25 June 2026
EMADOC-1700519818-3067648
Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of 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: EMA/PAM/0000340642

Note

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

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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	28 May 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

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1. Introduction

On 3 April 2026, the MAH submitted a completed paediatric study for Infanrix hexa, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that "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

A list of investigational products used in this study are presented in Table 1 below.

Table 1. Study interventions administered (Source: Report Body Table 5)

Study intervention name	**AltSonflex1-2-3 Dose A (diluted from Dose C)**		**AltSonflex1-2-3 Dose B (diluted from Dose C)**		**AltSonflex1-2-3 Dose C**	**altSonflex Placebo**	***MENVEO***		***BOOSTRIX***	***INFANRIX HEXA***		***TYPHIMVI***	***MR-VAC***	
Study intervention formulation	*Shigella sonnei* GMMA adsorbed on $Al(OH)_3$(3.75 µg OAg); *Shigella flexneri 1b* GMMA adsorbed on $Al(OH)_3$ (3.75 µg OAg); *Shigella flexneri 2a* GMMA adsorbed on $Al(OH)_3$ (3.75 µg OAg); *Shigella flexneri 3a* GMMA adsorbed on $Al(OH)_3$ (3.75 µg OAg);	$Al(OH)_3$ suspended in buffered saline (q.s. 0.375 mL)	*Shigella sonnei* GMMA adsorbed on $Al(OH)_3$ (7.5 µg OAg); *Shigella flexneri 1b* GMMA adsorbed on $Al(OH)_3$ (7.5 µg OAg); *Shigella flexneri 2a* GMMA adsorbed on $Al(OH)_3$ (7.5 µg OAg);	$Al(OH)_3$ suspended in buffered saline (q.s. 0.25 mL)	*Shigella sonnei* GMMA adsorbed on $Al(OH)_3$ (15 µg OAg); *Shigella flexneri 1b* GMMA adsorbed on $Al(OH)_3$ (15 µg OAg); *Shigella flexneri 2a* GMMA adsorbed on $Al(OH)_3$ (15 µg OAg); *Shigella flexneri 3a*	$Al(OH)_3$ suspended in buffered saline (q.s. 0.5 mL)	MenA(10 µg)-CRM_{197} (16.7-33.3 µg)	MenC(5 µg)-CRM_{197} (7.1-12.5 µg); MenW-135(5 µg)-CRM_{197}(3.3-8.3 µg); MenY(5 µg)-CRM_{197} (5.6-10 µg); Water for injections q.s. 0.5 mL	DT (≥ 2 IU) adsorbed on aluminium hydroxide and aluminium phosphate; TT (≥ 20 IU) adsorbed on aluminium hydroxide and aluminium phosphate; PT (8 µg) adsorbed on aluminium	DT[1] (≥ 30 IU); TT[1] (≥ 40 IU); PT (25 µg)[1]; FHA (25 µg)[1]; PRN (8 µg)[1]; HBsAg (10 µg)[2]; IPV1 (Mahoney strain) (40 DAgU); IPV2 (MEF-1 strain) (8 DAgU); IPV3 (Saukett strain)	Hib (10 µg)-TT (~25 µg) adsorbed on $AlPO_4$; $AlPO_4$	Vi capsular polysaccharide of *Salmonella typhi* (Ty2 strain) (25 µg); Water for Injections q.s. 0.5 mL	Measles Virus Edmonston strain (live, attenuated) (≥ 1000 $CCID_{50}$); Rubella Virus Wistar RA 27/3 strain (live, attenuated) (≥ 1000 $CCID_{50}$)	Water for injections (0.5 mL)

