30 November 2016
EMA/793588/2016
Human Medicines Evaluation Division

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

Infanrix hexa

diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed)

Procedure no: EMEA/H/C/000296/P46/124

Note

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

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1. Introduction

This report covers the following post-authorisation commitments undertaken by the MAH:

1.1. Steps taken for the assessment

Submission date:	19/08/2016
Start of procedure:	12/09/2016
CHMP Rapporteur's preliminary assessment report circulated on:	17/10/2016
CHMP Rapporteur's updated assessment report circulated on:	28/10/2016
CHMP opinion:	10/11/2016

2. Assessment of the post-authorisation measure PAM 124

[Study initiation date: 01-July-2010/ Study completion date: 10-September-2013 Data lock point (Date of database freeze): 21-August-2015]

This PAM is the stand-alone submission of the final study report for the study 113369 (MENACWY-TT-083), in accordance with Article 46 of Regulation (EC) No 1901/2006. A short critical expert overview has been provideThe Company concluded that currently no changes to the Product Information of Infanrix hexa are needed.

Methods:

This study was a phase IIIb open, multi-country, randomised, controlled study designed to demonstrate the non-inferiority of the immune response of GSK Biologicals' meningococcal serogroup A, C, W-135 and Y conjugate vaccine Nimenrix™ (MenACWY-TT) when given intramuscularly at 2, 4 and 12 months of age or given at 2, 3, 4 and 12 months of age compared to two licensed MenC conjugate vaccine given intramuscularly at 2, 4 and 12 months of age.

This multicentre study was conducted in 44 centres located in three countries (Estonia, Germany and Spain).

Duration of treatment: The duration of the study was approximately 16 months for each subject.

Study design

This was a phase IIIB self-contained, open, multi-country, randomized, controlled study with four parallel groups. Blood samples were collected from each subject at pre-vaccination (Day 0), one month after the last priming vaccination (Month 3), at pre-booster (Month 10) and post-booster (Month 11).

Study Population was composed of male or female infants between, and including, 6-12 weeks (42-90 days) of age at the time of the first study vaccination.

The study groups were as follows:

• Group ACWY_3: subjects received three primary vaccination doses of MenACWY-TT vaccine at 2, 3 and 4 months of age and one booster dose of MenACWY-TT vaccine at 12 months of age.

• Group ACWY_2: subjects received two primary vaccination doses of MenACWY-TT vaccine at 2 and 4 months of age and one booster dose of MenACWY-TT vaccine at 12 months of age.

• Group MenCCRM: subjects received two primary vaccination doses of Menjugate vaccine at 2 and 4 months of age and one booster dose of Menjugate vaccine at 12 months of age (active control group).

• Group MenC-TT: subjects received two primary vaccination doses of NeisVac-C vaccine at 2 and 4 months of age and one booster dose of NeisVac-C vaccine at 12 months of age (active control group).

All subjects were vaccinated with Infanrix hexa and Synflorix at 2, 3, 4 and 12 months of age.

Primary Outcome/Efficacy Variable concerned Immunogenicity with respect to components of the investigational vaccine.

- rSBA titres ≥ 1:8 for each of the four serogroups in all subjects, one month after the final priming vaccination.

Secondary Outcome for Infanrix hexa immunogenicity and safety assessment:

1. Immunogenicity with respect to components of the co-administered Infanrix hexa :

   Antibody concentrations/titres for

   - anti-diphtheria (≥0.1 IU/ml and concentrations),
   - anti-tetanus (≥0.1 IU/ml and concentrations),
   - anti-PT, anti-FHA, anti-PRN (≥ 5 EL.U/ml and concentrations),
   - anti-HBs (≥10 mIU/ml, ≥100 mIU/ml and concentrations),
   - anti-polio type 1, 2 and 3 (≥1:8 and titres),
   - anti-PRP (≥0.15 μg/ml, ≥1.0 μg/ml and concentrations) antibodies

   in a randomised subset of 25% of subjects, at pre-vaccination, one month after the final priming vaccination, pre-booster and one month post-booster dose.

2. Safety

   To evaluate the safety and reactogenicity of the investigational vaccine.

