ 1:128 and GMTs at one month and at 2 years post-dose;
- Anti-T concentrations ≥ 0.1 IU/mL, ≥ 1.0 IU/mL and GMCs at one month post-dose.

Results

There were 156 subjects vaccinated (see below) and 139 completed the study. No subject was withdrawn due to a SAE or AE.

Table 3 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal (Total Vaccinated cohort)

	HibMenC	Hib+MCC
Number of subjects vaccinated	119	37
Number of subjects completed	105	34
Number of subjects withdrawn	14	3
Reasons for withdrawal :		
Subject died	0	0
Serious Adverse Event	0	0
Non-Serious Adverse Event	0	0
Eligibility criteria not fulfilled (inclusion and exclusion criteria)	0	0
Protocol violation	0	0
Consent withdrawal (not due to an adverse event)	5	1
Migrated/moved from study area	1	0
Lost to follow-up (subjects with incomplete vaccination course)	0	0
Lost to follow-up (subjects with complete vaccination course)	7	2
Sponsor study termination	0	0
Others[1]	1	0

There were 139 included in ATP cohort for immunogenicity at Month 73 and 133 were included in the ATP cohort for persistence at Year 2. The mean age at the time of vaccination (month 73) was 7 years with 44.6% female and 55.4% male subjects.

Vaccine responses exceeded 97% for all meningococcal serogroups at one month after Nimenrix. In each case, response rates were lower for the small sub-groups who were seropositive at pre-vaccination.

Table 4 Vaccine response for rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY antibody titres one month after booster vaccination (ATP cohort for immunogenicity at Month 73)

				Vaccine response			
						95% CI	
Antibody	Group	Pre-vaccination status	N	n	%	LL	UL
rSBA-MenA	HibMenC	S-	92	92	100	96.1	100
		S+	12	10	83.3	51.6	97.9
		Total	104	102	98.1	93.2	99.8
	Hib+MCC	S-	31	31	100	88.8	100
		S+	3	2	66.7	9.4	99.2
		Total	34	33	97.1	84.7	99.9
rSBA-MenC	HibMenC	S-	85	85	100	95.8	100
		S+	19	16	84.2	60.4	96.6
		Total	104	101	97.1	91.8	99.4
	Hib+MCC	S-	29	29	100	88.1	100
		S+	5	4	80.0	28.4	99.5
		Total	34	33	97.1	84.7	99.9
rSBA-MenW-135	HibMenC	S-	92	92	100	96.1	100
		S+	12	10	83.3	51.6	97.9
		Total	104	102	98.1	93.2	99.8
	Hib+MCC	S-	26	26	100	86.8	100
		S+	8	7	87.5	47.3	99.7
		Total	34	33	97.1	84.7	99.9
rSBA-MenY	HibMenC	S-	83	83	100	95.7	100
		S+	21	18	85.7	63.7	97.0
		Total	104	101	97.1	91.8	99.4
	Hib+MCC	S-	29	29	100	88.1	100
		S+	5	4	80.0	28.4	99.5
		Total	34	33	97.1	84.7	99.9

At one month after Nimenrix, at least 97.1% of subjects had rSBA titres ≥ 1:8 for each serogroup. In each sub-group defined by prior vaccination history the highest rSBA GMTs were observed for MenW and the lowest for MenA. The comparisons between the sub-groups suggested slightly lower responses at one month and/or at 2 years in the Hib+MCC group but the 95% CI overlapped. At 2 years post-dose the lowest percentages with ≥1:8 or ≥1:128 occurred for rSBA-MenA.

Table 5 Number and percentage of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135, and rSBA-MenY titres equal to or above the cut-off values of 1:8 and 1:128 and GMTs (Adapted ATP cohort*)