	$Al(OH)_3$ suspended in buffered saline (q.s. 0.125 mL)		*Shigella flexneri 3a* GMMA adsorbed on $Al(OH)_3$ (7.5 µg OAg); $Al(OH)_3$ suspended in buffered saline (q.s. 0.25 mL)		GMMA adsorbed on $Al(OH)_3$ (15 µg OAg); $Al(OH)_3$ suspended in buffered saline (q.s. 0.5 mL)				hydroxide and aluminium phosphate; FHA (8 µg) adsorbed on aluminium hydroxide and aluminium phosphate; PRN (2.5 µg) adsorbed on aluminium hydroxide and aluminium phosphate; Aluminium hydroxide	(32 DAgU); [1]adsorbed on $Al(OH)_3$ and [2]adsorbed on $AlPO_4$ (0.7 mg Al^{3+}); Water for injections					

									(0.3 mg Al^{3+}); Aluminium phosphate (0.2 mg Al^{3+}); Water for injections q.s. 0.5 mL					
Presentation	Vial, suspension for suspension for injection	Vial, Suspension for suspension for injection	Vial, suspension for suspension for injection	Vial, Suspension for suspension for injection	Vial, suspension for injection	Vial, suspension for injection	Vial, powder for solution for injection	Vial, solution for solution for injection	Syringe, suspension for injection	Pre-filled syringe, suspension for suspension for injection	Vial, powder for suspension for injection	Syringe, solution for injection	Powder for suspension for injection	Solution for suspension for injection
Type	Investigational product		Investigational product		Investigational product	Placebo	Comparator		Comparator	Comparator		Comparator	Co-administered product	
Product category	Biologic		Biologic		Biologic	Drug	Biologic		Combination Product	Combination Product		Combination product	Biologic	

Route of administration	Intramuscular								Subcutaneous
Location	Deltoid in adults and children, thigh in infants			Deltoid	Deltoid in adults and children, anterolateral thigh in infants	Deltoid	Thigh	Deltoid	Deltoid
Directionality	Upper in adults and children, anterolateral in infants			Upper	Upper in adults and children, anterolateral in infants	Upper	Anterolateral	Upper	Upper
Laterality *	Non-dominant								
Number of doses to be administered:	3 in infants	3 in infants, 2 in children	2 in adults and children, 3 in infants	2 in adults (Stage 1)	1 in adults (Stage 2), 1 in children, 2 in infants	1 in adults (Stage 2)	1 in infants	1 in children	2 in infants
Volume to be administered	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.5 mL
Packaging and labelling	Mentioned in Study Procedures Manual								
Responsible for manufacture	Dilution at clinical site		GSK					Sanofi Pasteur	Serum Institute of India

*The non-dominant arm was the preferred arm of injection. In case it was not possible to administer the study intervention in the non-dominant arm, an injection in the dominant arm was performed.

2.3. Clinical aspects

Introduction

The MAH submitted a final report for the study (number 212149, EudraCT number: 2021-000891-12): "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

Shigellosis remains a major public health problem around the world; it is the leading bacterial cause of diarrheal deaths worldwide. GSK is developing a multicomponent Shigella vaccine to prevent the burden of shigellosis in infants and children in developing countries where shigellosis is endemic. Currently, there are no widely used vaccines against *Shigella sonnei (S. sonnei)* and *Shigella flexneri (S. flexneri)* serotypes despite several attempts in the last decades. GSK Vaccines Institute for Global Health (GVGH) has developed a new candidate Shigella 4-component generalised modules for membrane antigen (GMMA) vaccine (GSK4001785A or altSonflex1-2-3) against *S. sonnei* and *S. flexneri* serotypes 1b, 2a, and 3a, which is based on the previously developed GVGH monovalent *S. sonnei* vaccine (1790GAHB vaccine) using the GMMA-platform technology (Generalised Modules for Membrane Antigens).

SHIGELLA 4 GMMA GVGH-001 (H06_01TP) study was a Phase 1/2 observer-blind, controlled, randomised, multi-country, staged, age de-escalation study to evaluate the safety and immunogenicity of the altSonflex1-2-3 GMMA candidate vaccine against *S. sonnei* and *S. flexneri* serotypes 1b, 2a, and 3a. Infanrix hexa was part of the active control vaccines along with Menveo. MR-VAC was also administered as part of the National Immunisation Program (NIP). Infanrix hexa being an active control vaccine, was not 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.