Results:

Demography:

Primary epoch
Across all vaccine groups the mean age of the subjects in the Primary ATP cohort for immunogenicity was 8.7 weeks (range 6 to 12 weeks) with a standard deviation of 1.5. The distribution of males and females was similar with 50.5% male and 49.5% female. According to geographic ancestry, the majorityof subjects were White/Caucasian/European Heritage (94.2%), 2.6% of subjects were White - Arabic /
North African Heritage and 1.6% of subjects Other.

Booster epoch
Across all vaccine groups the mean age of the subjects in the Booster ATP cohort for immunogenicity was 12.1 months (range 12 to 13 months) with a standard deviation of 0.4. The distribution of males andfemales was similar with 49.9% male and 50.1% female. According to geographic ancestry, the majorityof subjects were White/Caucasian/European Heritage (95.1%), 2.1% of subjects were White - Arabic /
North African Heritage and 1.3% of subjects Other.

The demographic profile of the Primary and Booster Total Vaccinated Cohorts and Primary and Booster ATP cohorts for safety were similar to those described for the Primary and Booster ATP cohorts for immunogenicity.

Study population - primary epoch (Primary Total Vaccinated cohort)				
Number of subjects	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
Planned, N	515	515	515	515
Randomised, N (Primary Total Vaccinated cohort)	528	524	516	527
Completed Primary epoch, n (%)	508 (96.2)	517 (98.7)	508 (98.4)	509 (96.6)
Demographics	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
N (Primary Total Vaccinated cohort)	528	524	516	527
Females:Males	255:273	273:251	264:252	251:276
Mean Age, weeks (SD)	8.7 (1.5)	8.6 (1.5)	8.7 (1.5)	8.6 (1.5)
Median Age, weeks (minimum, maximum)	9 (5, 13)	8 (6, 12)	9 (6, 13)	9 (5, 12)
White - Caucasian / European Heritage, n (%)	500 (94.7)	497 (94.8)	486 (94.2)	495 (93.9)
White - Arabic / North African Heritage, n (%)	12 (2.3)	8 (1.5)	10 (1.9)	21 (4.0)
Other, n (%)	8 (1.5)	9 (1.7)	8 (1.6)	7 (1.3)
ACWY_3 = Subjects who received 3 primary doses of MenACWY-TT at 2, 3 and 4 months of age ACWY_2 = Subjects who received 2 primary doses of MenACWY-TT at 2 and 4 months of age MenCCRM = Subjects who received 2 primary doses of *Menjugate* at 2 and 4 months of age MenC-TT = Subjects who received 2 primary doses of *NeisVac-C* at 2 and 4 months of age				
Study population - booster epoch (Booster Total Vaccinated cohort)				
Number of subjects	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
Planned, N	515	515	515	515
Randomised, N (Booster Total Vaccinated cohort)	497	511	503	506
Completed Booster epoch, n (%)	494* (99.4)	509 (99.6)	498 (99.0)	505 (99.8)
Demographics	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
N (Booster Total Vaccinated cohort)	497	511	503	506
Females:Males	241:256	265:246	256:247	244:262
Mean Age, months (SD)	12.2 (0.6)	12.1 (0.4)	12.1 (0.4)	12.1 (0.4)
Median Age, months (minimum, maximum)	12 (11, 21)	12 (11, 14)	12 (11, 15)	12 (11, 14)
White - Caucasian / European Heritage, n (%)	471 (94.8)	485 (94.9)	475 (94.4)	475 (93.9)
White - Arabic / North African Heritage, n (%)	12 (2.4)	8 (1.6)	9 (1.8)	21 (4.2)
Other, n (%)	7 (1.4)	8 (1.6)	7 (1.4)	7 (1.4)
ACWY_3 = Subjects who received 3 primary doses of MenACWY-TT at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age ACWY_2 = Subjects who received 2 primary doses of MenACWY-TT at 2 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age MenCCRM = Subjects who received 2 primary doses of *Menjugate* at 2 and 4 months of age and 1 booster dose of *Menjugate* at 12 months of age MenC-TT = Subjects who received 2 primary doses of *NeisVac-C* at 2 and 4 months of age and 1 booster dose of *NeisVac-C* at 12 months of age did not receive booster dose at visit 5, however completed post booster visit, Visit 6. This subject is not considered in this table				

