▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – MENQUADFI® (MENINGOCOCCAL (GROUPS A, C, Y, W) POLYSACCHARIDE TETANUS TOXOID CONJUGATE VACCINE) SOLUTION FOR INJECTION

1 NAME OF THE MEDICINE

Meningococcal (Groups A, C, Y, W) Polysaccharide Tetanus Toxoid Conjugate Vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 mL dose of vaccine contains:

- Meningococcal polysaccharide* Group A 10.0 micrograms/dose
- Meningococcal polysaccharide* Group C 10.0 micrograms/dose
- Meningococcal polysaccharide* Group Y 10.0 micrograms/dose
- Meningococcal polysaccharide* Group W-135 10.0 micrograms/dose

* Each of the four polysaccharides is conjugated to tetanus toxoid (approximately 55 micrograms/dose)

MenQuadfi is a sterile solution of *Neisseria meningitidis* (*N. meningitidis*) purified capsular polysaccharides of groups A, C, W-135, and Y, individually conjugated to tetanus toxoid protein prepared from cultures of *Clostridium tetani*. No preservative or adjuvant is added during manufacture.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Solution for injection.

MenQuadfi is a clear, colourless, sterile, preservative-free solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

MenQuadfi is indicated for active immunisation of individuals from 6 weeks of age against invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W and Y.

The use of MenQuadfi should be in accordance with official recommendations.

4.2 DOSE AND METHOD OF ADMINISTRATION

MenQuadfi should be administered as a 0.5 mL single dose injection by the intramuscular route only.

Primary Vaccination

Table 1 - Dose schedules

Age at First Dose	Primary Vaccination
Infants from 6 weeks	3 doses with an interval of at least 2 months between doses and a 4th dose administered from 12 months of age at least 2 months after the third dose
Infants from 6 months to less than 12 months of age	2 doses with the 2nd dose from 12 months of age and at least 2 months after the first dose
Individuals from 12 months of age and older	One single dose

Booster Vaccination

- MenQuadfi may be given as a single booster dose to adolescents and adults who have previously been primed with meningococcal vaccine at least 3 years prior (see Section 5.1 Pharmacodynamic Properties).

Refer to official recommendations for further information regarding booster dosing.

Method of administration

MenQuadfi should be administered as a single 0.5 mL injection by intramuscular route into the deltoid region or anterolateral thigh, depending on the recipient's age and muscle mass.

No data are available to establish safety and efficacy of the vaccine using intradermal or subcutaneous routes of administration.

Refer to Section 4.5 Interactions with other medicines and other forms of interactions for concomitant administration with other vaccines.

The product is for single use only and must not be reused. Discard any remaining unused contents.

4.3 CONTRAINDICATIONS

MenQuadfi is contraindicated in anyone with a known systemic hypersensitivity reaction to any component of MenQuadfi or after previous administration of the vaccine or a vaccine containing the same components (See Section 2 Qualitative and quantitative composition and Section 6.1 List of excipients).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Appropriate observation and medical treatment should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Protection

As with any vaccine, vaccination with MenQuadfi may not protect all vaccine recipients.

MenQuadfi will not protect against *N meningitidis* serogroup B disease.

Immunisation with MenQuadfi does not substitute for routine tetanus immunisation.

Waning of serum bactericidal antibody titres against serogroup A when using human complement in the assay (hSBA) has been reported for MenQuadfi and other quadrivalent meningococcal vaccines. The clinical relevance of this observation is unknown.

Intercurrent illness

Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, should not result in the deferral of vaccination.

Syncope

Syncope can occur following or even before any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling and injury and to manage syncope.

Altered Immunocompetence

Reduced Immune Response

Some individuals with altered immunocompetence, including some individuals receiving immunosuppressant therapy, may have reduced immune responses to MenQuadfi.

Complement Deficiency

Individuals with certain complement deficiencies and individuals receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis*, including invasive disease caused by serogroups A, C, W, and Y, even if they develop antibodies following vaccination with MenQuadfi.

Use in the elderly

Safety and efficacy of MenQuadfi administration in individuals older than 56 years of age have been established. Refer to Section 4.8 Adverse Effects and Section 5.1 Pharmacodynamic Properties for more information.

Paediatric use

Safety and efficacy of MenQuadfi administration in individuals less than 6 weeks of age have not been established.

Safety and effectiveness of MenQuadfi were established in individuals from 6 weeks through 17 years of age. Data from MET41, MET42 and MET58 indicate that MenQuadfi can be given to infants with a history of preterm birth (31 to <37 weeks gestational age). The safety of MenQuadfi was evaluated in 237 infants with a history of preterm birth and no differences in adverse reactions following MenQuadfi were found between these infants and those who were born full term (see Section 4.8 Adverse Effects (Undesirable effects)). Additionally, the immune responses to MenQuadfi evaluated in 61-71 infants with a history of preterm birth (MET42) were comparable to those infants who were born full term (see Section 5.1 Clinical trials).

Infants with a history of preterm birth whose clinical condition is satisfactory should be immunised with full doses of vaccine at same chronological age and according to the same schedule as full-term infants, regardless of birth weight.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Use with other vaccines

MenQuadfi should not be mixed with any other vaccine in the same vial or syringe.

If MenQuadfi needs to be given at the same time as another injectable vaccine(s), immunisation should be carried out on separate limbs.

MenQuadfi can be given concomitantly with any of the following vaccines:

- Measles-mumps-rubella vaccine (MMR) and varicella vaccine (V).
- Combined diphtheria - tetanus - acellular pertussis (DTPa) vaccines, including combination DTPa vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b (HepB, IPV or Hib) such as DTPa-IPV-HepB-Hib vaccine or DTPa-IPV/Hib.
- 13-valent pneumococcal polysaccharide conjugate vaccine (PCV13).
- Human Papillomavirus Vaccine (Recombinant, adsorbed) (HPV).
- Rotavirus Vaccines
- Hepatitis B vaccine (HepB)
- Meningococcal Serogroup B vaccine (See Section 5.1 Pharmacodynamic properties – Concomitantly Administered Vaccines).

The anti-pertussis responses following dTpa administered concomitantly with MenQuadfi and HPV versus dTpa administered concomitantly with HPV did not meet non-inferiority for the

FHA, PRN, and FIM antigens. Because there are no established serological correlates of protection for pertussis, the clinical implications of the observed pertussis antigen responses are unknown.

MenQuadfi can be administered concomitantly with PCV13. Lower hSBA GMTs on day 30 post-dose for serogroup A have been observed when given concomitantly. The clinical relevance of this observation is unknown. As a precaution in children 12-23 months of age at high risk for serogroup A disease, consideration might be given for administration of MenQuadfi and PCV13 vaccines separately.

(See Section 4.8 Adverse effects and Section 5.1 Pharmacodynamic properties – Concomitantly administered vaccine for safety and immunogenicity data)

Use with systemic immunosuppressive medicinal products

It may be expected that in individuals receiving immunosuppressive treatment or individuals with immunodeficiency, an adequate immune response may not be elicited.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

A developmental and reproductive toxicity study was performed in female rabbits. The animals were administered a full human dose (0.5 mL) of MenQuadfi intramuscularly on two occasions before mating and three occasions during gestation. There were no effects on mating performances or female fertility. No study was conducted on male fertility.

Use in pregnancy (Category B1)

Limited data are available on the use of MenQuadfi in pregnant women. However, no conclusions can be drawn regarding whether or not MenQuadfi is safe for use during pregnancy.

A developmental and reproductive toxicity study was performed in female rabbits. The animals were administered a full human dose of MenQuadfi (0.5 mL) intramuscularly on two occasions before mating and three occasions during gestation. The study showed no adverse effects on embryo-fetal development (including an evaluation of teratogenicity) or early post-natal development.

MenQuadfi should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the fetus.

Use in lactation

There are no available data on the presence of MenQuadfi in human milk, milk production, or the effects on the breastfed infant. No conclusions can be drawn regarding whether or not MenQuadfi is safe for use during breastfeeding.

MenQuadfi should be used during breastfeeding only if the potential benefits to the mother outweigh the potential risks, including those to the breastfed child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects of MenQuadfi on the ability to drive or use machines have been performed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Summary of the safety profile

The safety of MenQuadfi in infants initiating vaccination from 6 weeks of age to less than 12 months of age is based on 6 studies in which participants received at least one dose of MenQuadfi concomitantly with routine paediatric vaccines (N=6060) or MenQuadfi concomitantly with MenB vaccine (N=314). The routine paediatric vaccines include DTPa-IPV/Hib or DTPa-IPV-HepB or DTPa-IPV-HepB-Hib or DTPa-HepB-IPV/Hib, Hib vaccine, PCV13 or PCV10, rotavirus vaccine, HepB, MMR, V or HepA. These studies evaluated the safety of a primary series consisting of either 1, 2 or 3 doses of MenQuadfi in the first year of life, following by a booster dose from 12 months of age in the second year of life.

The most frequently reported adverse reactions within 7 days after vaccination with any dose of MenQuadfi in infants initiating vaccination from 6 weeks of age to less than 12 months of age were irritability (74.6%) and injection site tenderness (64.6%). These adverse reactions were mostly mild or moderate in intensity.

The safety of a single dose of MenQuadfi in individuals 12 months of age and older was evaluated in seven randomised, active-controlled, multi-centre pivotal studies. In these studies, 6308 subjects received either a primary dose (N=5906) or a booster dose (N=402) of MenQuadfi and were included in the safety analyses. This included 1389 toddlers aged 12 through 23 months of age, 498 children aged 2 through 9 years, 2289 children and adolescents aged 10 through 17 years, 1684 adults aged 18 through 55 years, 199 older adults aged 56 through 64 years, and 249 elderly aged 65 years and older. Of these, 392 adolescents received MenQuadfi co-administered with dTpa and 4vHPV, and 589 toddlers received MenQuadfi co-administered with MMR+V (N=189), DTPa-IPV-HepB-Hib (N=200) or PCV-13 (N=200).

The most frequently reported adverse reactions within 7 days after vaccination with a single dose of MenQuadfi alone in toddlers 12 through 23 months of age were irritability (36.7%) and injection site tenderness (30.6%) and in ages 2 years and above were injection site pain (38.7%) and myalgia (30.5%). These adverse reactions were mostly mild or moderate in intensity.

Rates of adverse reactions after a booster dose of MenQuadfi in adolescents and adults at least 15 years of age were comparable to those seen in adolescents and adults who received a primary dose of MenQuadfi.

Tabulated list of adverse reactions

The following adverse reactions, as listed below, have been identified from clinical studies conducted with MenQuadfi when given alone to subjects 2 years of age and older. The safety profiles observed in infants initiating vaccination from 6 weeks to less than 12 months of age and toddlers aged 12 through 23 months are presented in the paediatric population section.

The adverse reactions are listed according to the following frequency categories:

Very common (≥1/10);

Common (≥1/100 to <1/10);

Uncommon (≥1/1,000 to <1/100);

Rare (≥1/10,000 to <1/1,000);

Very Rare (<1/10,000)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2 - Tabulated Summary of Adverse Reactions following Administration of MenQuadfi from Clinical Trials in Subjects 2 years of age and above

MedDRA System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Rare	Lymphadenopathy
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness
Gastrointestinal disorders	Uncommon	Vomiting, nausea
	Rare	Diarrhoea, stomach pain
Skin and subcutaneous tissue disorders	Rare	Urticaria, pruritus, rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia
	Rare	Pain in extremity
General disorders and administration site conditions	Very common	Malaise
		Injection site pain
	Common	Fever
		At the injection site: swelling, erythema
	Uncommon	Fatigue
		At the injection site: pruritus, warmth, bruising, rash
	Rare	Chills, axillary pain
		At the injection site: induration

Paediatric population

The safety profile of MenQuadfi in children and adolescents 2 through 17 years of age was generally comparable to that in adults. Injection site erythema and swelling at the MenQuadfi injection site were reported more frequently in children 2 through 9 years of age (very common) than in the older age groups.

When co-administered with routine paediatric vaccines, the safety profile of MenQuadfi when administered as a booster dose in the second year of life was similar to its safety profile in infants from 6 weeks to less than 12 months of age. Adverse reactions following MenQuadfi vaccination in individuals 12 through 23 months of age when administered as a booster dose or a single primary dose were generally comparable.