Methods

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).

Treatments

The candidate altSonflex1-2-3 vaccine was administered intramuscularly at 3 different doses (Dose A [low], Dose B [medium], and Dose C [high]) (Figure below). Study completion was defined as the date of last testing/reading released of the human biological samples or imaging data, related to primary and secondary endpoints.

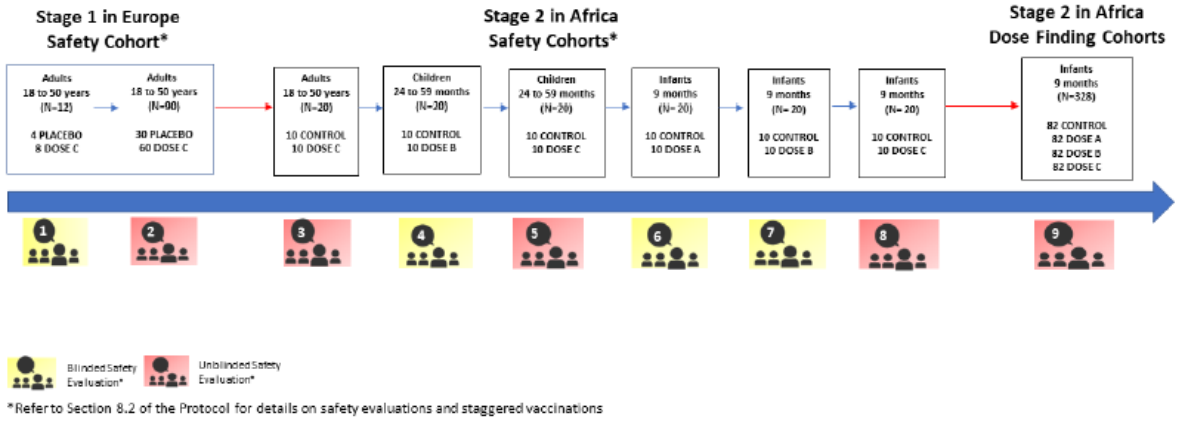

Figure 1. Study design (Source: Clinical Overview Figure 1)

In Stage 2 of the study, infant participants in the Control group received the following vaccines:

- Infants 9 months of age, Safety cohort: 2 doses of 0.5 mL Menveo 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 on Day 29 and Day 281.
- Infants 9 months of age, Dose-finding cohort: 2 doses of 0.5 mL Menveo 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 on Day 1 and Day 253.

The study groups, intervention, and blinding of Stage 2 Infants 9 months of age Safety cohort and Infants 9 months of age Dose-finding cohort are shown in Table below.

Table 2. Study groups, intervention, and blinding of Stage 2 Infants 9 months of age Safety cohort and Infants 9 months of age Dose-finding cohort (Source: Clinical Overview Table 1)

Study groups	Study groups analyzed	Number of participants	Study intervention	Blinding
				Screening → Visit 9 (observer-blind)
ST2_Infants_Control A_Safety	Control	10	*Menveo* (Day 1 and Day 85), *MR-VAC* (Day 29 and Day 281), *Infanrix hexa* (Day 253)	•
ST2_Infants_Control B_Safety		10	*Menveo* (Day 1 and Day 85), *MR-VAC* (Day 29 and Day 281), *Infanrix hexa* (Day 253)	•
ST2_Infants_Control C_Safety		10	*Menveo* (Day 1 and Day 85), *MR-VAC* (Day 29 and Day 281), *Infanrix hexa* (Day 253)	•
ST2_Infants_Dose A_Safety	Dose A (low)	10	Dose A altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 29 and Day 281)	•
ST2_Infants_Dose B_Safety	Dose B (medium)	10	Dose B altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 29 and Day 281)	•
ST2_Infants_Dose C_Safety	Dose C (high)	10	Dose C altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 29 and Day 281)	•
ST2_Infants_Control_Dose finding	Control	82	*Menveo* (Day 1 and Day 85), *MR-VAC* (Day 1 and Day 253), *Infanrix hexa* (Day 253)	•
ST2_Infants_Dose A_Dose finding	Dose A (low)	82	Dose A altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 1 and Day 253)	•
ST2_Infants_Dose B_Dose finding	Dose B (medium)	82	Dose B altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 1 and Day 253)	•
ST2_Infants_Dose C_Dose finding	Dose C (high)	82	Dose C altSonflex1-2-3 (Day 1, Day 85, and Day 253), *MR-VAC* (Day 1 and Day 253)	•

Abbreviations: *MR-VAC* = measles and rubella vaccine; ST= stage.

Objective(s)

There were no study objectives directly related to Infanrix hexa. Only the safety data obtained in the paediatric population pertaining to the Control group where Infanrix hexa was administered along with Menveo (active control vaccine) and MR-VAC (vaccine as part of NIP) were reported.

Outcomes/endpoints

Data on solicited events (up to 7 days post vaccination) and unsolicited adverse events (AEs) (up to 28 days post vaccination) were presented following a single vaccine administration (Day 253) 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 were erythema, pain, and swelling as per protocol requirement. 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. Haematological, renal, and hepatic panel test results, at 7 days after each vaccination were also evaluated.

Study participants

<u>Infants 9 months of age in Africa, safety cohort:</u>

A total of 60 participants were enrolled, 30 of which received a single dose of Infanrix hexa via IM on Day 253. A total of 27 (90%) participants completed the study, while 3 (10%) participants withdrew

from the study not due to AEs. Demographic and baseline characteristics were similar across the different intervention groups.

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

A total of 329 participants were enrolled and 328 participants received the study intervention, 82 of which received Infanrix hexa co-administered with MR-VAC on Day 253. A total of 71 participants completed the study, while 11 participants withdrew from the study. Demographic and baseline characteristics were similar across the different intervention groups.

Results

Infants 9 months of age in Africa, safety cohort:

Following a single dose of Infanrix hexa administration via IM on Day 253, at least 1 solicited event was reported in 10 (37%) participants including 6 (22.2%) participants with solicited administration-site event and 4 (14.8%) participants with at least 1 solicited systemic event (fever, ≥38.0°C). At least 1 solicited administration-site event of pain was reported in 6 (22.2%) participants and swelling in 3 (11.1%) participants, no cases of erythema were reported. Pain was the most frequently reported solicited administration-site event. All solicited administration site events were of Grade 1 intensity except for 1 (3.7%) participant with Grade 2 pain. At least 1 solicited systemic event of fever was reported in 4 (14.8%) participants, 3 (11.1%) participants had at least 1 event of fever related to study vaccination as assessed by the investigator. No cases of fever ≥40℃ were reported and all of the solicited systemic events of fever were of Grade 1 intensity. Four (14.8%) participants had at least 1 unsolicited AE within the 28 days post vaccination. The reported unsolicited AEs by Preferred Term, regardless of causality, included rhinitis, conjunctivitis, abdominal distension, cough, and pyrexia (1 [3.7%] participant each). There were no Grade 3 unsolicited AEs within 28 days post vaccination reported, and none of the unsolicited AEs within 28 days post vaccination were considered related to vaccination by the investigator. Following Infanrix hexa administration, no SAEs, deaths, or AEs leading to vaccine discontinuation or study withdrawal were reported. Safety laboratory test results did not reveal specific trends.