Study population - ESFU (Booster Total Vaccinated cohort)				
Number of subjects	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
Planned, N	515	515	515	515
Randomised, N (Booster Total Vaccinated cohort)	497	511	503	506
Completed ESFU, n (%)	492* (99.0)	502 (98.2)	496 (98.6)	505* (99.8)
Demographics	**ACWY_3**	**ACWY_2**	**MenCCRM**	**MenC-TT**
N (Booster Total Vaccinated cohort)	497	511	503	506
Females:Males	241:256	265:246	256:247	244:262
Mean Age, months (SD)	12.2 (0.6)	12.1 (0.4)	12.1 (0.4)	12.1 (0.4)
Median Age, months (minimum, maximum)	12 (11, 21)	12 (11, 14)	12 (11, 15)	12 (11, 14)
White - Caucasian / European Heritage, n (%)	471 (94.8)	485 (94.9)	475 (94.4)	475 (93.9)
White - Arabic / North African Heritage, n (%)	12 (2.4)	8 (1.6)	9 (1.8)	21 (4.2)
Other, n (%)	7 (1.4)	8 (1.6)	7 (1.4)	7 (1.4)
ACWY_3 = Subjects who received 3 primary doses of MenACWY-TT at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age ACWY_2 = Subjects who received 2 primary doses of MenACWY-TT at 2 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age MenCCRM = Subjects who received 2 primary doses of *Menjugate* at 2 and 4 months of age and 1 booster dose of *Menjugate* at 12 months of age MenC-TT = Subjects who received 2 primary doses of *NeisVac-C* at 2 and 4 months of age and 1 booster dose of *NeisVac-C* at 12 months of age did not receive booster dose at Visit 5, however completed ESFU visit, Visit 7. These subjects are not considered in this table				

<u>Immunogenicity</u> concerning Infanrix –hexa as Secondary objectives:

At one month post-primary vaccination the responses were:

Anti-D:

- The percentage of subjects with anti-D concentrations ≥0.1 IU/ml was 100% for all four vaccine groups. The percentage of subjects with anti-D concentrations ≥1.0 IU/ml ranged from 84.6% for the ACWY_3 group to 94.3% for the MenCCRM group.

GMCs ranged from 2.171 IU/ml in the ACWY_3 group to 3.005 IU/ml in the MenCCRM group.

Anti-TT:

- The percentage of subjects with anti-TT concentrations ≥ 0.1 IU/ml was 100% for all four vaccine groups. The percentage of subjects with anti-TT concentrations ≥1.0 IU/ml ranged from 95.6% for the ACWY_2 group to 99.1% for the MenC-TT group.

GMCs ranged from 2.847 IU/ml in the MenCCRM group to 4.339 IU/ml in the MenC-TT group.

Anti-PT, FHA and PRN:

- All subjects in all four groups had anti-PT, anti-FHA and anti-PRN antibody concentrations ≥5 EL.U/ml.

GMCs ranged from 52.7 EL.U/ml for PT in the ACWY_3 group to 149.2 EL.U/ml for FHA in the ACWY_2 group.

Anti-PT, FHA and PRN vaccine response:

- Vaccine response to the pertussis antigens ranged from 82.4% for FHA in the MenC-TT group to 95.5% for PT in the MenCCRM group.

Anti-HBs:

- The percentage of subjects with anti-HBs concentrations ≥ 10.0 mIU/ml was 98.9% % for the ACWY_3 98.8% in the MenC-TT groups and 100% for the ACWY_2 and MenCCRM groups.

- The percentage of subjects with anti-HBs concentrations ≥ 100 mIU/ml ranged from 86.2% for the ACWY_3 group to 94.7% for the MenCCRM group.

GMCs ranged from 697.1mIU/ml in the ACWY_3 group to 848.3 mIU/ml in the MenCCRM group.

Anti-PRP:

- The percentage of subjects with anti-PRP concentrations ≥ 0.15 µg/ml ranged from 98.4% (MenCCRM group) to 100% (ACWY_3 and ACWY_2 groups). The percentage of subjects with anti-PRP concentrations ≥ 1.0 µg/ml ranged from 76.4% (MenCCRM group) to 93.0% (MenC-TT group).

GMCs ranged from 2.752 µg/ml in the MenCCRM group to 4.662 µg/ml in the MenC-TT group.

Anti-polio (see Table 1.)