Table 3 - Tabulated Summary of Adverse Reactions following Administration of MenQuadfi with Routine Paediatric Vaccines from Clinical Trials in Infants Initiating Vaccination from 6 weeks to less than 12 months of age

MedDRA System Organ Class	Frequency	Adverse reactions
Infections and infestations	Uncommon	Nasopharyngitis
	Rare	Upper respiratory tract infection**, Rhinitis**
Immune system disorder	Rare	Anaphylactic reaction*
Metabolic and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
Nervous system disorders	Very common	Drowsiness
	Rare	Febrile convulsion****
Respiratory, thoracic and mediastinal disorders	Rare	Cough**
Gastrointestinal disorders	Very common	Vomiting
	Uncommon	Diarrhoea
	Rare	Constipation**
Skin and subcutaneous tissue disorders	Uncommon	Rash
	Rare	Petechiae***, urticaria**, erythema**, rash macular**, eczema**
General disorders and administration site conditions	Very common	Fever
		Abnormal crying
		At the injection site tenderness/pain, erythema, swelling
	Common	At the injection site: bruising
	Uncommon	At the injection site: haemorrhage, heamatoma, mass, induration, warmth, rash
	Rare	At the injection site: discolouration**, reaction**, scab**

MedDRA System Organ Class	Frequency	Adverse reactions

*Occurred at a frequency of < 0.1% in one subject from 12-18 months of age
** Occurred at frequency of <0.1% and more ≥3 subjects experiencing the event
*** Petechiae occurred at a frequency of <0.1% in one subject from 6 weeks to less than 12 months
**** Frequency based on vaccinated participants between 6 weeks and 23 months of age in the entire MenQuadfi development program

In toddlers 12 through 23 months of age, injection site erythema and swelling (very common) at the MenQuadfi injection site, vomiting (common) and diarrhoea (common), were reported more frequently than in the older age groups. The following additional reactions, as listed below in Table 4, have been reported following administration of MenQuadfi in toddlers during clinical trials:

Table 4 - Tabulated Summary of Adverse Reactions following Administration of MenQuadfi from Clinical Trials in Subjects 12 months through 23 months

MedDRA System Organ Class	Frequency	Adverse reactions
Metabolic and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
	Uncommon	Insomnia
Nervous system disorders	Very common	Drowsiness
	Rare	Febrile convulsion*
Gastrointestinal disorders	Common	Vomiting, diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
General disorders and administration site conditions	Very Common	Abnormal crying
		At the injection site: tenderness/pain, erythema, swelling
	Common	Fever
	Uncommon	At the injection site: pruritus, induration, bruising, rash

* Frequency based on vaccinated participants between 6 weeks and 23 months of age in the entire MenQuadfi development program

Older population

Overall, within 7 days after vaccination with a single dose of MenQuadfi, the same injection site and systemic adverse reactions were observed in older (≥56 years of age) and younger adults (18 through 55 years old) but at lower frequencies; except for injection site pruritus, which was more frequent (common) in older adults. These adverse reactions mostly were mild or moderate in intensity.

Concomitant use with other vaccines

Concomitant use with routine paediatric vaccines

MenQuadfi can be co-administered with routine paediatric vaccines. Infant studies investigated the safety of MenQuadfi in individuals initiating vaccination from 6 weeks to less than 12 months of age when given concomitantly with routine paediatric vaccines. See Section 4.5 Interactions with Other Medicines and Other Forms of Interactions - Use with other vaccines and Section 5.1 Clinical Trials – Concomitantly Administered Vaccines.

Concomitant use with MMR and V for ages 12-23 months

The safety of MenQuadfi administered concomitantly with MMR and V was evaluated in a randomised, controlled, open-label (the laboratory technicians were blinded to group assignment) trial (MET57).

The rates of local reactions at each of the injection sites were comparable when MenQuadfi was given concomitantly with MMR and V, MenQuadfi was given alone, and MMR and V were given without MenQuadfi.

The overall rates of solicited systemic reactions reported for participants receiving MenQuadfi + MMR + V (46.6%) were comparable to rates among participants who received MMR + V without MenQuadfi (43.2%), or MenQuadfi alone (54.3%). In the three groups the most common solicited systemic reactions were irritability (MenQuadfi + MMR + V, 23.8%; MMR +V, 26.3%; MenQuadfi alone, 24.5%), abnormal crying (MenQuadfi + MMR + V, 18.5%; MMR +V, 18.9%; MenQuadfi alone, 27.7%), and appetite lost (MenQuadfi + MMR + V, 21.2%; MMR +V, 13.7%; MenQuadfi alone, 23.4%).

Concomitant use with PCV13 for ages 12-23 months

The safety of MenQuadfi administered concomitantly with PCV13 as evaluated in a randomised, open-label (the laboratory technicians were blinded to group assignment) trial (MET57).

The rates of local reactions at the PCV13 injection sites tended to be higher when MenQuadfi was given concomitantly with PCV13 compared with PCV13 given without MenQuadfi.

The overall rates of solicited systemic reactions reported for participants receiving MenQuadfi + PCV13 (20.0%) were comparable to rates among participants who received MenQuadfi alone (19.0%). The overall rate of solicited systemic reactions was lower for participants receiving PCV13 without MenQuadfi (10.1%). In the three groups the most common systemic reactions were irritability (MenQuadfi + PCV13, 13.0%; PCV13, 9.1%; MenQuadfi alone, 16.0%), appetite lost (MenQuadfi + PCV13, 9.5%; PCV13, 7.1%; MenQuadfi alone, 12.0%), and drowsiness (MenQuadfi + PCV13, 12.5%; PCV13, 4.0%; MenQuadfi alone, 6.0%).

Concomitant use with dTpa and HPV for ages 10-17 years

The safety of MenQuadfi administered concomitantly with dTpa and HPV was evaluated in a randomised, controlled, open-label (the laboratory technicians were blinded to group assignment) trial (MET50).

The overall rate of solicited systemic reactions was higher when MenQuadfi was given concomitantly with dTpa and HPV (70.6%) than when MenQuadfi was given alone (52.0%) and comparable to when dTpa and HPV were given without MenQuadfi (65.9%). In the three groups the most common solicited systemic reactions were myalgia (MenQuadfi + dTpa + HPV, 61.3%; dTpa +HPV, 55.4%; MenQuadfi alone, 35.3%) and headache (MenQuadfi + dTpa + HPV, 33.8%; dTpa + HPV, 29%; MenQuadfi alone, 30.2%). The rates of local reactions at each of the injection sites were comparable when MenQuadfi was given concomitantly with dTpa and HPV, MenQuadfi was given alone, and dTpa and HPV were given without MenQuadfi.

Concomitant use with dTpa-IPV and 9vHPV for ages 10-17 years

The safety of MenQuadfi administered concomitantly with dTpa-IPV and 9vHPV was evaluated in a randomised, active controlled, partially observer-blind (open-label for one of the study groups) trial (MEQ00071). The safety analysis set included 458 participants who received MenQuadfi alone (171 participants), MenQuadfi concomitantly with dTpa-IPV and 9vHPV (116 participants), or a comparator meningococcal vaccine (171 participants, MenACWY-TT). The participants 10 years through 17 years of age who received MenQuadfi alone were a mean age of 12.4 years and 12.5 years for those who received MenQuadfi concomitantly with dTpa -IPV and 9vHPV.

The rates of systemic reactions were comparable between all groups. The most common solicited systemic reactions were myalgia, headache and malaise.

The most common solicited injection site reaction following MenQuadfi vaccination was pain. The rates of pain at the dTpa -IPV and 9vHPV injection site were numerically higher when given concomitantly with MenQuadfi compared to when dTpa-IPV and 9vHPV were given alone.

Majority of solicited reactions were Grade 1 or 2 and resolved within 3 days after vaccination.

No SAEs occurred following administration with MenQuadfi alone or concomitantly with dTpa-IPV and 9vHPV during the entire study period.

Table 5 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with dTpa -IPV and 9vHPV with or without MenQuadfi in Participants 10 through 17 Years of Age

	MenQuadfi and dTpa -IPV + 9vHPV given sequentially* (N=171)			**MenQuadfi + dTpa -IPV + 9vHPV given concomitantly** (N=116)**		
Participants experiencing at least one:	n/M	%	Frequency	n/M	%	Frequency
General disorders and administration site conditions						
Local reactions						
Injection Site Pain						
MenQuadfi	91/169	53.8	Very common	69/116	59.5	Very common
dTpa-IPV	116/168	69.0	Very common	95/116	81.9	Very common
9vHPV	113/168	67.3	Very common	97/116	83.6	Very common

	MenQuadfi and dTpa -IPV + 9vHPV given sequentially* (N=171)			MenQuadfi + dTpa -IPV + 9vHPV given concomitantly** (N=116)		
Injection Site Erythema						
MenQuadfi	19/169	11.2	Common	11/116	9.5	Common
dTpa -IPV	9/168	5.4	Common	13/116	11.2	Common
9vHPV	7/168	4.2	Common	6/116	5.2	Common
Injection Site Swelling						
MenQuadfi	17/169	10.1	Common	12/116	10.3	Common
dTpa-IPV	9/168	5.4	Common	10/116	8.6	Common
9vHPV	4/168	2.4	Common	7/116	6.0	Common
Systemic reactions						
Malaise	65/169	38.5	Very common	42/116	36.2	Very common
Fever	12/169	7.1	Common	6/116	5.2	Common
Nervous system disorders						
Headache	75/169	44.4	Very common	52/116	44.8	Very common
Musculoskeletal and connective tissue disorders						
Myalgia	84/169	49.7	Very common	67/116	57.8	Very common

*Participants received MenQuadfi on D01 and dTpa-IPV + 9vHPV on D31
**Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01
n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Concomitant use with meningococcal serogroup B (MenB) vaccines

In clinical study (MET52), the safety of MenQuadfi administered concomitantly with meningococcal serogroup B (MenB) vaccine was evaluated in an open-label, randomised, parallel-group, active-controlled trial, where 303 participants received the second dose of MenQuadfi concomitantly with MenB and 306 participants received the second dose of MenQuadfi alone at 12-13 months of age.

Rates and intensity of injection site reactions within 7 days following vaccination tended to be higher when MenQuadfi was given concomitantly with MenB than when MenQuadfi was given alone. The most common solicited injection site reaction was erythema, which was experienced more frequently in participants who received MenQuadfi with MenB (71.2%) compared to those who received MenQuadfi alone (66.3%). The most common solicited systemic reaction was irritability, which was experienced more frequently in participants who received MenQuadfi with MenB (98.7%) compared to those who received MenQuadfi alone (95.8%). Crying abnormal and drowsiness were reported at higher rates in subjects who received MenB with MenQuadfi (60.1% and 45.3%, respectively) compared to MenQuadfi alone (36.1% and 23.2%).

Additionally, in clinical study (MET59), adolescents and adults 13-26 years of age primed with MenQuadfi 3-6 years previously received MenQuadfi co-administered with meningococcal serogroup B (MenB) vaccine, Trumenba (N=93) or Bexsero (N=92).

Rates and intensity of systemic reactions within 7 days following vaccination tended to be higher when MenQuadfi was given concomitantly with MenB vaccine than when MenQuadfi was given alone. The most common solicited systemic reaction was myalgia, of mild intensity, which was experienced more frequently in adolescents and adults who received MenQuadfi and MenB vaccine concomitantly (Trumenba, 65.2%; Bexsero, 63%) compared to those who received MenQuadfi alone (32.8%).

Post Marketing

In addition to the adverse events observed during the clinical trials, the following events have been reported during the post marketing use of MenQuadfi. The frequency is qualified as "not known" (cannot be estimated from available data).

- *Immune system disorders*: Hypersensitivity including anaphylaxis
- *Nervous system disorders*: Convulsions with or without fever

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For general advice on overdose management, contact the Poisons Information Centre, telephone number 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: meningococcal vaccine, ATC code: J07AH08

Mechanism of action

Invasive meningococcal disease (IMD) is caused by the bacterium *N. meningitidis*, a gram-negative diplococcus found exclusively in humans. The presence of bactericidal anti-capsular meningococcal antibodies has been associated with protection from IMD. MenQuadfi induces the production of bactericidal antibodies specific to the capsular polysaccharides of *N. meningitidis* serogroups A, C, W, and Y.

Clinical trials

The immunogenicity of MenQuadfi in infants initiating vaccination from 6 weeks to less than 12 months of age was assessed in two pivotal studies where the primary vaccination series consisted of one or three doses in the first year of life (depending on the age at first dose) and a booster dose in the second year of life. The immunogenicity of a single dose of MenQuadfi for primary vaccination in toddlers (12 – 23 months of age), children and adolescents (2 – 17 years of age), adults (18 – 55 years of age) and older adults (56 years and above) was assessed in six pivotal studies and in one additional study (MEQ65) in toddlers (12 – 23 months of age); the immunogenicity of a single dose of MenQuadfi for booster vaccination (ages 15-55 years of age) was assessed in one pivotal study. In addition, antibody persistence after primary vaccination and immunogenicity of a booster dose was assessed in three studies in children (4-5 years of age), adolescents and adults (13-26 years of age), and older adults (≥59 years of age). Ten out of eleven studies were randomised (one partially randomised), parallel-group, multi-centre studies. Nine out of eleven studies were active controlled. Clinical study comparators were MenACWY-TT, MenACWY-CRM, MenACWY-DT, MenC-TT and MenACWY-PS. Five out of eleven studies were open-label. The other six studies were modified, double-blind.

Primary immunogenicity analyses were conducted by measuring serum bactericidal activity (SBA) using human serum as the source of exogenous complement (hSBA). Rabbit complement (rSBA) data are available in subsets in all age groups and generally follows the trends observed with human complement (hSBA) data. In addition, all participants were assessed for primary immunogenicity measured by hSBA and rSBA for serogroup C in MEQ00065 study.

Clinical data on the persistence of antibody response ≥3 years after primary vaccination with MenQuadfi in children (4-5 years of age), adolescents and adults (13-26 years of age), and older adults (≥ 59 years of age) are available. Clinical data on booster vaccination with MenQuadfi in those participants are also available (MET62).

Immunogenicity in individuals initiating vaccination from 6 weeks through less than 12 months of age

Immunogenicity in infants initiating vaccination from 6 weeks through 6 months of age

MET42 compared the immunogenicity of three doses (given at 2, 4, and 6 months of age) and a booster dose (given at 12-18 months of age) of MenQuadfi to MenACWY-CRM 30 days after the third and booster vaccination. The hSBA seroresponse rate, percentage of participants with hSBA titers ≥ 1:8 (seroprotection rate) and GMTs are presented in Table 6.

Immune non-inferiority, based on seroresponse rates, after the booster dose was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups.

Immune non-inferiority, based on seroprotection rates, after the third dose was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups.

Table 6 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-CRM 30 Days after Vaccination with Routine Infant Vaccines at 2, 4, 6, and a Booster Dose at 12-18 Months (MET42[*])

	Post 3rd Dose		Pre booster dose		Post booster dose	
Endpoint	**MenQuadfi (95% CI)**	**MenACWY-CRM (95% CI)**	**MenQuadfi (95% CI)**	**MenACWY-CRM (95% CI)**	**MenQuadfi (95% CI)**	**MenACWY-CRM (95% CI)**
A	N=682-852	N=322-409	N=607	N=282	N=501-642	N=223-296
% Participants achieving Seroresponse[†‡]	64.4 (60.6; 68.0)	50.6 (45.0; 56.2)	-	-	79.4 (75.6; 82.9)	77.6 (71.5; 82.9)
% ≥1:8 (seroprotection)[‡]	77.9 (75.0; 80.7)	67.7 (63.0; 72.2)	62.8 (58.8; 66.6)	46.5 (40.5; 52.5)	87.7 (84.9; 90.1)	88.2 (83.9; 91.6)
GMT	25 (23; 28)	15 (13; 18)	11 (10; 12)	7 (6; 8)	67 (58; 78)	57 (47; 70)
C	N=691-835	N=338-421	N=612	N=284	N=530-655	N=238-300
% Participants achieving Seroresponse[†‡]	96.4 (94.7; 97.6)	82.8 (78.4; 86.7)	-	-	97.0 (95.1; 98.3)	88.2 (83.4; 92.0)
% ≥1:8 (seroprotection)[‡]	99.0 (98.1; 99.6)	91.2 (88.1; 93.7)	93.1 (90.8; 95.0)	30.6 (25.3; 36.4)	99.4 (98.4; 99.8)	93.3 (89.9; 95.9)
GMT	391 (356; 428)	53 (46; 61)	61 (54; 69)	4 (4; 5)	678 (606; 758)	91 (76; 109)
W	N=739-883	N=369-438	N=619	N=288	N=540-651	N=250-305
% Participants achieving Seroresponse[†‡]	92.8 (90.7; 94.6)	85.6 (81.6; 89.1)	-	-	97.6 (95.9; 98.7)	96.4 (93.3; 98.3)
% ≥1:8 (seroprotection)[‡]	98.6 (97.6; 99.3)	92.9 (90.1; 95.1)	97.1 (95.4; 98.3)	61.5 (55.6; 67.1)	99.4 (98.4; 99.8)	99.0 (97.2; 99.8)
GMT	98 (91; 106)	49 (43; 55)	58 (53; 64)	9 (8; 10)	387 (352; 426)	175 (149; 206)
Y	N=701-861	N=347-423	N=611	N=287	N=523-651	N=233-295
% Participants achieving Seroresponse[†‡]	88.7 (86.2; 91.0)	81.8 (77.4; 85.8)	-	-	96.4 (94.4; 97.8)	92.3 (88.1; 95.4)
% ≥1:8 (seroprotection)[‡]	98.3 (97.1; 99.0)	91.7 (88.7; 94.2)	96.2 (94.4; 97.6)	67.9 (62.2; 73.3)	99.1 (98.0; 99.7)	98.6 (96.6; 99.6)
GMT	88 (81; 96)	41 (36; 46)	44 (40; 48)	10 (9; 11)	296 (268; 327)	186 (158; 219)

	Post 3rd Dose	Pre booster dose	Post booster dose

* Clinical trial identifier NCT03537508
† Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer <1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.
‡Non-inferiority criterion met (lower limit of the 2-sided 95% CI is > -10%)
N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method

MET52 evaluated the immunogenicity of MenQuadfi in infants following a single dose at 3 months and a booster dose at 12-13 months of age. The percentages of participants who achieved seroprotection (hSBA titers ≥1:8) 30 days following administration of MenQuadfi booster dose alone or co-administered with Bexsero at 12-13 months were 99.4% -100% for all four serogroups (see Section 5.1 Clinical Trials - Concomitantly Administered Vaccines).

Immunogenicity in infants initiating vaccination from 6 months to less than 12 months of age

MET61 compared the immunogenicity of one dose (given at 6-7 months of age) and a booster dose (given at 12-13 months of age) of MenQuadfi to MenACWY-CRM 30 days after each vaccination. The hSBA seroresponse rate, percentage of participants with hSBA titers ≥ 1:8 (seroprotection rate) and GMTs are presented in Table 7.

Immune non-inferiority, based on seroresponse and seroprotection rates after the booster dose, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups.

Table 7 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-CRM 30 Days after vaccination with routine infant vaccines at 6-7months and 12-13 months (MET61*)

	Post 1st Dose		Pre booster dose		Post booster dose	
Endpoint	**MenQuadfi (95% CI)**	**Menveo (95% CI)**	**MenQuadfi (95% CI)**	**Menveo (95% CI)**	**MenQuadfi (95% CI)**	**Menveo (95% CI)**
A	N=108-130	N=111-132	N=103	N=91	N=141-170	N=123-158
% Participants achieving Seroresponse†‡	30.6 (22.1; 40.2)	15.3 (9.2; 23.4)	-	-	89.4 (83.1; 93.9)	82.9 (75.1; 89.1)
% ≥1:8 (seroprotection)‡	54.6 (45.7; 63.4)	37.9 (29.6; 46.7)	77.7 (68.4; 85.3)	73.6 (63.3; 82.3)	95.3 (90.9; 97.9)	93.0 (87.9; 96.5)
GMT	8 (7; 10)	5 (4; 7)	20 (15; 27)	15 (11; 20)	184 (143; 237)	119 (90.6; 157)
C	N=104-127	N=107-133	N=118	N=118	N=134-162	N=126-160

	Post 1st Dose		Pre booster dose		Post booster dose	
% Participants achieving Seroresponse†‡	92.3 (85.4; 96.6)	81.3 (72.6; 88.2)	-	-	99.3 (95.9; 100)	97.6 (93.2; 99.5)
% ≥1:8 (seroprotection)‡	96.9 (92.1; 99.1)	90.2 (83.9; 94.7)	98.1 (93.2; 99.8)	69.1 (58.8; 78.3)	100 (97.7; 100)	98.1 (94.6; 99.6)
GMT	167 (129; 217)	41 (33; 52)	150 (117; 193)	13 (10; 17)	1473 (1236; 1756)	319 (263; 388)
W	N=108-134	N=112-134	N=120	N=117	N=143-171	N=127-159
% Participants achieving Seroresponse†‡	18.5 (11.7; 27.1)	8.0 (3.7; 14.7)	-	-	99.3 (96.1; 100)	92.9 (86.9; 96.7)
% ≥1:8 (seroprotection)‡	38.1 (29.8; 46.8)	28.4 (20.9; 36.8)	96.2 (90.6; 99.0)	50.5 (40.0; 61.1)	100 (97.9; 100)	95.6 (91.1; 98.2)
GMT	6 (4; 7)	4 (3; 5)	47 (36; 61)	6 (5; 8)	442 (367; 533)	106 (83; 135)
Y	N=102-125	N=106-128	N=120	N=116	N=140-170	N=128-160
% Participants achieving Seroresponse†‡	30.4 (21.7; 40.3)	7.5 (3.3;14.32)	-	-	98.6 (94.9; 99.8)	97.7 (93.3; 99.5)
% ≥1:8 (seroprotection)‡	60.8 (51.7; 69.4)	26.6 (19.1; 35.1)	96.2 (90.6; 99.0)	54.8 (44.2; 65.2)	100 (97.9; 100)	97.5 (93.7; 99.3)
GMT	8 (7; 11)	4 (3; 5)	46 (36; 59)	7 (5; 8)	423 (358; 499)	133 (107; 166)

*Clinical trial identifier NCT03691610

N: number of participants in per-protocol analysis set with valid serology results

†Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer <1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

‡Non-inferiority criterion met (lower limit of the 2-sided 95% CI is > -10%)

95% CI of the single proportion calculated from the exact binomial method

Immunogenicity in toddlers 12 to 23 month of age

Immunogenicity in participants 12 through 23 months of age was evaluated in three clinical studies (MET51, MET57 and MEQ00065).

MET51 was conducted in participants who were either meningococcal vaccine naive or had been primed with monovalent meningococcal C vaccines (MenC-TT or MenC-CRM) in the first year of life.

Non-inferiority of immune response, based on percentage of participants achieving a post-vaccination hSBA titre ≥ 1:8 at Day 30 regardless of their meningococcal vaccine background, was demonstrated for MenQuadfi versus MenACWY-TT vaccine for all serogroups.

Non-inferiority of immune response, based on percentage of participants achieving a post-vaccination hSBA titre ≥ 1:8 at Day 30 in meningococcal vaccine naive toddlers, was demonstrated for MenQuadfi versus MenACWY-TT vaccine for all serogroups (see Table 8).

The point estimates of the immune response endpoints (with corresponding 95% confidence intervals [CIs]) and the differences or ratios observed between the two vaccines administered (with corresponding 95% CIs) in naive toddlers are summarised in Table 8 below.

Table 8 - Comparison of Bactericidal Antibody Responses at D30 following Vaccination with MenQuadfi or MenACWY-TT in Meningococcal Vaccine naive Participants 12 through 23 Months of Age (MET51)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	% difference MenQuadfi - MenACWY-TT (95% CI)	MenQuadfi / MenACWY-TT (95% CI)
A				
% ≥1:8 (Seroprotection)§	90.8 (86.9; 93.8) N=293	89.5 (85.4; 92.7) N=295	1.3 (-3.60; 6.20)	
% Seroresponse	76.8 (71.5; 81.5) N=293	72.5 (67.1; 77.6) N=295	4.2 (-2.78;11.2)	
hSBA GMT	28.7 (25.2; 32.6) N=293	28.0 (24.4; 32.1) N=295		1.03 (0.850; 1.24)
C				
% ≥1:8 (Seroprotection)§	99.3 (97.6; 99.9) N=293	81.4 (76.4; 85.6) N=295	18.0 (13.6; 22.8)	
% Seroresponse	98.3 (96.1; 99.4) N=293	71.5 (66.0; 76.6) N=295	26.8 (21.4; 32.3)	
hSBA GMT	436 (380; 500) N=293	26.4 (22.5; 31.0) N=295		16.5 (13.4; 20.4)
W				
% ≥1:8 (Seroprotection)§	83.6 (78.9; 87.7) N=293	83.4 (78.7; 87.5) N=296	0.2 (-5.85; 6.18)	
% Seroresponse	67.6 (61.9; 72.9) N=293	66.6 (60.9; 71.9) N=296	1.0 (-6.54; 8.57)	
hSBA GMT	22.0 (18.9; 25.5) N=293	16.4 (14.4; 18.6) N=296		1.34 (1.10; 1.63)
Y				
% ≥1:8 (Seroprotection)§	93.2 (89.7; 95.8) N=293	91.6 (87.8; 94.5) N=296	1.6 (-2.76; 6.03)	

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	% difference MenQuadfi - MenACWY-TT (95% CI)	MenQuadfi / MenACWY-TT (95% CI)
% Seroresponse	81.9 (77.0; 86.1) N=293	79.1 (74.0; 83.5) N=296	2.9 (-3.56; 9.25)	
hSBA GMT	38.0 (33.0; 43.9) N=293	32.2 (28.0; 37.0) N=296		1.18 (0.970; 1.44)

N: number of participants in per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

MET57 was conducted in meningococcal vaccine naive toddlers 12 through 23 months of age to assess the immunogenicity and safety of concomitant administration of MenQuadfi with paediatric vaccines (MMR+V, DTPa-IPV-HepB-Hib or PCV). Overall, the post vaccination hSBA seroprotection rates in participants who received MenQuadfi was high for all serogroups (between 88.9% and 100%), and GMTs were higher for serogroup C than for serogroups A, W and Y.

MEQ00065 study was conducted in meningococcal vaccine naïve toddlers 12 through 23 months of age to assess the immunogenicity of serogroup C using hSBA and rSBA assays following administration of a single dose of MenQuadfi compared to MenACWY-TT or to MenC-TT.

Superiority of MenQuadfi was demonstrated in comparison to MenACWY-TT vaccine for the hSBA seroprotection (titers ≥1:8) rate and hSBA and rSBA GMTs to meningococcal serogroup C. Non-inferiority was demonstrated for the rSBA seroprotection rate to meningococcal serogroup C.

Superiority of MenQuadfi was also demonstrated in comparison to MenC-TT vaccine for the rSBA and hSBA GMTs to meningococcal serogroup C and non-inferiority was demonstrated for the rSBA and hSBA seroprotection rates to meningococcal serogroup C (see Table 9).

Table 9 - Comparison of hSBA and rSBA bactericidal antibody responses for serogroup C at D30 following vaccination with MenQuadfi, MenACWY-TT or MenC-TT in meningococcal vaccine naïve participants 12 through 23 months of age (study MEQ00065)

Endpoints	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	MenC-TT (95% CI)	MenQuadfi (95% CI)	MenACWYTT (95% CI)	MenC-TT (95% CI)
		hSBA			rSBA	
	N=214	N=211	N= 216	N=213	N=210	N= 215
% ≥1:8 (Seroprotection)	99.5#§ (97.4; 100)	89.1 (84.1; 93.0)	99.5 (97.4; 100)	100¶ (98.3; 100)	94.8 (90.8; 97.4)	100 (98.3; 100)
% Seroresponse	99.5 (97.4; 100)	83.4 (77.7; 88.2)	99.1 (96.7; 99.9)	99.5 (97.4; 100)	92.9 (88.5; 95.9)	99.5 (97.4; 100)

Endpoints	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	MenC-TT (95% CI)	MenQuadfi (95% CI)	MenACWYTT (95% CI)	MenC-TT (95% CI)
GMTs	515[$] (450; 591)	31.6 (26.5; 37.6)	227 (198; 260)	2143[¥] (1870; 2456)	315 (252; 395)	1624 (1425; 1850)

superiority of MenQuadfi demonstrated versus MenACWY-TT (hSBA seroprotection rates)
§ non inferiority of MenQuadfi demonstrated versus MenC-TT (hSBA seroprotection rates)
$ superiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (hSBA GMTs)
¶ non inferiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (rSBA seroprotection rates)
¥ superiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (rSBA GMTs)
N = number of participants in the per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method

Immunogenicity in children 2 through 9 years of age

Immunogenicity in participants 2 through 9 years of age was evaluated in study MET35 (stratified by ages 2 through 5 and 6 through 9 years) comparing seroresponses following administration of either MenQuadfi or MenACWY-CRM.

Overall for participants 2 through 9 years of age, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM. For Serogroup A, the post vaccination hSBA seroprotection rates and GMTs were similar in participants who received MenQuadfi than those who received MenACWY-CRM. The point estimates of the immune response endpoints (with corresponding 95% confidence intervals [CIs]) and the differences or ratios observed between the two vaccines administered (with corresponding 95% CIs) in naive children are summarised in Table 10 below.

Table 10 - Comparison of Bactericidal Antibody Response to MenQuadfi or MenACWY-CRM 30 Days after Vaccination of Participants 2 through 5 years and 6 through 9 Years of Age (MET35)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
		2-5 years		
A				
% ≥1:8 (Seroprotection)	84.6 (79.3; 89.1) N=228	76.5 (70.3; 81.9) N=221	8.2 (0.9; 15.5)	
% Seroresponse [§]	52.4 (45.7; 59.1) N=227	44.8 (38.1; 51.6) N=221	7.6 (-1.6; 16.7)	
hSBA GMT	21.6 (18.2; 25.5) N=228	18.9 (15.5; 23.0) N=221		1.14 (0.883; 1.47)
C				

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
% ≥1:8 (Seroprotection)	97.4 (94.4; 99.0) N=229	64.6 (57.9; 70.8) N=223	32.8 (26.1; 39.4)	
% Seroresponse §	94.3 (90.5; 96.9) N=229	43.2 (36.6; 50.0) N=222	51.1 (43.5; 57.8)	
hSBA GMT	208 (175; 246) N=229	11.9 (9.79; 14.6) N=223		17.4 (13.4; 22.6)
W				
% ≥1:8 (Seroprotection)	90.8 (86.3; 94.2) N=229	80.6 (74.8; 85.6) N=222	10.2 (3.8; 16.7)	
% Seroresponse §	73.8 (67.6; 79.4) N=229	61.3 (54.5; 67.7) N=222	12.5 (3.9; 20.9)	
hSBA GMT	28.8 (24.6; 33.7) N=229	20.1 (16.7; 24.2) N=222		1.43 (1.12; 1.83)
Y				
% ≥1:8 (Seroprotection)	97.8 (95.0; 99.3) N=229	86.9 (81.8; 91.1) N=222	10.9 (6.1; 16.1)	
% Seroresponse §	88.2 (83.3; 92.1) N=229	77.0 (70.9; 82.4) N=222	11.2 (4.2; 18.1)	
hSBA GMT	49.8 (43.0; 57.6) N=229	36.1 (29.2; 44.7) N=222		1.38 (1.07; 1.78)
		6-9 years		
A				
% ≥1:8 (Seroprotection)	88.2 (83.2; 92.0) N=228	81.9 (76.3; 86.5) N=237	6.3 (-0.2; 12.8)	
% Seroresponse §	58.3 (51.6; 64.8) N=228	50.6 (44.1; 57.2) N=237	7.7 (-1.3; 16.6)	
hSBA GMT	28.4 (23.9; 33.8) N=228	26.8 (22.0; 32.6) N=237		1.06 (0.816; 1.38)
C				
% ≥1:8 (Seroprotection)	98.3 (95.6; 99.5) N=229	69.5 (63.2; 75.3) N=236	28.8 (22.6; 35.0)	
% Seroresponse §	96.1 (92.7; 98.2) N=229	52.1 (45.5; 58.6) N=236	44.0 (36.8; 50.6)	
hSBA GMT	272 (224; 330) N=229	23.7 (18.2; 31.0) N=236		11.5 (8.24; 16.0)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
W				
% ≥1:8 (Seroprotection)	98.7 (96.2; 99.7) N=229	91.6 (87.3; 94.8) N=237	7.1 (3.3; 11.5)	
% Seroresponse §	83.8 (78.4; 88.4) N=229	66.7 (60.3; 72.6) N=237	17.2 (9.4; 24.7)	
hSBA GMT	48.9 (42.5; 56.3) N=229	33.6 (28.2; 40.1) N=237		1.45 (1.16; 1.82)
Y				
% ≥1:8 (Seroprotection)	99.1 (96.9; 99.9) N=229	94.5 (90.8; 97.0) N=237	4.6 (1.4; 8.3)	
% Seroresponse §	94.8 (91.0; 97.3) N=229	81.4 (75.9; 86.2) N=237	13.3 (7.6; 19.2)	
hSBA GMT	95.1 (80.2; 113) N=229	51.8 (42.5; 63.2) N=237		1.84 (1.41; 2.38)

N: number of participants in per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

Immunogenicity in children and adolescents 10 through 17 years of age

Immunogenicity in participants aged 10 through 17 years of age was evaluated in two studies comparing seroresponses following administration of MenQuadfi with either MenACWY-CRM (MET50) or MenACWY-DT (MET43) and in one study comparing seroprotection following administration of MenACWY-TT MEQ00071.

MET50 was conducted in meningococcal vaccine naive participants and evaluated seroresponses following administration with either MenQuadfi alone; MenACWY-CRM alone; MenQuadfi co-administered with dTpa and HPV; or dTpa and HPV alone.

Overall immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups. The post vaccination hSBA seroprotection rates for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM. The post vaccination hSBA GMTs for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM and comparable for serogroup A. The point estimates of the immune response endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adolescents is summarised in Table 11 below.

Table 11 - Comparison of Bactericidal Antibody Responses at D30 following administration with MenQuadfi or MenACWY-CRM Vaccination of Participants 10 through 17 Years of Age (MET50)

Endpoint[1] by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
A				
% ≥1:8 (Seroprotection)	93.5 (90.9; 95.6) N=463	82.8 (79.0; 86.1) N=464	10.8 (6.7; 14.9)	
% Seroresponse§	75.6 (71.4; 79.4) N=463	66.4 (61.9; 70.7) N=464	9.2 (3.4; 15.0)	
hSBA GMT	44.1 (39.2; 49.6) N=463	35.2 (30.3; 41.0) N=464		1.25 (1.033; 1.517)
C				
% ≥1:8 (Seroprotection)	98.5 (96.9; 99.4) N=462	76.0 (71.9; 79.8) N=463	22.5 (18.5; 26.6)	
% Seroresponse§	97.2 (95.2; 98.5) N=462	72.6 (68.3; 76.6) N=463	24.6 (20.3; 29.0)	
hSBA GMT	387 (329; 456) N=462	51.4 (41.2; 64.2) N=463		7.53 (5.717; 9.919)
W				
% ≥1:8 (Seroprotection)	99.1 (97.8; 99.8) N=463	90.7 (87.7; 93.2) N=464	8.4 (5.7; 11.4)	
% Seroresponse§	86.2 (82.7; 89.2) N=463	66.6 (62.1; 70.9) N=464	19.6 (14.2; 24.8)	
hSBA GMT	86.9 (77.8; 97.0) N=463	36.0 (31.5; 41.0) N=464		2.42 (2.035; 2.868)
Y				
% ≥1:8 (Seroprotection)	97.2 (95.2; 98.5) N=463	83.2 (79.5; 86.5) N=464	14.0 (10.3; 17.9)	
% Seroresponse§	97.0 (95.0; 98.3) N=462	80.8 (76.9; 84.3) N=464	16.2 (12.3; 20.2)	
hSBA GMT	75.7 (66.2; 86.5) N=463	27.6 (23.8; 32.1) N=464		2.74 (2.244; 3.351)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.
[1]Seroresponse rate (primary end point) for each serogroup: post-vaccination hSBA titers ≥1:8 for participants with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre to post-vaccination for participants with pre-vaccination hSBA titers ≥1:8.

Study MET43 was performed to evaluate the efficacy of MenQuadfi compared to MenACWY-DT in meningococcal vaccine naïve participants 10 through 55 years of age.

In MET 43, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-DT. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adolescents is summarised in Table 12 below.

Table 12 - Comparison of Bactericidal Antibody Response at D30 following administration with MenQuadfi or MenACWY-DT Vaccination of Participants 10 through 17 Years of Age (MET43)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	96.2 (94.9; 97.2) N=1,097	89.0 (84.9; 92.3) N=300	7.2 (3.8; 11.3)	
% Seroresponse§	74.0 (71.3; 76.6) N=1,097	55.3 (49.5; 61.0) N=300	18.7 (12.5; 24.9)	
hSBA GMT	78 (71.4; 85.2) N=1,097	44.2 (36.4; 53.7) N=300		1.76 (1.42; 2.18)
C				
% ≥1:8 (Seroprotection)	98.5 (97.5; 99.1) N=1,098	74.7 (69.3; 79.5) N=300	23.8 (19.1; 29.0)	
% Seroresponse§	95.6 (94.2; 96.8) N=1,097	53.3 (47.5; 59.1) N=300	42.3 (36.6; 48.0)	
hSBA GMT	504 (456; 558) N=1,098	44.1 (33.7; 57.8) N=300		11.4 (8.57; 15.2)
W				
% ≥1:8 (Seroprotection)	98.3 (97.3; 99.0) N=1,097	93.7 (90.3; 96.1) N=300	4.6 (2.2; 8.0)	
% Seroresponse§	84.5 (82.2; 86.6) N=1,097	72.0 (66.6; 77.0) N=300	12.5 (7.22; 18.2)	
hSBA GMT	97.2 (88.3; 107) N=1,097	59.2 (49.1; 71.3) N=300		1.64 (1.33; 2.03)
Y				
% ≥1:8 (Seroprotection)	99.1 (98.3; 99.6) N=1,097	94.3 (91.1; 96.7) N=300	4.8 (2.5; 8.0)	

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
% Seroresponse§	95.6 (94.2; 96.8) N=1,097	85.7 (81.2; 89.4) N=300	10.0 (6.18; 14.5)	
hSBA GMT	208 (189; 228) N=1,097	80.3 (65.6; 98.2) N=300		2.59 (2.07; 3.23)

N: number of participants in per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

MEQ00071 was performed to evaluate the efficacy of MenQuadfi compared to MenACWY-TT in participants 10 through 17 years of age.

MEQ00071 was conducted in participants who were either meningococcal vaccine naïve or had been primed with monovalent MenC vaccines (MenC-TT or MenC-CRM) before two years of age. The participants were randomized to receive either a single dose of MenQuadfi alone, a single dose of the licensed MenACWY-TT vaccine, or a single dose of MenQuadfi given concomitantly with dTpa-IPV and 9vHPV.

Non-inferiority of immune response 30 days following vaccination, based on the percentages of participants with hSBA titers ≥ 1:8 (seroprotection rates), was demonstrated for MenQuadfi versus MenACWY-TT vaccine for all serogroups (Table 13).

The post vaccination hSBA seroresponse rates were higher in participants who received MenQuadfi than those who received MenACWY-TT for all serogroups. The post vaccination hSBA GMTs for serogroups C, W, and Y were higher in participants who received MenQuadfi versus those who received MenACWY-TT and comparable for serogroup A (see Table 13).

Immune response was also measured 6 days following vaccination in a subset of participants who received MenQuadfi concomitantly with dTpa-IPV and 9vHPV (N=60). A rapid and robust immune response was observed, with hSBA GMTs increasing mainly within the first 6 days after vaccination. hSBA GMTs ranged from 2.36 to 9.23 before vaccination, from 22.2 to 2224 six days after vaccination and from 39.5 to 2358 thirty days after vaccination.

Table 13 – MEQ00071* – Comparison of hSBA antibody response at D30 following vaccination with MenQuadfi or MenACWY-TT in adolescents 10 through 17 years of age – PPASM

Endpoint by Serogroup	MenQuadfi (95% CI) N=159	MenACWY-TT (95% CI) N=161	Difference (%) MenQuadfi minus MenACWY-TT (95% CI)
A			
% ≥1:8 (Seroprotection)**	97.5 (93.7; 99.3)	92.5 (87.3; 96.1)	4.98 (0.06; 10.36)
% Seroresponse	88.0 (81.9; 92.6)	75.5 (68.0; 81.9)	

Endpoint by Serogroup	MenQuadfi (95% CI) N=159	MenACWY-TT (95% CI) N=161	Difference (%) MenQuadfi minus MenACWY-TT (95% CI)
GMT	78.2 (64.6; 94.7)	56.0 (44.0; 71.2)	
C			
% ≥1:8 (Seroprotection)**	100 (97.7; 100)	95.0 (90.4; 97.8)	4.97 (1.58; 9.50)
% Seroresponse	99.4 (96.5; 100)	88.8 (82.8; 93.2)	
GMT	2294 (1675; 3142)	619 (411; 931)	
W			
% ≥1:8 (Seroprotection)**	100 (97.7; 100)	98.8 (95.6; 99.8)	1.24 (-1.28; 4.42)
% Seroresponse	93.1 (88.0; 96.5)	81.4 (74.5; 87.1)	
GMT	134 (109; 164)	64.6 (52.5; 79.4)	
Y			
% ≥1:8 (Seroprotection)**	99.4 (96.5; 100)	98.1 (94.6; 99.6)	1.24$ (-1.88; 4.77)
% Seroresponse	98.7 (95.5; 99.8)	88.1 (82.1; 92.7)	
GMT	169 (141; 202)	84.8 (68.3; 105)	

*Clinical trial identifier NCT04490018
**Non-inferiority of MenQuadfi demonstrated versus MenACYW-TT
N: number of participants in the Per-Protocol Analysis Set and includes both meningococcal vaccine naïve and MenC primed participants
95% CI of the single proportion calculated from the exact binomial method
The two-sided 95% CI is calculated based on the Wilson score method without continuity correction as described by Newcombe R.G. The non-inferiority will be demonstrated if the lower limit of the 95% CI of the difference is greater than -10%.
hSBA vaccine seroresponse is defined as a post-vaccination titer ≥ 1:16 for participants with pre-vaccination hSBA titer < 1:8, or a post-vaccination titer ≥ 4-fold increase from baseline for participants with pre-vaccination hSBA titer ≥ 1:8

Response in participants according to MenC vaccination status

The immunogenicity of serogroup C following a single dose of MenQuadfi compared to a single dose of MenACWY-TT 30 days after vaccination was assessed in both meningococcal vaccine naïve and MenC primed (before two years of age) participants (MEQ00071).

Overall, the post vaccination hSBA seroprotection rates, hSBA seroresponse rates, and hSBA GMTs were higher in meningococcal vaccine naïve participants who received MenQuadfi than those who received MenACWY-TT. In MenC primed participants, the post vaccination hSBA seroprotection and seroresponse rates against meningococcal serogroup C were comparable between both study groups and the hSBA GMTs tended to be higher in participants who received MenQuadfi than those who received MenACWY-TT (see Table 14).

Table 14 – MEQ00071* - Comparison of hSBA bacterial antibody responses for serogroup C D30 following vaccination with MenQuadfi or MenACWY-TT in meningococcal vaccine naïve or MenC primed participants 10 through 17 years of age– PPASM

Endpoint for Serogroup C	MenC Naïve (95% CI)		MenC primed (95% CI)	
	MenQuadfi N=45	MenACWY-TT N=49	MenQuadfi N=114	MenACWY-TT N=112
% ≥1:8 (Seroprotection)	100 (92.1; 100)	85.7 (72.8; 94.1)	100 (96.8; 100)	99.1 (95.1; 100)
% Seroresponse	100 (92.1; 100)	65.3 (50.4; 78.3)	99.1 (95.2; 100)	99.1 (95.1; 100)
GMT	489 (252; 949)	29 (17.5; 47.9)	4222 (3166; 5632)	2361 (1740; 3204)

*Clinical trial identifier NCT04490018
N: number of participants in the Per-Protocol Analysis Set
95% CI of the single proportion calculated from the exact binomial method
The two-sided 95% CI is calculated based on the Wilson score method without continuity correction as described by Newcombe R.G.
hSBA vaccine seroresponse is defined as a post-vaccination titer ≥ 1:16 for participants with pre-vaccination hSBA titer < 1:8, or a post-vaccination titer ≥ 4-fold increase from baseline for participants with pre-vaccination hSBA titer ≥ 1:8

Immunogenicity in adults 18 through 55 years of age

Immunogenicity in participants from 18 through 55 years of age was evaluated in study MET43 comparing MenQuadfi to MenACWY-DT. Immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-DT. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adults is summarised in Table 15 below.

Table 15 - Comparison of Bactericidal Antibody Responses at D30 following administration with MenQuadfi or MenACWY-DT Vaccination of Participants 18 through 55 Years of Age (MET43)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	93.5 (92.1; 94.8) N=1,408	88.1 (83.8; 91.5) N=293	5.5 (2.0; 9.9)	
% Seroresponse§	73.5 (71.2; 75.8) N=1,406	53.9 (48.0; 59.7) N=293	19.6 (13.5; 25.8)	
hSBA GMT	106 (97.2; 117) N=1,408	52.3 (42.8; 63.9) N=293		2.03 (1.63; 2.53)
C				

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
% ≥1:8 (Seroprotection)	93.5 (92.0; 94.7) N=1,408	77.8 (72.6; 82.4) N=293	15.7 (11.0; 20.9)	
% Seroresponse§	83.4 (81.4; 85.3) N=1,406	42.3 (36.6; 48.2) N=293	41.1 (35.0; 46.9)	
hSBA GMT	234 (210; 261) N=1,408	37.5 (29.0; 48.5) N=293		6.24 (4.77; 8.16)
W				
% ≥1:8 (Seroprotection)	94.5 (93.2; 95.7) N=1,410	80.2 (75.2; 84.6) N=293	14.3 (10.0; 19.4)	
% Seroresponse§	77.0 (74.7; 79.2) N=1,408	50.2 (44.3; 56.0) N=293	26.8 (20.7; 32.9)	
hSBA GMT	75.6 (68.7; 83.2) N=1,410	33.2 (26.3; 42.0) N=293		2.27 (1.77; 2.93)
Y				
% ≥1:8 (Seroprotection)	98.6 (97.8; 99.1) N=1,410	81.2 (76.3; 85.5) N=293	17.4 (13.2; 22.2)	
% Seroresponse§	88.1 (86.3; 89.8) N=1,408	60.8 (54.9; 66.4) N=293	27.4 (21.7; 33.3)	
hSBA GMT	219 (200; 239) N=1,410	54.6 (42.3; 70.5) N=293		4.00 (3.05; 5.24)

N: number of participants in per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups

Immunogenicity in adults 56 years of age and above

Immunogenicity in adults ≥ 56 years of age was assessed in study MET49 comparing the immunogenicity of MenQuadfi to MenACWY-PS.

In study MET49, the overall mean age of participants who received MenQuadfi was 66.9 years. The age range of participants was 56 through 89.8 years of age. The immune response to MenQuadfi based on hSBA seroresponse was non-inferior to that of MenACWY-PS for all four serogroups. The percentages of participants with hSBA titres ≥ 1:8 increased from baseline for all serogroups and in both groups (see Table 16).

In participants 56 through 64 years of age, participants ≥ 65 years, participants 65 through 74 years and participants ≥ 75 years of age, seroprotection rates were comparable between

MenQuadfi and MenACWY-PS for serogroup A and higher for serogroups C, Y and W in participants who received MenQuadfi than those who received MenACWY-PS. In participants 56 through 64 years of age and ≥ 65 years the GMTs were higher for all serogroups in those who received MenQuadfi than those who received MenACWY-PS. In participants 65 through 74 years of age, the GMTs were higher for serogroups C, Y and W, and comparable for serogroup A in those who received MenQuadfi than those who received MenACWY-PS. In participants ≥ 75 years of age the GMTs were higher for serogroup C, and comparable for serogroups A, Y and W in those who received MenQuadfi than those who received MenACWY-PS.

Overall for adults ≥ 56 years of age, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY PS for all four serogroups. The post vaccination hSBA GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-PS. The post vaccination hSBA seroprotection rates for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-PS. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive older adults is summarised in Table 16 below.

Table 16 - Comparison of Bactericidal Antibody Responses at D30 following administration with MenQuadfi or MenACWY-PS in naive Older Adults (MET49)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	% difference MenQuadfi – MenACWY-PS (95% CI)	MenQuadfi / MenACWY-PS (95% CI)
A				
% ≥1:8 (Seroprotection)	89.4 (86.1; 92.1) N=433	84.2 (80.4; 87.5) N=431	5.2 (0.6; 9.7)	
% Seroresponse§	58.2 (53.4; 62.9) N=433	42.5 (37.7; 47.3) N=431	15.7 (9.08; 22.2)	
hSBA GMT	55.1 (46.8; 65.0) N=433	31.4 (26.9; 36.7) N=431		1.75 (1.40; 2.20)
C				
% ≥1:8 (Seroprotection)	90.1 (86.9; 92.7) N=433	71.0 (66.5; 75.2) N=431	19.1 (13.9; 24.2)	
% Seroresponse§	77.1 (72.9; 81.0) N=433	49.7 (44.8; 54.5) N=431	27.5 (21.2; 33.5)	
hSBA GMT	101 (83.8; 123) N=433	24.7 (20.7; 29.5) N=431		4.10 (3.16; 5.33)
W				
% ≥1:8 (Seroprotection)	77.4 (73.1; 81.2) N=433	63.1 (58.4; 67.7) N=431	14.3 (8.2; 20.2)	

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	% difference MenQuadfi – MenACWY-PS (95% CI)	MenQuadfi / MenACWY-PS (95% CI)
% Seroresponse§	62.6 (57.8; 67.2) N=433	44.8 (40.0; 49.6) N=431	17.8 (11.2; 24.2)	
hSBA GMT	28.1 (23.7; 33.3) N=433	15.5 (13.0; 18.4) N=431		1.81 (1.42; 2.31)
Y				
% ≥1:8 (Seroprotection)	91.7 (88.7; 94.1) N=433	67.7 (63.1; 72.1) N=431	23.9 (18.8; 29.0)	
% Seroresponse§	74.4 (70.0; 78.4) N=433	43.4 (38.7; 48.2) N=431	31.0 (24.6; 37.0)	
hSBA GMT	69.1 (58.7; 81.4) N=433	21.0 (17.4; 25.3) N=431		3.30 (2.57; 4.23)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

Persistence of immune response and MenQuadfi booster response

Antibody persistence after primary vaccination and immunogenicity of a MenQuadfi booster dose was assessed in four studies in children (4-5 years of age, and 6-7 years of age), adolescents and adults (13-26 years of age), and older adults (≥59 years of age).

Persistence of immune response and MenQuadfi booster response in children 4 through 5 years of age

MET62 evaluated the antibody persistence of a primary dose, immunogenicity and the safety of a booster dose of MenQuadfi in children approximately 4 years of age. These children were primed with a single dose of MenQuadfi or MenACWY-TT 3 years before as part of the phase II study MET54 when they were 12-23 months old. The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-TT) children had received 3 years ago (see Table 17).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for MenQuadfi or MenACWY-TT. The pre-booster GMTs were higher than the pre-primary dose, indicative of long-term persistence of immune response.

After the booster dose, seroprotection rates were nearly 100% for all serogroups in children primed with MenQuadfi.

Table 17 - Comparison of bactericidal antibody response 30 days after booster vaccination, and persistence in children (approximately 4 through 5 years of age) primed with MenQuadfi or MenACWY-TT 3 years before as toddlers 12 through 23 months of age in study MET54 – (study MET62)

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)			MenQuadfi Booster in MenACWY-TT primed (95% CI)			MenQuadfi Booster in MenQuadfi primed + MenACWY-TT primed (95% CI)		
	Persistence[#]		Booster[$]	Persistence[#]		Booster[$]	Persistence[#]		Booster[$]
	N=42		N=40	N=49		N=44	N=91		N=84
	D30 Post primary dose	D0-Pre-booster dose		D30 Post primary dose	D0-Pre-booster dose		D30 Post primary dose	D0-Pre-booster dose	
A									
% ≥1:8	97.6	66.7	100	89.8	83.7	100	93.4	75.8	100
(Seroprotection) %	(87.4; 99.9) -	(50.5; 80.4) -	(91.2; 100) 100	(77.8; 96.6) -	(70.3; 92.7) -	(92.0; 100) 95.5	(86.2; 97.5) -	(65.7; 84.2) -	(95.7; 100) 97.6
Seroresponse			(91.2; 100)			(84.5; 99.4)			(91.7; 99.7)
hSBA GMT	83.3 (63.9; 109)	11.9 (8.11; 17.4)	763 (521; 1117)	49.6 (32.1; 76.7)	14.7 (10.7; 20.2)	659 (427; 1017)	63.0 (48.3; 82.2)	13.3 (10.5; 17.0)	706 (531; 940)
C									
% ≥1:8	100	100	100	87.8	57.1	100	93.4	76.9	100
(Seroprotection) %	(91.6; 100) -	(91.6; 100) -	(91.2; 100) 95.0	(75.2; 95.4) -	(42.2; 71.2) -	(92.0; 100) 100	(86.2; 97.5) -	(66.9; 85.1) -	(95.7; 100) 97.6
Seroresponse			(83.1; 99.4)			(92.0; 100)			(91.7; 99.7)
hSBA GMT	594 (445; 793)	103 (71.7; 149)	5894 (4325; 8031)	29.4 (20.1; 43.1)	11.6 (7.28; 18.3)	1592 (1165; 2174)	118 (79.3; 175)	31.8 (21.9; 46.1)	2969 (2293; 3844)
W									
% ≥1:8	100	97.6	97.5	95.9	83.7	100	97.8	90.1	98.8
(Seroprotection) %	(91.6; 100) -	(87.4; 99.9) -	(86.8; 99.9) 97.5	(86.0; 99.5) -	(70.3; 92.7) -	(92.0; 100) 100	(92.3; 99.7) -	(82.1; 95.4) -	(93.5; 100) 98.8
Seroresponse			(86.8; 99.9)			(92.0; 100)			(93.5; 100

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)			MenQuadfi Booster in MenACWY-TT primed (95% CI)			MenQuadfi Booster in MenQuadfi primed + MenACWY-TT primed (95% CI)		
hSBA	71.8	50.0	2656	40.1	21.2	3444	52.5	31.5	3043
GMT	(53.3; 96.7)	(35.9; 69.5)	(1601; 4406)	(30.6; 52.6)	(14.6; 30.9)	(2387; 4970)	(42.7; 64.5)	(24.2; 41.0)	(2248; 4120)
Y									
% ≥1:8	100	97.6	100	100	89.8	100	100	93.4	100
(Seroprotection) %	(91.6; 100)	(87.4; 99.9)	(91.2; 100)	(92.7; 100)	(77.8; 96.6)	(92.0; 100)	(96.0; 100)	(86.2; 97.5)	(95.7; 100)
Seroresponse	-	-	100	-	-	100	-	-	100
			(91.2; 100)			(92.0; 100)			(95.7; 100)
hSBA	105	32.5	2013	75.8	18.2	2806	88.1	23.8	2396
GMT	(73.9; 149)	(24.8; 42.7)	(1451; 2792)	(54.2; 106)	(13.8; 24.0)	(2066; 3813)	(69.3; 112)	(19.4; 29.1)	(1919; 2991)

$ N calculated using per protocol analysis set (PPAS) with valid serology results; booster dose = D30 MET62.
# N calculated using full analysis set for persistence (FASP) with valid serology results; post-primary dose = D30 MET54, pre-booster dose = D0 MET62.
Vaccine seroresponse:titre is < 1:8 at baseline with post-vaccination titre ≥ 1:16 or titre is ≥ 1:8 at baseline with a ≥ 4-fold increase at post- vaccination.
95% CI of the single proportion calculated from the exact binomial method

Persistence of immune response and MenQuadfi booster response in children 6 through 7 years of age

MEQ00073 evaluated the antibody response of a booster dose of MenQuadfi in children 6 through 7 years of age who had previously received a primary dose of MenQuadfi 5 years earlier as part of study MET51 when they were 12 through 23 months of age and were either meningococcal vaccine naive or primed with a MenC vaccine in their first year of life.

For all serogroups, 5Y post-primary (pre-booster) GMTs were higher than the pre-primary GMTs, indicative of long-term persistence of immune response.

At D30 post-booster dose, the proportion of individuals exhibiting ≥1:8 seroprotection rates were as follows: 98.9% for serogroup A, 97.7% for serogroup C, and 100% for serogroups W and Y in children primed with MenQuadfi (see Table 18).

The antibody responses against serogroup C at D30 post-booster dose of MenQuadfi were comparable regardless of MenC vaccination status during the first year of life before priming with MenQuadfi 5 years earlier.

Table 18 - Comparison of bactericidal antibody response at D30 following booster vaccination, and persistence with children 6 through 7 years of age primed with MenQuadfi 5 years earlier as toddlers 12 through 23 months of age in study MET51 (study MEQ00073)

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)			
		Persistence[#] N=208		Booster* N=88
	D0 Pre-Primary	D30 Post-Primary	5Y Post-Primary D0 Pre-Booster	
A				
% ≥1:8 (Seroprotection)	17.8 (12.8; 23.7)	90.4 (85.5; 94.0)	76.0 (69.6; 81.6)	98.9 (93.8; 100)
% Seroresponse	-	-	-	93.2 (85.7; 97.5)
hSBA GMT	4.09 (3.83; 4.38)	28.9 (24.5; 34.0)	14.5 (12.0; 17.5)	1143 (820; 1594)
C				
% ≥1:8 (Seroprotection)	40.4 (33.7; 47.4)	99.5 (97.4; 100)	85.1 (79.5; 89.6)	97.7 (92.0; 99.7)
% Seroresponse	-	-	-	97.7 (92.0; 99.7))
hSBA GMT	8.03 (6.35; 10.1)	1315 (1002; 1724)	37.6 (29.8; 47.4)	8933 (6252; 12764)
W				
% ≥1:8 (Seroprotection)	3.8 (1.7; 7.4)	83.7 (77.9; 88.4)	84.6 (79.0; 89.2)	100 (95.9; 100)
% Seroresponse	-	-	-	98.9 (93.8; 100)
hSBA GMT	2.29 (2.15; 2.43)	25.7 (21.3; 31.0)	30.7 (24.9; 37.9)	8656 (6393; 11721)
Y				
% ≥1:8 (Seroprotection)	6.8 (3.7; 11.1)	92.3 (87.8; 95.5)	68.8 (62.0; 75.0)	100 (95.9; 100)
% Seroresponse	-	-	-	98.9 (93.8; 100)
hSBA GMT	2.51 (2.35; 2.68)	41.6 (35.0; 49.6)	12.7 (10.5; 15.4)	3727 (2908; 4776)

*MEQ00073 – NCT04936685.
[#] MET51 – NCT02955797.
**D30 Post Booster MEQ00073 = Per Protocol Analysis Set 1 (PPAS1).

Vaccine seroresponse: titer is < 1:8 at baseline with post-vaccination titer ≥ 1:16 or titer is ≥ 1:8 at baseline with a ≥ 4-fold increase at post-vaccination.
N: number of participants in full analysis set for persistence (FASP) with valid serology results. The number of participants varies depending on the timepoints.
95% CI of the single proportion calculated from the exact binomial method.

Persistence of immune response and MenQuadfi booster response in adolescents and adults 13 through 26 years of age

MET59 evaluated the antibody persistence of primary dose, immunogenicity and safety of a booster dose of MenQuadfi in adolescents and adults 13 through 26 years of age who had received a single dose of MenQuadfi in study MET50 or MET43 or MenACWY-CRM in study MET50 or outside of Sanofi trials 3-6 years prior. The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-CRM) participants had received 3-6 years previously (see Table 19).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster for MenQuadfi and MenACWY-CRM primed participants. The pre-booster GMTs were higher than the pre-primary dose, indicative of long-term persistence of immune response.

After the booster dose, seroprotection rates were nearly 100% for all serogroups in adolescents and adults primed with MenQuadfi.

Table 19 - Comparison of bactericidal antibody response 6 and 30 days after booster vaccination, and persistence in adolescents and adults (13 through 26 years) primed with MenQuadfi or MenACWY-CRM 3-6 years before in study MET50*, MET43 or outside of Sanofi trials – (study MET59***)**

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)				MenQuadfi Booster in MenACWY-CRM primed (95% CI)			
	Persistence^		Booster$		Persistence^		Booster$	
	D30 – Post primary dose N=376	D0 – Pre-booster dose N=379-380	D06 – Post booster dose N=46	D30 – Post booster dose N=174	D30 Post primary dose N=132-133	D0-Pre-booster dose N=140	D06- Post booster dose N=45	D30 – Post booster dose N=176
A								
% ≥1:8 (Seroprotection)	94.7 (91.9; 96.7)	72.8 (68.0; 77.2)	91.3 (79.2; 97.6)	99.4 (96.8; 100)	81.2 (73.5; 87.5)	71.4 (63.2; 78.7)	95.6 (84.9; 99.5)	99.4 (96.9; 100)
% Seroresponse	-	-	82.6 (68.6; 92.2)	94.8 (90.4; 97.6)	-	-	77.8 (62.9; 88.8)	93.2 (88.4; 96.4)
hSBA GMT	45.2 (39.9; 51.1)	12.5 (11.1; 14.1)	289 (133; 625)	502 (388; 649)	32.8 (25.0; 43.1)	11.6 (9.41; 14.3)	161 (93.0; 280)	399 (318; 502)
C								

% ≥1:8 (Seroprotection)	98.1 (96.2; 99.2)	86.3 (82.4; 89.6)	100 (92.3; 100)	100 (97.9; 100)	74.2 (65.9; 81.5)	49.3 (40.7; 57.9)	97.8 (88.2; 99.9)	100 (97.9; 100)
% Seroresponse	-	-	89.1 (76.4; 96.4)	97.1 (93.4; 99.1)	-	-	93.3 (81.7; 98.6)	98.9 (96.0; 99.9)
hSBA GMT	417 (348; 500)	37.5 (31.6; 44.5)	3799 (2504; 5763)	3708 (3146; 4369)	49.7 (32.4; 76.4)	11.0 (8.09; 14.9)	919 (500; 1690)	2533 (2076; 3091)
W								
% ≥1:8 (Seroprotection)	100 (99.0; 100)	88.9 (85.3; 91.9)	100 (92.3; 100)	100 (97.9; 100)	93.2 (87.5; 96.9)	76.4 (68.5; 83.2)	100 (92.1; 100)	100 (97.9; 100)
% Seroresponse	-	-	97.8 (88.5; 99.9)	97.7 (94.2; 99.4)	-	-	88.9 (75.9; 96.3)	98.9 (96.0; 99.9)
hSBA GMT	82.7 (73.6; 92.9)	28.8 (25.1; 33.0)	1928 (1187; 3131)	2290 (1934; 2711)	45.1 (34.3; 59.4)	14.9 (11.9; 18.6)	708 (463; 1082)	2574 (2178; 3041)
Y								
% ≥1:8 (Seroprotection)	97.9 (95.9; 99.1)	81.8 (77.5; 85.5)	97.8 (88.5; 99.9)	100 (97.9; 100)	88.7 (82.1; 93.5)	52.1 (43.5; 60.7)	100 (92.1; 100)	100 (97.9; 100)
% Seroresponse	-	-	95.7 (85.2; 99.5)	98.9 (95.9; 99.9)	-	-	91.1 (78.8; 97.5)	100 (97.9; 100)
hSBA GMT	91.0 (78.6; 105)	21.8 (18.8; 25.1)	1658 (973; 2826)	2308 (1925; 2767)	36.1 (27.2; 47.8)	8.49 (6.50; 11.1)	800 (467; 1371)	3036 (2547; 3620)

*MET50 – The study was conducted in adolescents (10-17 years of age).
**MET43 – The study was conducted in children, adolescents and adults (10-55 years of age).
***MET59 – NCT04084769
$N calculated using per protocol analysis set (PPAS 1 and 2) with valid serology results; post-booster dose = D06 or D30 of MET59
^N calculated using full analysis set for persistence (FASP) with valid serology results. The number of participants varies depending on the timepoints and serogroup; post-primary dose = D30 MET50 or MET43, pre-booster dose = D0 MET59.
Vaccine seroresponse: titre is <1:8 at baseline with post-vaccination titre ≥1:16 or titre is ≥1:8 at baseline with a ≥4-fold increase at post-vaccination.
95% CI of the single proportion calculated from the exact binomial method.

Persistence of immune response and MenQuadfi booster response in adults 59 years of age and older

MEQ00066 evaluated the antibody persistence of primary dose, immunogenicity, and safety of a booster dose of MenQuadfi in older adults who had received a single dose of MenQuadfi or MenACWY-PS ≥3 or 5 years previously in study MET49 or MET44.

3 year persistence

The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-PS) participants had received 3 years previously at ≥ 56 years of age in MET49 (see Table 20).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for both MenQuadfi-primed and MenACWY-PS-primed adults. In addition, for both primed groups, the pre-booster GMTs were higher than the pre-primary dose for serogroups C, W and Y (indicative of long-term persistence of immune response for these serogroups) and were comparable for serogroup A.

Table 20 - Comparison of bactericidal antibody response at D6 and D30 days following booster vaccination, and persistence in adults (≥59 years) primed with MenQuadfi or MenACWY-PS 3 years before at ≥ 56 years of age in study MET49* – (study MEQ00066#)

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)				MenQuadfi Booster in MenACWY-PS primed (95% CI)			
	Persistence^		Booster$		Persistence^		Booster$	
	D30 - Post primary dose N=212	D0 - Pre-booster dose N=214	D06 – Post booster dose N=58	D30 - Post booster dose N=145	D30 Post primary dose N=168	D0-Pre-booster dose N=169	D06 - Post booster dose N=62	D30 - Post booster dose N=129-130
A								
% ≥1:8 (Seroprotection)	89.6 (84.7; 93.4)	65.0 (58.2; 71.3)	91.4 (81.0; 97.1)	93.8 (88.5; 97.1)	85.7 (79.5; 90.6)	65.7 (58.0; 72.8)	72.6 (59.8; 83.1)	87.7 (80.8; 92.8)
% Seroresponse	-	-	36.2 (24.0; 49.9)	79.3 (71.8; 85.6)	-	-	8.1 (2.7; 17.8)	60.8 (51.8; 69.2)
hSBA GMT	48.9 (39.0; 61.5)	12.2 (10.2; 14.6)	43.7 (26.5; 71.9)	162 (121; 216)	37.7 (29.3; 48.7)	11.6 (9.53; 14.1)	13.1 (9.60; 17.8)	56.6 (41.5; 77.2)
C								
% ≥1:8 (Seroprotection)	88.2 (83.1; 92.2)	73.4 (66.9; 79.2)	98.3 (90.8; 100)	99.3 (96.2; 100)	71.4 (64.0; 78.1)	47.9 (40.2; 55.7)	51.6 (38.6; 64.5)	85.3 (78.0; 90.9)
% Seroresponse	-	-	77.6 (64.7; 87.5)	93.1 (87.7; 96.6)	-	-	8.1 (2.7; 17.8)	55.0 (46.0; 63.8)
hSBA GMT	84.8 (64.0; 112)	17.7 (14.3; 21.9)	206 (126; 339)	638 (496; 820)	26.7 (19.8; 36.0)	8.47 (6.76; 10.6)	11.1 (7.17; 17.1)	56.0 (39.7; 78.9)
W								
% ≥1:8 (Seroprotection)	78.8 (72.6; 84.1)	66.8 (60.1; 73.1)	89.7 (78.8; 96.1)	98.6 (95.1; 99.8)	60.1 (52.3; 67.6)	39.6 (32.2; 47.4)	46.8 (34.0; 59.9)	80.8 (72.9; 87.2)
% Seroresponse	-	-	70.7 (57.3; 81.9)	90.3 (84.3; 94.6)	-	-	6.5 (1.8; 15.7)	49.2 (40.4; 58.1)

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)				MenQuadfi Booster in MenACWY-PS primed (95% CI)			
hSBA GMT	28.0 (22.2; 35.3)	14.2 (11.6; 17.4)	118 (64.0; 216)	419 (317; 553)	14.7 (11.0; 19.8)	6.54 (5.28; 8.11)	9.89 (6.45; 15.2)	31.0 (22.6; 42.6)
Y								
% ≥1:8 (Seroprotection)	92.5 (88.0; 95.6)	68.2 (61.5; 74.4)	94.8 (85.6; 98.9)	100 (97.5; 100)	65.5 (57.8; 72.6)	40.8 (33.3; 48.6)	45.2 (32.5; 58.3)	81.5 (73.8; 87.8)
% Seroresponse	-	-	72.4 (59.1; 83.3)	92.4 (86.8; 96.2)	-	-	8.1 (2.7; 17.8)	49.2 (40.4; 58.1)
hSBA GMT	65.3 (51.8; 82.2)	15.3 (12.3; 19.1)	151 (83.4; 274)	566 (433; 740	19.6 (14.4; 26.7)	7.49 (5.72; 9.82)	11.1 (6.31; 19.4)	40.5 (29.0; 56.4)

* Clinical trial identifier: NCT02842866
# Clinical trial identifier: NCT04142242
^N calculated using full analysis set for persistence (FAS3) with valid serology results; Post primary dose = D30 of MET49, Pre-booster dose = D0 of MEQ00066
$N calculated using per protocol analysis Set 2 and 1 (PPAS2 and PPAS1) with valid serology results. The number of participants varies depending on the timepoints and serogroup; Post booster dose = D06 or D30 of MEQ00066
Vaccine seroresponse - titer is < 1:8 at baseline with post-vaccination titer ≥ 1:16 or titer is ≥ 1:8 at baseline with a ≥ 4-fold increase at post-vaccination.
95% CI of the single proportion calculated using the exact binomial method.

5 year persistence

A subset of participants who were assessed for antibody persistence at 3 years and did not receive the MenQuadfi booster dose were re-assessed for antibody persistence at 5 years at which time they received a booster dose of MenQuadfi.

In MenQuadfi-primed subjects, hSBA GMTs for serogroups C, W and Y 5Y post-primary dose were higher than the pre-priming GMTs (and were comparable for serogroup A), indicating long-term persistence of immune response.

Following the MenQuadfi booster dose, seroprotection rates were 100% for serogroups A, C, and Y, and 95.0% for serogroup W in subjects primed with MenQuadfi and 87.5%, 62.5%, 87.5% and 68.8% for serogroups A, C, W and Y, respectively, for those primed with MenACWY-PS.

6-7 year persistence

The antibody persistence was assessed according to the vaccine (MenQuadfi or MenACWY-PS) participants had received 6-7 years previously in study MET44 (see Table 21).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for MenQuadfi-primed adults. The pre-booster GMTs were higher than the pre-primary dose

for serogroup C, W, and Y in MenQuadfi-primed adults, indicative of long-term persistence of immune response for these serogroups, and were comparable for serogroup A.

Table 21 - Comparison of bactericidal antibody persistence in adults (≥59 years) primed with MenQuadfi or MenACWY-PS 6-7 years before in MET44^ – (study MEQ00066[#])

Endpoint by Serogroup	6-7 years Persistence^			
	MenQuadfi primed (95% CI)		MenACWY-PS primed (95% CI)	
	D30 - Post primary dose$	D0 - Pre-booster dose#	D30 - Post primary dose$	D0 - Pre-booster dose#
	N=58	N=59	N=26	N=26
A				
% ≥1:8 (Seroprotection)	91.4 (81.0; 97.1)	55.9 (42.4; 68.8)	76.9 (56.4; 91.0)	50.0 (29.9; 70.1)
GMT	48.0 (30.6; 75.4)	9.00 (6.44; 12.6)	27.3 (13.8; 54)	9.64 (5.18; 17.9)
C				
% ≥1:8 (Seroprotection)	74.1 (61.0; 84.7)	59.3 (45.7; 71.9)	76.9 (56.4; 91.0)	42.3 (23.4; 63.1)
GMT	52.2 (27.4; 99.7)	11.9 (7.67; 18.5)	23.9 (11.9; 48.1)	7.58 (4.11; 14.0)
W				
% ≥1:8 (Seroprotection)	75.9 (62.8; 86.1)	66.1 (52.6; 77.9)	73.1 (52.2; 88.4)	38.5 (20.2; 59.4)
GMT	31.2 (18.8; 52.0)	11.9 (7.97; 17.8)	18.8 (10.1; 34.9)	4.95 (3.39; 7.22)
Y				
% ≥1:8 (Seroprotection)	81.0 (68.6; 90.1)	59.3 (45.7; 71.9)	73.1 (52.2; 88.4)	46.2 (26.6; 66.6)
GMT	45.8 (26.9; 78.0)	11.2 (7.24; 17.5)	25.9 (12.4; 53.8)	7.19 (4.09; 12.6)

^Clinical trial identifier: NCT01732627
[#]Clinical trial identifier: NCT04142242
N: number of participants in full analysis set for persistence (FAS3) with valid serology results.
$ Post primary dose = D30 of MET44
# Pre-booster dose = D0 of MEQ00066
95% CI of the single proportion calculated from the exact binomial method.

Booster response in adolescents and adults at least 15 years of age primed with other MenACWY vaccines

Study MET56 compared the immunogenicity of a booster dose of MenQuadfi to a booster dose of MenACWY-DT in participants at least 15 years of age and primed with quadrivalent meningococcal conjugate vaccine (MCV4; MenACWY-CRM or MenACWY-DT) 4 to 10 years earlier.

At baseline, hSBA seroprotection and GMT were similar for serogroups A, C, W, and Y.

The hSBA seroresponse following a booster dose of MenQuadfi was non-inferior to that following a booster dose of MenACWY-DT for all four serogroups.

The percentages of participants with hSBA titres ≥ 1:8 increased from baseline for all serogroups and in both groups. The percentages were comparable in MenQuadfi and MenACWY-DT for all serogroups (see Table 22).

Table 22 - Comparison of Bactericidal Antibody Responses at D30 following booster vaccination with MenQuadfi and MenACWY-DT in participants at least 15 years of age primed with MenACWY-CRM or MenACWY-DT 4 to 10 years earlier (MET56)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	%difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	100.0 (99.0; 100.0) N=384	99.0 (97.4; 99.7) N=389	1.0 (-0.1; 2.6)	
% Seroresponse§	92.2 (89.0; 94.7) N=384	87.1 (83.4; 90.3) N=389	5.0 (0.735; 9.38)	
hSBA GMT	497 (436; 568) N=384	296 (256; 343) N=389		1.68 (1.38; 2.05)
C				
% ≥1:8 (Seroprotection)	99.5 (98.1; 99.9) N=384	99.0 (97.4; 99.7) N=389	0.5 (-1.0; 2.1)	
% Seroresponse§	97.1 (94.9; 98.6) N=384	91.8 (88.6; 94.3) N=389	5.4 (2.16; 8.76)	
hSBA GMT	2,618 (2,227; 3,078) N=384	599 (504; 711) N=389		4.37 (3.45; 5.53)
W				
% ≥1:8 (Seroprotection)	100.0 (99.0; 100.0) N=384	99.7 (98.6; 100.0) N=389	0.3 (-0.8; 1.4)	
% Seroresponse§	98.2 (96.3; 99.3) N=384	90.7 (87.4; 93.4) N=389	7.4 (4.30; 10.9)	
hSBA GMT	1,747 (1,508; 2,025) N=384	723 (614; 853) N=389		2.42 (1.94; 3.01)
Y				
% ≥1:8 (Seroprotection)	99.7 (98.6; 100.0) N=384	99.5 (98.2; 99.9) N=389	0.3 (-1.0; 1.6)	
% Seroresponse§	97.4 (95.3; 98.7) N=384	95.6 (93.1; 97.4) N=389	1.8 (-0.907; 4.55)	
hSBA GMT	2,070 (1,807; 2,371) N=384	811 (699; 941) N=389		2.55 (2.09; 3.12)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	%difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups

Concomitantly Administered Vaccines

Immunogenicity of MenQuadfi when given concomitantly with routine paediatric vaccines in infants initiating vaccination from 6 weeks of age – Studies MET42, MET61, MET33, MET52

MenQuadfi can be co-administered with routine paediatric vaccines. In a clinical trial conducted in the US initiating vaccination in infants as early as 6 weeks of age, MenQuadfi was given concomitantly with routine paediatric vaccines including DTPa-IPV/Hib, PCV13, rotavirus vaccine, HepB, MMR, V, and HepA (MET42). In another clinical trial conducted in the US initiating vaccination in older infants aged 6-7 months (MET61), MenQuadfi was administered concomitantly with DTPa-IPV/Hib or DTPa-IPV-HepB, Hib vaccine, rotavirus vaccine, HepB, PCV13, MMR, and V.

The immune response of routine paediatric vaccines was assessed in MET42 and no interference was observed when DTPa-IPV/Hib, PCV13, rotavirus vaccine, HepB, MMR and V were given concomitantly with MenQuadfi compared to when the vaccines were given concomitantly with MenACWY-CRM. Non-inferiority of immune responses to DTPa-IPV/Hib, PCV13, rotavirus vaccine, and HepB following vaccinations at 6 months and DTPa-IPV/Hib, PCV13, MMR and V following vaccinations at 12-18 months was demonstrated.

In two other supporting clinical trials (MET33 and MET52), MenQuadfi was administered concomitantly with DTPa-IPV-HepB-Hib or DTPa-IPV/Hib or DTPa-HepB-IPV/Hib, HepB, rotavirus vaccine, and PCV13. In MET33, MenQuadfi was also administered concomitantly with MMR.

Overall, the immunogenicity profile of the routine paediatric vaccines when co-administered with MenQuadfi or MenACWY-CRM or when administered alone was comparable following the infant vaccination series and the booster vaccination in the second year of life in Mexico and the Russian Federation (MET33).

Immunogenicity of a single dose of MenQuadfi when given concomitantly with routine paediatric vaccines or when routine paediatric vaccines were given alone in meningococcal naïve infants 12 through 23 months of age – Study MET57

A Phase III study MET57 was performed in meningococcal vaccine naive toddlers to evaluate the efficacy of MenQuadfi concomitantly administered with MMR, V, PCV13, and DTPa-IPV-HepB-Hib and showed no clinically relevant interference on antibody responses to each of the antigens. Overall, the immunogenicity profile of MenQuadfi administered alone was comparable to the

MenQuadfi administered concomitantly with licensed paediatric vaccines (MMR+V, DTPa-IPV-HepB-Hib, or PCV13).

Overall, the immunogenicity profile of licensed paediatric vaccines (MMR+V, DTPa-IPV-HepB-Hib, or PCV13) administered alone without MenQuadfi was comparable to that of the licensed paediatric vaccines administered concomitantly with MenQuadfi.

Immunogenicity of a single dose of MenQuadfi given alone, MenQuadfi given concomitantly with dTpa and HPV or dTpa and HPV given alone in meningococcal vaccine naïve adolescents 10 to 17 years of age – Study MET50

A Phase II Study (MET50) was performed in meningococcal naive children and adolescents to evaluate the efficacy of MenQuadfi administered concomitantly with dTpa and HPV vaccines.

The antibody responses to MenQuadfi and to HPV, tetanus and diphtheria antigens were similar in both study groups. The anti-pertussis responses of the dTpa administered concomitantly with MenQuadfi and HPV versus dTpa administered concomitantly with HPV only were non-inferior for the PT antigen and did not meet non-inferiority for the FHA, PRN, FIM antigens. Vaccine response rates were robust and comparable across both groups. This trend is in line with the data available with the existing quadrivalent meningococcal conjugate vaccines. Because there are no established serological correlates of protection for pertussis, the clinical implications of the observed pertussis antigen responses are unknown.

Immunogenicity of MenQuadfi given alone or with MenB vaccine in infants initiating vaccination from 3 months of age

Study MET52 evaluated the antibody response of a booster dose of MenQuadfi when given alone or concomitantly with MenB vaccine (Bexsero) in infants. MenQuadfi was given at 3 months and 12-13 months of age and Bexsero was given at 2, 4, and 12-13 months of age.

Immune non-inferiority, based on seroprotection rate, was demonstrated when MenQuadfi booster dose was given concomitantly with Bexsero compared to when MenQuadfi was given alone.

Overall, no clinically relevant interference of immune response to serogroups A, C, W, and Y was observed when MenQuadfi booster was co-administered with licensed MenB vaccine.

Immunogenicity of Booster dose of MenQuadfi given alone or concomitantly with MenB vaccine in adolescents and adults 13 through 26 years of age who had received a single dose of MenQuadfi 3-6 years before as part of study MET50 or MET43 – Study MET59

Concomitant administration of MenQuadfi with MenB vaccine (Trumenba, N=90 or Bexsero, N=89) in adolescents and adults 13 through 26 years of age was evaluated in MET59. There was no suggestion of interference in MenQuadfi hSBA seroresponse rates when the vaccine was coadministered with MenB vaccine. The potential impact of MenQuadfi on MenB vaccine immune response was not assessed.

Immunogenicity of a single dose of MenQuadfi when given separately or concomitantly with dTpa-IPV and 9vHPV in meningococcal vaccine naïve or MenC primed (before two years of age) adolescents 10 to 17 years of age – Study MEQ00071

MEQ00071 was performed to evaluate the antibody responses of MenQuadfi when given alone compared to that of MenACWY-TT and when MenQuadfi was given concomitantly with tetanus, diphtheria, acellular pertussis with inactivated poliomyelitis [dTpa-IPV] vaccine and human papillomavirus 9-valent [9vHPV] vaccine in participants 10 through 17 years of age.

Participants were randomised to receive one of the following study regimens: MenQuadfi alone (N=173), MenACWY-TT alone (N=173) or MenQuadfi + dTpa-IPV + 9vHPV (N = 117).

The post vaccination hSBA seroprotection rates for each serogroup were comparable in participants who received MenQuadfi alone or concomitantly with dTpa -IPV and 9vHPV. The post vaccination hSBA GMTs were higher for serogroups A and W in participants who received MenQuadfi alone compared to those who received MenQuadfi concomitantly with dTpa-IPV + 9vHPV and comparable for serogroups C and Y between study groups. The post vaccination hSBA seroresponse rates for serogroup A were higher in participants who received MenQuadfi alone compared to those who received MenQuadfi concomitantly with dTpa-IPV + 9vHPV and comparable for serogroups C, Y and W between study groups (see Table 23).

The anti-diphtheria, -polio type 2, -FHA and -FIM geometric means (GMs) were similar when dTpa-IPV + 9vHPV were given concomitantly with MenQuadfi or when dTpa-IPV + 9vHPV were given separately from MenQuadfi.

Anti-PT, -polio type 1 and 3 and -PRN GMs were lower when dTpa-IPV + 9vHPV were given concomitantly with MenQuadfi than when given separately from MenQuadfi. Higher GMs were observed to tetanus when dTpa-IPV + 9vHPV were given concomitantly with MenQuadfi than when dTpa-IPV + 9vHPV were given separately from MenQuadfi (see Table 24).

The response rates of antibody titers/concentrations against antigens contained in dTpa-IPV were comparable when given concomitantly with 9vHPV + MenQuadfi compared to when dTpa -IPV + 9vHPV were given separately from MenQuadfi (see Table 25).

All anti-HPV antibodies, as measured by GMs, before and after vaccination were similar between study groups except anti-HPV type-6 and type-58, for which the GMs were lower in participants who received dTpa-IPV + 9vHPV concomitantly with MenQuadfi compared to those who received dTpa-IPV + 9vHPV separately from MenQuadfi. The proportions of participants who achieved seroconversion were comparable between both study groups (see Table 26 and Table 27).

Although antibody responses, when assessed by GMs, tended to be lower when MenQuadfi was given concomitantly with dTpa-IPV + 9vHPV compared to when dTpa-IPV + 9vHPV were given separately from MenQuadfi, no clinically relevant differences were observed.

Table 23 - MEQ00071* - Comparison of hSBA antibody response 30 days after vaccination with MenQuadfi when administered separately or concomitantly with dTpa-IPV + 9vHPV in adolescents (10 through 17 years) - PPASM

Endpoint by Serogroup	MenQuadfi** (95% CI) N=159	MenQuadfi+dTpa-IPV+9vHPV$ (95% CI) N=113
A		
% ≥1:8 (Seroprotection)	97.5 (93.7; 99.3)	91.2 (84.3; 95.7)
% Seroresponse	88.0 (81.9; 92.6)	63.4 (68.0; 81.9)
GMT	78.2 (64.6; 94.7)	42.2 (32.5; 54.7)
C		
% ≥1:8 (Seroprotection)	100 (97.7; 100)	99.1 (95.2; 100)
% Seroresponse	99.4 (96.5; 1000	97.3 (92.4; 99.4)
GMT	2294 (1675; 3142)	1938 (1365; 2752)
W		
% ≥1:8 (Seroprotection)	100 (97.7; 100)	100 (96.8; 100)
% Seroresponse	93.1 (88.0; 96.5)	85.7 (77.8; 91.6)
GMT	134 (109; 164)	74.6 (61.8; 90.1)
Y		
% ≥1:8 (Seroprotection)	99.4 (96.5 ; 100)	99.1 (95.2 ; 100)
% Seroresponse	98.7 (95.5; 99.8)	99.1 (95.2; 100)
GMT	169 (141; 202)	171 (138; 211)

*Clinical trial identifier NCT04490018

**Participants received MenQuadfi on D01 and dTpa-IPV+9vHPV on D31

$Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01

N: number of subjects in the Per-Protocol Analysis Set and includes both meningococcal vaccine naïve and MenC primed participants

95% CI of the single proportion calculated from the exact binomial method

The two-sided 95% CI is calculated based on the Wilson score method without continuity correction as described by Newcombe R.G.

hSBA vaccine seroresponse is defined as a post-vaccination titer ≥ 1:16 for participants with pre-vaccination hSBA titer < 1:8, or a post-vaccination titer ≥ 4-fold increase from baseline for participants with pre-vaccination hSBA titer ≥ 1:8

Table 24 - MEQ00071* - Summary of geometric means of antibody titers/concentrations against antigens contained in dTpa-IPV 30 days after concomitant administration with 9vHPV or concomitant administration with 9vHPV and MenQuadfi – PPASC

	dTpa-IPV+9vHPV** (N=149)			MenQuadfi+ dTpa-IPV+9vHPV$ (N=113)		
Antigens	M	GM	(95% CI)	M	GM	(95% CI)
Tetanus	149	17.3	(14.9; 20.1)	113	34.5	(30.1; 39.6)
Diphtheria	149	3.75	(3.24; 4.35)	113	2.91	(2.46; 3.44)
PT	149	58.4	(50.6; 67.4)	113	41.4	(36.1; 47.4)
Polio 1	149	3135	(2692; 3650)	113	1593	(1306; 1943)
Polio 2	147	3344	(2635; 4245)	113	2950	(2409; 3613)
Polio 3	149	7059	(5861; 8502)	113	3166	(2553; 3926)
FHA	149	177	(156; 200)	113	146	(128; 166)
PRN	149	331	(265; 414)	113	236	(184; 303)
FIM	149	152	(112; 207)	113	106	(75.3; 149)

*Clinical trial identifier NCT04490018

**Participants received MenQuadfi on D01 and dTpa-IPV+9vHPV on D31

$Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01

M: number of subjects with valid serology results for the particular antigen and time point N: number of subjects in Per-Protocol Analysis Set (PPAS)

Table 25 - MEQ00071* - Summary of response rates of antibody titers/concentrations against antigens contained in dTpa-IPV 30 days after concomitant administration with 9vHPV or concomitant administration with 9vHPV and MenQuadfi – PPASC

		dTpa-IPV+9vHPV** (N=149)			MenQuadfi+dTpa-IPV+9vHPV$ (N=113)		
Antigens	Criteria	n/M	%	(95% CI)	n/M	%	(95% CI)
Diphtheria	≥0.1 IU/mL	149/149	100	(97.6; 100)	112/113	99.1	(95.2; 100)
	≥1 IU/mL	139/149	93.3	(88.0; 96.7)	102/113	90.3	(83.2; 95.0)
Tetanus	≥0.1 IU/mL	149/149	100	(97.6; 100)	113/113	100	(96.8; 100)
	≥1 IU/mL	148/149	99.3	(96.3; 100)	113/113	100	(96.8; 100)
PT	Vaccine response*	118/145	81.4	(74.1; 87.4)	86/113	76.1	(67.2; 83.6)
Polio 1	≥8 (1/dil)	149/149	100	(97.6; 100)	113/113	100	(96.8; 100)
Polio 2	≥8 (1/dil)	147/147	100	(97.5; 100)	113/113	100	(96.8; 100)
Polio 3	≥8 (1/dil)	149/149	100	(97.6; 100)	113/113	100	(96.8; 100)

		dTpa-IPV+9vHPV** (N=149)			MenQuadfi+dTpa-IPV+9vHPV$ (N=113)		
FHA	Vaccine response*	110/147	74.8	(67.0; 81.6)	80/113	70.8	(61.5; 79.0)
PRN	Vaccine response*	144/147	98.0	(94.2; 99.6)	103/113	91.2	(84.3; 95.7)
FIM	Vaccine response*	138/147	93.9	(88.7; 97.2)	108/113	95.6	(90.0; 98.5)

*Clinical trial identifier NCT04490018

**Participants received MenQuadfi on D01 and dTpa-IPV+9vHPV on D31

$Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01 n: number of participants with titers that meet the criteria

M: number of participants with valid serology results for the particular antigen

% are percentages for dTpa-IPV+9vHPV and MenQuadfi+dTpa-IPV+9vHPV. Percentages are based on M

*Seroresponse is defined as post-vaccination concentration ≥ 4 × baseline concentration, if the anti-pertussis antibody concentration at baseline is < 4 × LLOQ, or ≥ 2 × baseline concentration, if the anti-pertussis antibody concentration at baseline is ≥ 4 × LLOQ.

Table 26 - MEQ00071* Summary of geometric means of antibody concentrations against antigens contained in 9vHPV 30 days after concomitant administration with dTpa-IPV or concomitant administration with dTpa-IPV and MenQuadfi- PPAS

	dTpa-IPV+9vHPV** (N=149)			MenQuadfi+ dTpa-IPV+9vHPV$ (N=113)		
HPV Type	M	GM	(95% CI)	M	GM	(95% CI)
6	149	73.9	(64.3; 85.0)	113	50.6	(42.0; 60.9)
11	149	43.9	(38.9; 49.5)	113	36.3	(30.8; 42.8)
16	149	199	(171; 231)	113	146	(118; 179)
18	149	46.5	(38.4; 56.4)	113	31.2	(24.0; 40.6)
31	149	31.7	(26.5; 38.1)	113	24.7	(19.2; 31.8)
33	149	21.1	(17.8; 24.9)	113	15.0	(12.2; 18.6)
45	149	11.5	(9.35; 14.1)	113	8.24	(6.30; 10.8)
52	149	47.4	(41.1; 54.7)	113	40.9	(33.5; 49.8)
58	149	29.6	(25.5; 34.3)	113	20.6	(16.9; 25.1)

*Clinical trial identifier NCT04490018

**Participants received MenQuadfi on D01 and dTpa-IPV+9vHPV on D31

$Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01

M: number of participants with valid serology results for the particular HPV type

GMT: geometric mean titer

Table 27 - MEQ00071* – Summary of seroconversion of antibody concentrations against antigens contained in 9vHPV 30 days after concomitant administration with dTpa-IPV or concomitant administration with dTpa-IPV and MenQuadfi - PPASC

	dTpa-IPV+9vHPV** (N=149)			MenQuadfi+dTpa-IPV+9vHPV$ (N=113)		
HPV Type	n/M	(%)	(95% CI)	n/M	(%)	(95% CI)

	dTpa-IPV+9vHPV** (N=149)			MenQuadfi+dTpa-IPV+9vHPV$ (N=113)		
6	129/147	87.8	(81.3; 92.6)	96/113	85.0	(77.0; 91.0)
11	146/147	99.3	(96.3; 100)	110/113	97.3	(92.4; 99.4)
16	146/147	99.3	(96.3; 100)	111/113	98.2	(93.8; 99.8)
18	139/147	94.6	(89.6; 97.6)	100/113	88.5	(81.1; 93.7)
31	142/147	96.6	(92.2; 98.9)	100/113	88.5	(81.1; 93.7)
33	140/147	95.2	(90.4; 98.1)	99/113	87.6	(80.1; 93.1)
45	120/147	81.6	(74.4; 87.5)	85/113	75.2	(66.2; 82.9)
52	146/147	99.3	(96.3; 100)	109/113	96.5	(91.2; 99.0)
58	140/147	95.2	(90.4; 98.1)	104/113	92.0	(85.4; 96.3)

*Clinical trial identifier NCT04490018

**Participants received MenQuadfi on D01 and dTpa-IPV+9vHPV on D31

$Participants received MenQuadfi + dTpa-IPV + 9vHPV on D01

n: number of participants with titers that meet the HPV seroconversion criteria M: number of participants with valid serology results for the particular HPV type Percentages are based on M

Seroconversion is changing serostatus from seronegative to seropositive after vaccination. Cutoff values for HPV seropositivity for types 6, 11, 16, 18, 31, 33, 45, 52, and 58 are 9, 6, 5, 5, 3, 4, 3, 5, and 5 milli-Merck units (mMU)/mL, respectively.

5.2 PHARMACOKINETIC PROPERTIES

No pharmacokinetic studies have been performed.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

MenQuadfi has not been evaluated for genotoxic potential.

Carcinogenicity

MenQuadfi has not been evaluated for carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium chloride, sodium acetate and water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 SHELF LIFE

48 months when stored at 2°C to 8°C.

Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period, MenQuadfi must be used or discarded. It must not be returned to storage. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C (Refrigerate. Do not freeze).

6.5 NATURE AND CONTENTS OF CONTAINER

Pack of 1 or 10 single dose (0.5 mL) vials.

Vial stopper is not made with natural latex.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

After use, any remaining vaccine and container must be disposed of safely, according to locally acceptable procedures.

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 Prescription Only Medicine

8 SPONSOR

sanofi-aventis australia pty ltd
International Tower 3, Level 23
300 Barangaroo Avenue
Sydney NSW 2000
Freecall: 1800 818 806
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

29 October 2020

10 DATE OF REVISION

19 November 2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4	Additional clarification for preterm birth
4.8	Addition of febrile convulsion and clarifying footnotes for rare frequency
5.1	Removed ‘Pasteur’ from the sponsor name