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

Following a single dose of Infanrix hexa via IM and second dose of MR-VAC subcutaneously on Day 253, at least 1 solicited event was reported in 32 (45.1%) participants including 31 (43.7%) participants with at least 1 solicited administration-site event and 5 (7%) participants with at least 1 solicited systemic events. At least 1 solicited administration-site event of pain was reported in 26 (36.6%) participants, swelling in 14 (19.7%) participants, and erythema in 8 (11.3%) participants. Majority of the solicited administration site events were of Grade 1 intensity except for 8 (11.3%) participants with Grade 2 pain and 1 (1.4%) participant with Grade 3 pain. Pain was the most frequently reported solicited administration-site event. At least 1 solicited systemic events of fever were reported in 5 (7%) participants; 4 (5.6%) participants had at least 1 event of fever related to study vaccination as assessed by the investigator. No cases of fever ≥40℃ were reported. All the solicited systemic events of fever were of Grade 1 intensity except for 1 (1.4%) participant with Grade 2 fever. A total of 26 (36.6%) participants had at least 1 unsolicited AE within 28 days post vaccination. The most commonly reported unsolicited AEs by Preferred Term include upper respiratory tract infection (8 [11.3%] participants), rhinitis and rhinorrhoea (4 [5.6%] participants each). All other AEs were reported in ≤4.2% participants. There were no Grade 3 unsolicited AEs within 28 days post vaccination reported and none of the unsolicited AEs within 28 days post vaccination were considered related to vaccination by the investigator. Following Infanrix hexa administration, no SAEs, deaths, or

AEs leading to vaccine discontinuation/withdrawal were reported. Safety laboratory test results did not reveal specific trends.

Discussion on clinical aspects

This study was 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).

The study had 2 adult safety cohorts (18 to 50 years age in Europe and Africa), 2 child safety cohorts (24 to 59 months of age in Africa), 3 infant safety cohorts (9 months of age in Africa), and 1 infant dose-finding cohort (9 months of age in Africa).

Infanrix hexa was part of the active control vaccines along with Menveo only in stage 2 for the infants 9 months of age. MR-VAC was also administered as part of the National Immunization Program (NIP).

In the safety cohort in Africa, 30 infants 9 months of age received a single dose of Infanrix hexa on Day 253 from which 27 completed the study (3 participants withdrew not due to AEs); the second dose of MR-VAC was administrated at Day 281.

In the dose-finding cohort in Africa, 82 infants 9 months of age received a single dose of Infanrix hexa co-administered with the second dose of MR-VAC on Day 253, from which 71 completed the study, while 11 participants withdrew from the study (reason not provided).

In the safety cohort in Africa, from the 27 infants 9 months of age, following a single dose of Infanrix hexa IM administration, the most frequently reported solicited AEs were pain (22.2%) and fever (14.8%) participants. Up to 28 days post vaccination, the reported unsolicited AEs included rhinitis, conjunctivitis, abdominal distension, cough, and pyrexia (1 [3.7%] participant each). None of them were considered related to vaccination by the investigator. Most of the reported (solicited) AEs were grade 1 or 2.

In the dose-finding cohort in Africa, from the 71 infants 9 months of age, following a single dose of Infanrix hexa via IM and second dose of MR-VAC subcutaneously on Day 253, the most frequently reported solicited AEs were pain (36.6%), swelling (19.7%), erythema (11.3%), and fever (7%). Up to 28 days post vaccination, the most commonly reported unsolicited AEs were upper respiratory tract infection (8 [11.3%] participants), rhinitis and rhinorrhoea (4 [5.6%] participants each). None of them were considered related to vaccination by the investigator. Most of the reported (solicited) AEs were grade 1 or 2.

To conclude, the study findings are of limited relevance for Infanrix hexa and relate only to safety outcomes, as no Infanrix hexa-specific immunogenicity assessments were performed. Given the limited number of infants who received Infanrix hexa alone, the safety data provide only limited information specific to this vaccine. Nevertheless, the safety profile of Infanrix hexa is in line with the approved SmPC without any new identified safety concerns. Therefore, it is agreed that no update to the Infanrix hexa SmPC is deemed necessary.

3. CHMP overall conclusion and recommendation

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

☒ **Fulfilled:**

No regulatory action required.