- The percentage of subjects with anti-polio titres ≥ 1:8 ranged from:
  - 97.7% (MenC-TT group) to 100% (ACWY_3 and ACWY_2 groups) for anti-polio 1.
  - 97.2% (MenC-TT group) to 100.0% (ACWY_3 and MenCCRM groups) for anti-polio 2.
  - 98.7% (MenC-TT group) to 100.0% (ACWY_2, ACWY_3 and MenCCRM groups) for anti-polio 3.

Table 1 Number and percentage of subjects with anti-Polio 1, anti-Polio 2 and anti-Polio 3 antibody titres equal to or above 1:8 and GMTs (Primary ATP cohort for immunogenicity)

				≥ 1:8				GMT		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
anti-Polio 1	ACWY_3	PRE	71	52	73.2	61.4	83.1	32.7	22.5	47.5
		PIII(M3)	91	91	100	96.0	100	279.6	222.4	351.5
	ACWY_2	PRE	58	46	79.3	66.6	88.8	40.2	27.3	59.3
		PIII(M3)	83	83	100	95.7	100	317.9	227.6	444.0
	MenCCRM	PRE	72	54	75.0	63.4	84.5	28.1	20.1	39.3
		PIII(M3)	90	89	98.9	94.0	100	424.1	323.1	556.6
	MenC-TT	PRE	58	46	79.3	66.6	88.8	30.7	21.5	43.9
		PIII(M3)	86	84	97.7	91.9	99.7	277.7	200.7	384.1
anti-Polio 2	ACWY_3	PRE	64	39	60.9	47.9	72.9	19.4	13.2	28.7
		PIII(M3)	81	81	100	95.5	100	225.2	173.2	292.6
	ACWY_2	PRE	54	40	74.1	60.3	85.0	28.0	18.4	42.5
		PIII(M3)	71	70	98.6	92.4	100	244.8	173.3	345.9
	MenCCRM	PRE	66	44	66.7	54.0	77.8	17.4	12.7	23.8
		PIII(M3)	81	81	100	95.5	100	274.5	202.1	372.8
	MenC-TT	PRE	62	41	66.1	53.0	77.7	22.9	15.6	33.5
		PIII(M3)	72	70	97.2	90.3	99.7	232.7	160.8	336.6
anti-Polio 3	ACWY_3	PRE	58	21	36.2	24.0	49.9	11.5	7.6	17.5
		PIII(M3)	93	93	100	96.1	100	642.7	478.7	862.8
	ACWY_2	PRE	52	21	40.4	27.0	54.9	11.7	7.8	17.5
		PIII(M3)	79	79	100	95.4	100	675.0	486.3	936.9
	MenCCRM	PRE	60	11	18.3	9.5	30.4	5.9	4.7	7.5
		PIII(M3)	87	87	100	95.8	100	674.0	525.5	864.5
	MenC-TT	PRE	51	23	45.1	31.1	59.7	14.2	8.8	22.8
		PIII(M3)	78	77	98.7	93.1	100	494.3	347.4	703.3

At one month post-booster vaccination responses were:

Anti-D:

The percentage of subjects with anti-D concentrations post-booster ≥0.1 IU/ml was 100% for all four vaccine groups. The percentage of subjects with anti-D concentrations ≥1.0 IU/ml ranged from 94.6% for the ACWY_2 group to 100% for the MenCCRM group. GMCs ranged from 5.032 IU/ml in the ACWY_3 group to 9.078 IU/ml in the MenCCRM group.

Anti-TT:

The percentage of subjects with anti-TT concentrations post-booster ≥0.1 IU/ml was 100% for all four vaccine groups. The percentage of subjects with anti-TT concentrations ≥1.0 IU/ml was from 99.2% for the MenCCRM group and 100% for the other three vaccine groups. GMCs ranged from 8.400 IU/ml in the MenCCRM group to 13.016 IU/ml in the MenC-TT group.

Anti-PT, FHA and PRN:

All subjects in all four groups had anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 EL.U/ml. GMCs ranged from 78.2 EL.U/ml for PT in the ACWY_2 group to 334.3 EL.U/ml for PRN in the MenC-TT group.

Anti-PT, FHA and PRN booster response:

Booster response to the pertussis antigens ranged from 92.2% for PT in the MenCCRM group to 100% for PRN in the ACWY_2 group.