				≥ 1:8				≥ 1:128				GMT		
						95% CI				95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	n	%	LL	UL	value	LL	UL
rSBA-MenA	HibMenC	PI(M72)	104	12	11.5	6.1	19.3	8	7.7	3.4	14.6	6.0	4.7	7.7
		PII(M73)	104	102	98.1	93.2	99.8	102	98.1	93.2	99.8	3421.4	2659.3	4402.0
		PII(M96)	100	72	72.0	62.1	80.5	67	67.0	56.9	76.1	174.9	102.4	298.7
	Hib+MCC	PI(M72)	34	3	8.8	1.9	23.7	2	5.9	0.7	19.7	6.0	3.6	10.1
		PII(M73)	35	35	100	90.0	100	35	100	90.0	100	2925.1	1949.5	4389.0
		PII(M96)	33	21	63.6	45.1	79.6	17	51.5	33.5	69.2	79.0	29.6	210.4
rSBA-MenC	HibMenC	PI(M72)	104	19	18.3	11.4	27.1	9	8.7	4.0	15.8	7.1	5.3	9.5
		PII(M73)	104	102	98.1	93.2	99.8	102	98.1	93.2	99.8	11819.2	9026.4	15476.1
		PII(M96)	100	100	100	96.4	100	90	90.0	82.4	95.1	333.1	278.3	398.8
	Hib+MCC	PI(M72)	34	5	14.7	5.0	31.1	2	5.9	0.7	19.7	6.5	4.0	10.6
		PII(M73)	35	35	100	90.0	100	34	97.1	85.1	99.9	7419.7	4543.2	12117.3
		PII(M96)	33	31	93.9	79.8	99.3	26	78.8	61.1	91.0	175.4	104.1	295.5
rSBA-MenW-135	HibMenC	PI(M72)	104	12	11.5	6.1	19.3	12	11.5	6.1	19.3	7.8	5.4	11.2
		PII(M73)	104	102	98.1	93.2	99.8	102	98.1	93.2	99.8	17166.5	12745.9	23120.3
		PII(M96)	100	96	96.0	90.1	98.9	96	96.0	90.1	98.9	1002.9	742.1	1355.5
	Hib+MCC	PI(M72)	34	8	23.5	10.7	41.2	8	23.5	10.7	41.2	13.9	6.0	31.9
		PII(M73)	35	35	100	90.0	100	35	100	90.0	100	15747.7	10033.0	24717.7
		PII(M96)	33	30	90.9	75.7	98.1	30	90.9	75.7	98.1	941.5	448.4	1976.9
rSBA-MenY	HibMenC	PI(M72)	104	21	20.2	13.0	29.2	21	20.2	13.0	29.2	10.8	7.3	16.0
		PII(M73)	104	103	99.0	94.8	100	103	99.0	94.8	100	4871.0	3932.7	6033.1
		PII(M96)	100	95	95.0	88.7	98.4	95	95.0	88.7	98.4	929.3	678.0	1273.7
	Hib+MCC	PI(M72)	34	5	14.7	5.0	31.1	5	14.7	5.0	31.1	8.3	4.4	15.8
		PII(M73)	35	34	97.1	85.1	99.9	34	97.1	85.1	99.9	3495.9	2126.6	5746.8
		PII(M96)	33	29	87.9	71.8	96.6	29	87.9	71.8	96.6	512.0	250.1	1048.3

All subjects had anti-T antibody concentration ≥ 0.1 IU/mL at one month post-dose in both sub-groups defined by prior vaccination.

Table 6 Number and percentage of subjects with anti-T antibody concentrations equal to or above 0.1 IU per ml and 1.0 IU per ml and GMCs (ATP cohort for immunogenicity at Month 73)

				≥ 0.1 IU/ml				≥ 1 IU/ml				GMC		
						95% CI				95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	n	%	LL	UL	value	LL	UL
anti-T	HibMenC	PII(M73)	103	103	100	96.5	100	102	99.0	94.7	100	15.6	13.1	18.6
	Hib+MCC	PII(M73)	34	34	100	89.7	100	33	97.1	84.7	99.9	12.5	8.4	18.7

HibMenC = Vaccinated with Hib-MenC-TT + *Priorix* in study Hib-MenC-TT-016 and MenACWY-TT in study MenACWY-TT-106

Hib+MCC = Vaccinated with *Meningitec* + *Hiberix* + *Priorix* in study Hib-MenC-TT-016 and MenACWY-TT in study MenACWY-TT-106

During the 4-day (Days 0-3) post-dose follow-up period for solicited local symptoms, pain was reported slightly less often in the Hib+MCC sub-group but rates for redness and swelling were comparable. Grade 3 pain was reported by one subject (0.8%) in the HibMenC sub-group and Grade 3 redness and swelling were reported by no more than 5.4% of subjects in the two sub-groups.

Table 7 Incidence of solicited local symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated cohort at Month 73)

		HibMenC					Hib+MCC				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Pain	All	118	69	58.5	49.0	67.5	37	15	40.5	24.8	57.9
	Grade 3	118	1	0.8	0.0	4.6	37	0	0.0	0.0	9.5
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
Redness (mm)	All	118	56	47.5	38.2	56.9	37	19	51.4	34.4	68.1
	>50	118	4	3.4	0.9	8.5	37	2	5.4	0.7	18.2
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
Swelling (mm)	All	118	30	25.4	17.9	34.3	37	8	21.6	9.8	38.2
	>50	118	2	1.7	0.2	6.0	37	0	0.0	0.0	9.5
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5

Fatigue was the most frequently reported solicited general symptom (at most 27%), followed by gastrointestinal symptoms and headache by at most 24.6%. There were no very high fevers reported.

Table 8 Incidence of solicited general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated cohort at Month 73)

		HibMenC					Hib+MCC				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Fatigue	All	118	31	26.3	18.6	35.2	37	10	27.0	13.8	44.1
	Grade 3	118	2	1.7	0.2	6.0	37	1	2.7	0.1	14.2
	Related	118	29	24.6	17.1	33.4	37	9	24.3	11.8	41.2
	Grade 3 Related	118	2	1.7	0.2	6.0	37	1	2.7	0.1	14.2
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
Gastrointestinal symptoms	All	118	29	24.6	17.1	33.4	37	5	13.5	4.5	28.8
	Grade 3	118	1	0.8	0.0	4.6	37	0	0.0	0.0	9.5
	Related	118	22	18.6	12.1	26.9	37	5	13.5	4.5	28.8
	Grade 3 Related	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
Headache	All	118	29	24.6	17.1	33.4	37	6	16.2	6.2	32.0
	Grade 3	118	1	0.8	0.0	4.6	37	2	5.4	0.7	18.2
	Related	118	26	22.0	14.9	30.6	37	6	16.2	6.2	32.0
	Grade 3 Related	118	1	0.8	0.0	4.6	37	2	5.4	0.7	18.2
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
Temperature/(Oral) (°C)	All	118	6	5.1	1.9	10.7	37	1	2.7	0.1	14.2
	≥37.5	118	6	5.1	1.9	10.7	37	1	2.7	0.1	14.2
	>38.0	118	2	1.7	0.2	6.0	37	0	0.0	0.0	9.5
	>38.5	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
	>39.0	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
	Related	118	5	4.2	1.4	9.6	37	1	2.7	0.1	14.2
	>39.0 Related	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5
	Medical advice	118	0	0.0	0.0	3.1	37	0	0.0	0.0	9.5

During the 31-day post-vaccination period at least one unsolicited AE was reported by 30.3% and 18.9% in the HibMenC and Hib+MCC sub-groups, respectively, while Grade 3 unsolicited AEs were reported by 6.7% and 5.4% (see table below). Unsolicited AEs assessed by the investigator as causally related to vaccination were reported by 6.7% of subjects in the HibMenC sub-group, one of which was Grade 3.

No SAEs or AEs leading to premature discontinuation of study vaccine and/or study were reported. Also, there were no NOCIs or pIMDs reported.

Table 9 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total Vaccinated cohort at Month 73)

		HibMenC N = 119				Hib+MCC N = 37			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		8	6.7	2.9	12.8	2	5.4	0.7	18.2
Gastrointestinal disorders (10017947)	Abdominal pain upper (10000087)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
General disorders and administration site conditions (10018065)	Injection site pruritus (10022093)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Infections and infestations (10021881)	Bronchitis (10006451)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
	Gastroenteritis (10017888)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
	Gastroenteritis viral (10017918)	0	0.0	0.0	3.1	1	2.7	0.1	14.2
	Subcutaneous abscess (10042343)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
	Upper respiratory tract infection (10046306)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Investigations (10022891)	Body temperature increased (10005911)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Nervous system disorders (10029205)	Headache (10019211)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	3.1	1	2.7	0.1	14.2
Skin and subcutaneous tissue disorders (10040785)	Eczema (10014184)	1	0.8	0.0	4.6	0	0.0	0.0	9.5

Table 10 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term that are causally related to vaccination, within the 31-day (Days 0-3) post-vaccination period (Total Vaccinated cohort at Month 73)

		HibMenC N = 119				Hib+MCC N = 37			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		8	6.7	2.9	12.8	0	0.0	0.0	9.5
General disorders and administration site conditions (10018065)	Injection site bruising (10022052)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
	Injection site inflammation (10022078)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
	Injection site pruritus (10022093)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Infections and infestations (10021881)	Upper respiratory tract infection (10046306)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Nervous system disorders (10029205)	Dizziness (10013573)	2	1.7	0.2	5.9	0	0.0	0.0	9.5
Psychiatric disorders (10037175)	Irritability (10022998)	1	0.8	0.0	4.6	0	0.0	0.0	9.5
Respiratory, thoracic and mediastinal disorders (10038738)	Oropharyngeal pain (10068319)	1	0.8	0.0	4.6	0	0.0	0.0	9.5

2.3.3. Discussion on clinical aspects

Children enrolled into MEN-ACWY-TT-106 had received either Menitorix (MenC-T and PRP-T) or Meningitec (MenC-CRM_{197}) plus Hiberix (PRP-T) at about one year of age. At 7 years of age, the proportions still seropositive for MenC were 19/104 (18%) in the Menitorix group and 5/34 (15%) in the Meningitec group. Some of these Australian children had naturally acquired antibody to MenA, W or Y but pre-vaccination seropositive rates were mostly <20%.

For each meningococcal serotype, all children who were seronegative at 7 years of age had a vaccine response (as defined in the protocol) after a single dose of Nimenrix compared to about 80% for the smaller subsets of children who were seropositive at pre-vaccination.

For MenC, 102/104 primed with Menitorix and 34/35 primed with Meningitec had rSBA-MenC titres ≥1:128 at one month after a dose of Nimenrix, with GMTs of 11,819 and 7420, respectively. The 95% CI around these GMTs overlapped and the imbalance in denominators should be noted. This difference in rSBA-MenC titres persisted at 2 years post-dose, when the percentages with titres ≥1:128 were 90% vs. 78.8% and the GMTs were 333 and 175 in respective priming groups. Whilst the differences between groups may not be clinically important (with 100% and 94% having titres at least 1:8 at 96 months), the findings would be in keeping with observations made in several previous studies in which the same or different conjugates were used for priming and boosting. It should be noted that the MAH's claim that Nimenrix "boosted" the rSBA-MenC titres cannot be verified based solely on the data presented. However, several previous studies have conclusively demonstrated the ability of Nimenrix to boost rSBA-MenC titres regardless of the type of conjugate used for priming.

For MenA, W and Y the percentages with rSBA titres at the 1:8 and 1:128 cut-offs and the GMTs at one month and at 2 years post-dose were numerically higher in the group primed with Menitorix but all 95% CI overlapped. It is difficult to comment further due to the imbalance in numbers and the possibility that the results reflect just a few subjects with unusually low responses.

Between one month and 2 years post-dose, the largest drops in percentages with rSBA titres at least 1:8 or 1:128 were observed for MenA. This finding is in keeping with previous studies in which SBA titres have declined more notably for MenA compared to the other serogroups. The hSBA titres were not estimated in this study. If they had been it would be expected that they would show even larger drops in titres vs. MenA compared to the rSBA data.

The safety profile of a single dose of Nimenrix at age 7 years was as expected. Although slightly higher total rates of solicited symptoms were reported in the sub-group primed with Menitorix, there was no excess of Grade 3 or related AEs in this sub-group.

In conclusion

There results reported at up to 2 years after a dose of Nimenrix administered to 7-year-old children who had been primed with a meningococcal serogroup C conjugate vaccine were very much as expected. There were no issues raised by the safety data. There is no need to make any changes to the SmPC based on these results.

3. Rapporteur's overall conclusion and recommendation

☒ Fulfilled:

No further action required.