Anti-HBs:

The percentage of subjects with anti-HBs concentrations ≥ 10.0 mIU/ml was 97.9% for the ACWY_3 and 100% for the ACWY_2 and MenCCRM and MenC-TT groups. The percentage of subjects with anti-HBs concentrations post-booster ≥ 100 mIU/ml ranged from 95.9% for the ACWY_3 group to 100% for the ACWY_2 group. GMCs ranged from 3624.9 mIU/ml in the ACWY_3 group to 4866.4 mIU/ml in the MenCCRM group.

Anti-PRP:

All subjects in all four groups had anti-PRP concentrations ≥ 0.15 µg/ml. The percentage of subjects with anti-PRP concentrations ≥1.0 µg/ml ranged from 96.6% for the MenC-TT group to 100% for the ACWY_2 and MenCCRM groups. GMCs ranged from 17.350 µg/ml in the ACWY_3 group to 23.973 µg/ml in the MenC-TT group.

Anti-polio (see Table 2.)

At 1 month post-boost, all subjects in all groups had anti-polio 1, 2, 3 titres ≥ 1:8.

Table 2 Number and percentage of subjects with anti-Polio 1, anti-Polio 2 and anti-Polio 3 antibody titres equal to or above 1:8 and GMTs (Booster ATP cohort for immunogenicity)

				≥ 1:8				GMT		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
anti-Polio 1	ACWY_3	PRE	65	49	75.4	63.1	85.2	34.7	23.5	51.1
		PIII(M3)	85	85	100	95.8	100	275.6	218.0	348.5
		PIII(M10)	80	74	92.5	84.4	97.2	74.9	56.3	99.6
		PIV(M11)	85	85	100	95.8	100	909.8	694.1	1192.6
	ACWY_2	PRE	55	43	78.2	65.0	88.2	39.0	26.0	58.3
		PIII(M3)	80	80	100	95.5	100	300.3	214.1	421.3
		PIII(M10)	68	63	92.6	83.7	97.6	84.7	60.0	119.7
		PIV(M11)	85	85	100	95.8	100	1070.9	812.5	1411.4
	MenCCRM	PRE	70	55	78.6	67.1	87.5	33.0	23.5	46.4
		PIII(M3)	89	88	98.9	93.9	100	418.3	316.5	552.9
		PIII(M10)	82	80	97.6	91.5	99.7	120.8	92.5	157.8
		PIV(M11)	81	81	100	95.5	100	1524.5	1214.9	1913.0
	MenC-TT	PRE	55	43	78.2	65.0	88.2	30.3	20.9	43.8
		PIII(M3)	90	88	97.8	92.2	99.7	282.1	205.9	386.4
		PIII(M10)	87	81	93.1	85.6	97.4	90.0	65.8	123.0
		PIV(M11)	84	84	100	95.7	100	1217.7	956.5	1550.2
anti-Polio 2	ACWY_3	PRE	56	35	62.5	48.5	75.1	20.4	13.4	31.0
		PIII(M3)	75	75	100	95.2	100	221.8	171.9	286.3
		PIII(M10)	71	69	97.2	90.2	99.7	93.7	71.1	123.5
		PIV(M11)	70	70	100	94.9	100	1205.7	902.2	1611.3
	ACWY_2	PRE	54	38	70.4	56.4	82.0	26.4	17.2	40.6
		PIII(M3)	70	69	98.6	92.3	100	258.4	181.2	368.6
		PIII(M10)	70	66	94.3	86.0	98.4	80.1	57.6	111.5
		PIV(M11)	74	74	100	95.1	100	1306.3	985.1	1732.2
	MenCCRM	PRE	65	44	67.7	54.9	78.8	18.2	13.1	25.1
		PIII(M3)	79	79	100	95.4	100	280.9	204.1	386.6
		PIII(M10)	86	83	96.5	90.1	99.3	112.5	86.7	146.1
		PIV(M11)	71	71	100	94.9	100	2068.0	1602.7	2668.5
	MenC-TT	PRE	60	40	66.7	53.3	78.3	24.2	16.2	36.3
		PIII(M3)	77	75	97.4	90.9	99.7	231.0	162.3	328.6
		PIII(M10)	77	72	93.5	85.5	97.9	78.1	57.6	105.9
		PIV(M11)	68	68	100	94.7	100	1419.0	1088.4	1849.9
anti-Polio 3	ACWY_3	PRE	51	20	39.2	25.8	53.9	12.4	7.9	19.6
		PIII(M3)	88	88	100	95.9	100	653.5	488.7	873.9
		PIII(M10)	61	57	93.4	84.1	98.2	115.0	80.1	165.2
		PIV(M11)	79	79	100	95.4	100	1681.0	1285.1	2198.9
	ACWY_2	PRE	48	17	35.4	22.2	50.5	10.7	7.0	16.4
		PIII(M3)	77	77	100	95.3	100	704.7	517.5	959.5
		PIII(M10)	65	62	95.4	87.1	99.0	104.6	77.9	140.3
		PIV(M11)	67	67	100	94.6	100	2167.8	1645.7	2855.6
	MenCCRM	PRE	57	11	19.3	10.0	31.9	6.3	4.8	8.4
		PIII(M3)	84	84	100	95.7	100	666.8	518.3	857.8
		PIII(M10)	63	62	98.4	91.5	100	155.2	118.3	203.7
		PIV(M11)	74	74	100	95.1	100	2136.2	1688.1	2703.4
anti-Polio 3	MenC-TT	PRE	48	20	41.7	27.6	56.8	13.8	8.3	22.9
		PIII(M3)	82	81	98.8	93.4	100	532.0	380.5	743.9
		PIII(M10)	68	64	94.1	85.6	98.4	108.6	77.6	152.1
		PIV(M11)	69	69	100	94.8	100	1852.2	1425.6	2406.4

ACWY_3 = Subjects who received 3 primary doses of MenACWY-TT at 2, 3 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age
ACWY_2 = Subjects who received 2 primary doses of MenACWY-TT at 2 and 4 months of age and 1 booster dose of MenACWY-TT at 12 months of age
MenCCRM = Subjects who received 2 primary doses of *Menjugate* at 2 and 4 months of age and 1 booster dose of *Menjugate* at 12 months of age
MenC-TT = Subjects who received 2 primary doses of *NeisVac-C* at 2 and 4 months of age and 1 booster of *NeisVac-C* at 12 months of age
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-primary vaccination at Month 0
PIII(M3) = Post primary vaccination at Month 3
PIII(M10) = Pre-booster vaccination at Month 10
PIV(M11) = Post booster vaccination at Month 11

Safety:

In Primary phase

Unsolicited AEs

- At least one unsolicited symptom was reported by 52.1% - 56.4% of subjects across the four study groups during the 31-day period after primary vaccination**.**

SAEs

- At least one SAE was reported by 6.4% of subjects (MenCCRM group) to 8.1% of subjects (ACWY_3 group) from study start up to the day preceding the booster vaccination.
- One subject in the ACWY_3 group reported a SAE (epilepsy) which was considered by the investigator to be vaccine related.

In Booster phase

Unsolicited AEs

- At least one unsolicited symptom was reported by 32.6% - 36.4% of subjects across the four study groups during the 31-day period after booster vaccination**.**

SAEs

- At least one SAE was reported by 2.8% of subjects (ACWY_3 and MenCCRM groups) to 3.5% of subjects (ACWY_2 group) from the booster vaccination up to the end of the ESFU, none of which were considered by the investigator to be related to study vaccination.

3. Rapporteur's overall conclusion

Stand-alone submission of the final study report for this study, in accordance with Article 46 of Regulation (EC) No 1901/2006. A short critical expert overview has been provided. Vaccination with MenACWY-TT (Nimenrix) in infants when co-administered with Infanrix hexa (DTPa-HBV-IPV/ Hib) and Synflorix (PCV10) was immunogenic and well tolerated and no safety concerns were identified. The Company concluded that currently no changes to the Product Information of Infanrix hexa are needed.

The Rapporteur endorses the discussion and conclusion of the MAH concerning immunogenicity and safety of the post-primary and booster results of Infanrix hexa in this standalone submission of the paediatric study MENACWY-TT-083 (GSK Study 113369).

☒ PAM fulfilled (all commitments fulfilled) - No further action required

☐ PAM not fulfilled (not all commitments fulfilled) and further action required: