Nimenrix™
Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine

1. NAME OF THE MEDICINAL PRODUCT

Nimenrix™

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains 5 micrograms of polysaccharide for *Neisseria meningitidis* groups A*, C*, W-135* and Y*.
* conjugated to tetanus toxoid carrier protein 44 micrograms

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

4. CLINICAL PARTICULARS

4.1. Indications

Nimenrix™ is indicated for active immunization of individuals from 6 weeks of age against invasive meningococcal diseases caused by *Neisseria meningitidis* groups A, C, W-135 and Y.

4.2. Dosage and Administration

Posology
Nimenrix™ should be used in accordance with available official recommendations.

Table 1: Posology

Age Group	Primary Immunization	Booster
Infants from 6 weeks to less than 6 months of age*	Two doses, each of 0.5 ml, with the first dose given from 6 weeks of age, with an interval of 2 months between doses	At 12 months of age
Unvaccinated infants from 6 months to less than 12 months of age**	One dose of 0.5 ml given from 6 months of age	At 12 months of age with a minimum interval of at least 2 months after the primary dose
Children from 12 months of age, adolescents and adults**	One dose of 0.5 ml	Not routinely administered

* See section 5.1 for further information.
** In some situations, consideration may be given to administering an additional primary dose or a booster dose of **Nimenrix™** (see sections 4.4 and 5.1 for further information).

Previously vaccinated children from 12 months of age, adolescents and adults
Nimenrix™ may be given as a booster dose to individuals who have previously received primary vaccination with a conjugated or plain polysaccharide meningococcal vaccine (see section 5.1).

Special populations
Individuals who have underlying conditions predisposing them to meningococcal infection due to anatomic or functional asplenia (such as sickle cell disease) may receive at least one dose of **Nimenrix™** (see sections 4.8 and 5.1).

Method of administration
Immunization should be carried out by intramuscular injection only.

In infants, the recommended injection site is the anterolateral aspect of the thigh.

In individuals from 1 year of age, the recommended injection site is the anterolateral aspect of the thigh or the deltoid muscle (see sections 4.4 and 4.5).

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3. Contraindications

Nimenrix™ should not be administered to subjects with hypersensitivity to the active substances or to any of the excipients contained in the vaccine (see sections 2 and 6.1).

4.4. Warnings and Precautions

Nimenrix™ should under no circumstances be administered intravascularly, intradermally or subcutaneously.

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Intercurrent illness
As with other vaccines, vaccination with **Nimenrix™** should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Syncope
Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

Subjects previously vaccinated with a plain polysaccharide meningococcal vaccine and vaccinated with **Nimenrix™** 30 to 42 months later had lower Geometric Mean Titres (GMTs) measured with rabbit complement serum bactericidal assay (rSBA) than subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years. Clinical relevance of this observation is unknown.

Thrombocytopenia and coagulation disorders
As with other vaccines administered intramuscularly, **Nimenrix™** should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

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

Persons with certain complement deficiencies and persons receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* groups A, C, W-135 and Y even if they develop antibodies following vaccination with **Nimenrix™**.

Special populations
Limited data are available on the safety and immunogenicity in individuals with increased susceptibility to meningococcal infection due to anatomic or functional asplenia (such as sickle cell disease) (see sections 4.2, 4.8 and 5.1).

Protection against meningococcal disease
Nimenrix™ will only confer protection against *Neisseria meningitidis* groups A, C, W-135 and Y. The vaccine will not protect against other *Neisseria meningitidis* groups.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

Immune response in infants aged 6 months to less than 12 months
A single-dose administered at 6 months was associated with lower human complement serum bactericidal assay (hSBA) titres to groups W-135 and Y compared with three doses administered at 2, 4, and 6 months (see section 5.1). The clinical relevance of this observation is unknown. If an infant aged 6 months to less than 12 months is expected to be at immediate risk of invasive meningococcal disease due to exposure to groups W-135, and/or Y, consideration may be given to administering a second primary dose of **Nimenrix™** after an interval of 2 months.

Immune responses in toddlers aged 12-14 months
At 1 month post vaccination, toddlers aged 12-14 months had similar rSBA titres to groups A, C, W-135, and Y following one dose of **Nimenrix™** or two doses of **Nimenrix™** given 2 months apart. At 1 year post vaccination, the rSBA titres to groups A, C, W-135 and Y were similar in both the one and the two dose groups (see section 5.1).

Measured with a serum bactericidal assay using hSBA, 1 month post vaccination, responses to groups W-135 and Y were lower after a single dose than after 2 doses given 2 months apart, while responses to groups A and C were similar in the two groups (see section 5.1). The clinical relevance of these observations is unknown. If a toddler is expected to be at

immediate risk of invasive meningococcal disease due to the exposure to groups W-135 and/or Y, consideration may be given to administering a second primary dose after an interval of 2 months. At 1 year post vaccination, the hSBA responses for groups A, C, W-135 and Y were similar in both the one and the two dose groups (see section 5.1). Regarding waning of antibody against group A or group C after a first dose of **Nimenrix™** in children aged 12-23 months, see under Persistence of serum bactericidal antibody titres.

Persistence of serum bactericidal antibody titres

Persistence of antibodies has been evaluated up to 10 years after vaccination. The persistence studies with **Nimenrix™** have shown a waning of serum bactericidal antibody titres against group A when using human complement in the assay (hSBA) (see section 5.1). The clinical relevance of this observation is unknown. However, if an individual is expected to be at particular risk of exposure to group A and received a dose of **Nimenrix™** more than approximately 1 year previously, consideration may be given to administering a booster dose.

A decline in antibody titres over time has been observed. The clinical relevance of this observation is unknown. A booster dose might be considered in individuals remaining at high risk of exposure to meningococcal disease caused by groups A, C, W-135 and Y (see section 5.1).

Although **Nimenrix™** contains tetanus toxoid, this vaccine does not substitute for tetanus immunization.

4.5. Interactions with Other Medicinal Products and Other Forms of Interaction

In infants, **Nimenrix™** can be given concomitantly with combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliovirus and *Haemophilus influenzae* type b vaccines (DTaP/IPV/Hib/HepB), as well as 10-valent pneumococcal conjugate vaccine.

From age 1 year and above, **Nimenrix™** can be given concomitantly with any of the following vaccines: hepatitis A (HAV) and hepatitis B (HBV) vaccines, measles - mumps - rubella (MMR) vaccine, measles - mumps - rubella - varicella (MMRV) vaccine, 10-valent pneumococcal conjugate vaccine or unadjuvanted seasonal influenza vaccine.

Nimenrix™ can also be given concomitantly with combined diphtheria - tetanus - acellular pertussis vaccines, including combination DTaP vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b, such as DTaP/IPV/Hib/HepB vaccine and 13-valent pneumococcal conjugate vaccine in the second year of life.

Safety and immunogenicity of **Nimenrix™** was evaluated when sequentially administered or co-administered with a DTaP/IPV/Hib/HepB vaccine in the second year of life. The administration of **Nimenrix™** 1 month after the DTaP/IPV/Hib/HepB vaccine resulted in lower MenA, MenC and MenW-135 GMTs as measured with a serum bactericidal assay using rSBA. The clinical relevance of this observation is unknown, since at least 99.4% of subjects (N=178) had rSBA titres ≥8 for each group (A, C, W-135, and Y). Whenever possible, **Nimenrix™** and a tetanus toxoid (TT) containing vaccine, such as DTaP/IPV/Hib/HepB vaccine, should be co-administered or **Nimenrix™** should be administered at least 1 month before the TT-containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine in toddlers aged 12-23 months, lower Geometric Mean antibody Concentrations (GMCs) and opsonophagocytic assay (OPA) antibody GMTs were observed for one pneumococcal serotype (18C conjugated to tetanus toxoid carrier protein). The clinical relevance of this observation is unknown. There was no impact of co-administration on the other nine pneumococcal serotypes.

In individuals aged 9 to 25 years, **Nimenrix™** can be given concomitantly with human papillomavirus bivalent [Type 16 and 18] vaccine, recombinant (HPV2).

One month after co-administration with a combined tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, adsorbed (Tdap) in subjects aged 9 to 25 years, lower GMCs were observed to each pertussis antigen (pertussis toxoid [PT], filamentous haemagglutinin [FHA] and pertactin [PRN]). More than 98% of subjects had anti-PT, FHA or PRN concentrations above the assay cut-off thresholds. The clinical relevance of these observations is unknown. There was no impact of co-administration on immune responses to **Nimenrix™** or the tetanus or diphtheria antigens included in Tdap.

If **Nimenrix™** is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

As with other vaccines, it may be expected that in patients receiving immunosuppressive treatment an adequate response may not be elicited.

4.6. Pregnancy and Lactation

Pregnancy
There is limited experience with use of **Nimenrix™** in pregnant women.

Animal studies with **Nimenrix™** do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3).

Nimenrix™ should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

Lactation
The safety of **Nimenrix™** when administered to breast-feeding women has not been evaluated. It is unknown whether **Nimenrix™** is excreted in human breast milk.

Nimenrix™ should only be used during breast-feeding when the possible advantages outweigh the potential risks.

4.7. Effects on Ability to Drive and Use Machines

No studies on the effects of **Nimenrix™** on the ability to drive and use machines have been performed.

4.8. Adverse Reactions

The safety profile presented in Table 2 is based on two data sets:

- a pooled analysis in more than 9,000 subjects from the age of 1 year on, who have been vaccinated with 1 dose of **Nimenrix™** in clinical studies.
- data from approximately 1,000 infants (6 weeks to 12 months of age) who have been primed and boosted with **Nimenrix™**.

Table 2: Adverse Reactions by System Organ Class and Council for International Organizations of Medical Science (CIOMS) Frequency Category Listed in Order of Decreasing Medical Seriousness or Clinical Importance Within Each Frequency Category and SOC

System Organ Class	**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**	**Frequency Not Known (cannot be estimated from the available data)**
Metabolism and nutrition disorders	Appetite lost					
Psychiatric disorders	Irritability		Insomnia Crying			
Nervous system disorders	Drowsiness Headache[1]		Hypoaesthesia[1] Dizziness[1]			
Gastrointestinal disorders		Gastrointestinal symptoms (including diarrhoea, vomiting and nausea[2])				
Skin and subcutaneous tissue disorders			Rash[3] Urticaria Pruritus			
Musculoskeletal and connective tissue disorders			Myalgia[1] Pain in extremity[1]			
General disorders and administration site conditions	Fever Injection site swelling Injection site pain	Injection site haematoma[2]	Malaise Injection site reaction (including induration, pruritus, warmth, anaesthesia)			Extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb*

System Organ Class	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	Frequency Not Known (cannot be estimated from the available data)
	Injection site redness Fatigue[1]					

*Adverse reaction identified post-marketing.

1. Not reported in the infant clinical study (MenACWY-TT-083)
2. Occurred at a frequency of Uncommon in infants
3. Occurred at a frequency of Common in infants

In a separate study a single dose of **Nimenrix™** was administered to 274 individuals aged 56 years and older. All adverse reactions reported in this study were already observed in younger age groups.

Local and general adverse reactions

In all age groups, the local adverse reactions of pain, redness and swelling at the injection site were reported at a very common frequency after vaccination.

In the infant and toddler groups, the general adverse reactions of drowsiness, fever, irritability/fussiness and loss of appetite were reported at a very common frequency after vaccination.

In a separate infant study, 554 infants were primed with one or three doses of **Nimenrix™** and 508 received booster doses in the second year of life. Local and general adverse reactions in this study were similar in frequency to the larger infant study.

In the 12-14 months age group who received two doses of **Nimenrix™** given 2 months apart, the first and second doses were associated with similar local and systemic reactogenicity.

In an additional clinical study of age-matched subjects who were either healthy or at increased risk of meningococcal disease due to anatomical or functional asplenia (such as sickle cell disease), the safety profile of **Nimenrix™** in at-risk children and adolescents was generally similar to that observed in the non-asplenic population (see section 5.1).

The 2-5 year group reported general adverse reactions at a frequency ranging from common (irritability, loss of appetite and fever) to very common (drowsiness).

In the 6-10, 11-17 and ≥18 years age groups, the general adverse reactions were reported at a frequency ranging from common (gastrointestinal symptoms and fever) to very common (headache and fatigue).

In a clinical study of 11 to 25 year old subjects co-administered **Nimenrix™** and Tdap or given the vaccines separately, the local reactions (injection site pain, redness, and swelling) and general reactions (fatigue and headache) occurred at a similar frequency in both groups and in the subjects in the pooled analysis (very common). The general reactions gastrointestinal events (nausea, vomiting, diarrhoea, abdominal pain) occurred more frequently (very common) and fever occurred less frequently (common) compared to subjects

in the pooled analysis, but occurred at a similar frequency in subjects co-administered the vaccines and subjects given the vaccines separately in the study.

In a clinical study of female subjects 9 to 25 years old, the local reactions (pain, redness, and swelling at the **Nimenrix™** injection site) and general reactions (headache, fever, and fatigue) occurred at a similar frequency in subjects co-administered **Nimenrix™**, Tdap and HPV2 and in subjects given **Nimenrix™** alone, as they did in subjects in the pooled analysis (very common). The general reactions gastrointestinal events (nausea, vomiting, diarrhoea, abdominal pain) and myalgia occurred at a similar frequency in the two groups but more frequently than in the pooled analysis (very common), as did the general reaction rash (common).

The local and general adverse reaction profile of a booster dose of **Nimenrix™** given to subjects from 12 months of age after primary vaccination with **Nimenrix™** or other conjugated or plain polysaccharide meningococcal vaccines, was similar to the local and general adverse reaction profile observed after primary vaccination with **Nimenrix™**, except gastrointestinal symptoms (including diarrhoea, vomiting, and nausea) which ranged from common to very common among subjects 6 years of age and older (versus common after primary vaccination).

4.9. Overdose

No cases of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: bacterial vaccines, ATC code J07AH08

Mechanism of Action
Anti-capsular meningococcal antibodies protect against meningococcal disease via complement mediated bactericidal killing. **Nimenrix™** induces the production of bactericidal antibodies against capsular polysaccharides of *Neisseria meningitidis* groups A, C, W-135 and Y when measured by assays using either rSBA or hSBA. By conjugating capsular polysaccharide to a protein carrier that contains T-cell epitopes, meningococcal conjugate vaccines like **Nimenrix™** change the nature of immune response to capsular polysaccharide from T-cell independent to T-cell dependent.

Vaccine efficacy was inferred from the demonstration of immunologic non inferiority (based mainly on comparing proportions with rSBA titres at least 1:8) to licensed meningococcal vaccines. Immunogenicity was measured by using rSBA or hSBA which are biomarkers for protective efficacy against meningococcal groups A, C, W-135 and Y.

Immunogenicity in infants
In Study MenACWY-TT-083, the immunogenicity of a 2-dose primary vaccination schedule administered at 2 and 4 months of age was evaluated. Routinely used infant vaccines DTaP/IPV/Hib/HepB and a 10-valent pneumococcal vaccine were co-administered. For group C, rSBA and hSBA titres elicited by **Nimenrix™** were compared to a 2-dose priming with licensed monovalent meningococcal conjugate group C vaccines, MenC-CRM and

MenC-TT vaccines. **Nimenrix™** elicited rSBA and hSBA titres against the four meningococcal groups. The response against group C was non-inferior to the one elicited by the licensed MenC-CRM and MenC-TT vaccines in terms of the percentage of subjects with rSBA titres ≥8 at 1 month after the second dose.

For subjects initially vaccinated in infancy with **Nimenrix™** at 2 and 4 months of age and receiving a **Nimenrix™** booster dose at 12 months of age, the increase in rSBA and hSBA titres 1 month post-booster dose ranged between 15 and 80-fold for all groups and more than 99.0% of all infants achieved post-booster titres above 8 for both assays. The observed booster response for group C was similar to that observed in subjects primed and boosted with a monovalent MenC conjugate vaccine (TT or CRM conjugated). Results are shown in Table 3.

Table 3: rSBA and hSBA titres following two doses of Nimenrix™ (or MenC-CRM or MenC-TT) given 2 months apart with the first dose administered to infants 6-12 weeks of age and following a booster at 12 months of age (Study MenACWY-TT-083)

Meningo-coccal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix™	M3	456	97.4% (95.4; 98.6)	203 (182; 227)	202	96.5% (93.0; 98.6)	157 (131; 188)
		M11	462	99.6% (98.4; 99.9)	1561 (1412; 1725)	214	99.5% (97.4; 100)	1007 (836; 1214)
C	Nimenrix™	M3	456	98.7% (97.2; 99.5)	612 (540; 693)	218	98.6% (96.0; 99.7)	1308 (1052; 1627)
		M11	463	99.8% (98.8; 100)	1177 (1059; 1308)	221	99.5% (97.5; 100)	4992 (4086; 6100)
	MenC-CRM vaccine	M3	455	99.6% (98.4; 99.9)	958 (850; 1079)	202	100% (98.2; 100)	3188 (2646; 3841)
		M11	446	98.4% (96.8; 99.4)	1051 (920; 1202)	216	100% (98.3; 100)	5438 (4412; 6702)
	MenC-TT vaccine	M3	457	100% (99.2; 100)	1188 (1080; 1307)	226	100% (98.4; 100)	2626 (2219; 3109)
		M11	459	100% (99.2; 100)	1960 (1776; 2163)	219	100% (98.3; 100)	5542 (4765; 6446)
W-135	Nimenrix™	M3	455	99.1% (97.8; 99.8)	1605 (1383; 1862)	217	100% (98.3; 100)	753 (644; 882)
		M11	462	99.8% (98.8; 100)	2777 (2485; 3104)	218	100% (98.3; 100)	5123 (4504; 5826)
Y	Nimenrix™	M3	456	98.2% (96.6; 99.2)	483 (419; 558)	214	97.7% (94.6; 99.2)	328 (276; 390)
		M11	462	99.4% (99.1; 99.9)	881 (787; 986)	217	100% (98.3; 100)	2954 (2498; 3493)

The analysis of immunogenicity was conducted on the primary according-to-protocol (ATP) cohort.
* rSBA analysis performed at Public Health England (PHE) laboratories in UK
** hSBA analysis performed at GSK laboratories
M3 = post-primary vaccination at Month 3
M11 = post-booster vaccination at Month 11

In Study MenACWY-TT-087, infants received either a single primary dose at 6 months followed by a booster dose at 15-18 months or three primary doses at 2, 4, and 6 months followed by a booster dose at 15-18 months. All subjects also received DTaP-IPV/Hib and 10-valent pneumococcal conjugate vaccines at all time points. A single primary dose administered at 6 months of age elicited robust rSBA titres to the four meningococcal groups,

as measured by the percentage of subjects with rSBA titres ≥8, that were comparable to responses after the last dose of a three-dose primary series. A booster dose produced robust responses, comparable between the two dosing groups, against all four meningococcal groups. Results are shown in Table 4.

Table 4: rSBA and hSBA titres following a single dose of Nimenrix™ in infants at 6 months of age and pre- and post-booster at 15-18 months of age (Study MenACWY-TT-087)

Mening-ococcal group	Time point	rSBA*			hSBA**		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Post dose 1[(1)]	163	98.8% (95.6; 99.9)	1333 (1035; 1716)	59	98.3% (90.9; 100)	271 (206; 355)
	Pre booster	131	81.7% (74; 87.9)	125 (84.4; 186)	71	66.2% (54; 77)	20.8 (13.5; 32.2)
	Post booster[(1)]	139	99.3% (96.1; 100)	2762 (2310; 3303)	83	100% (95.7; 100)	1416 (1140; 1758)
C	Post dose 1[(1)]	163	99.4% (96.6; 100)	592 (482; 726)	66	100% (94.6; 100)	523 (382; 717)
	Pre booster	131	65.6% (56.9; 73.7)	27.4 (20.6; 36.6)	78	96.2% (89.2; 99.2)	151 (109; 210)
	Post booster[(1)]	139	99.3% (96.1; 100)	2525 (2102; 3033)	92	100% (96.1; 100)	13360 (10953; 16296)
W-135	Post dose 1[(1)]	163	93.9% (89; 97)	1256 (917; 1720)	47	87.2% (74.3; 95.2)	137 (78.4; 238)
	Pre booster	131	77.9% (69.8; 84.6)	63.3 (45.6; 87.9)	53	100% (93.3; 100)	429 (328; 559)
	Post booster[(1)]	139	100% (97.4; 100)	3145 (2637; 3750)	59	100% (93.9; 100)	9016 (7045; 11537)
Y	Post dose 1[(1)]	163	98.8% (95.6; 99.9)	1470 (1187; 1821)	52	92.3% (81.5; 97.9)	195 (118; 323)
	Pre booster	131	88.5% (81.8; 93.4)	106 (76.4; 148)	61	98.4% (91.2; 100)	389 (292; 518)
	Post booster[(1)]	139	100% (97.4; 100)	2749 (2301; 3283)	69	100% (94.8; 100)	5978 (4747; 7528)

The analysis of immunogenicity was conducted on the primary ATP cohort.
* rSBA analysis performed at PHE laboratories in UK
** hSBA analysis performed at Neomed, Canada
[(1)] blood sampling performed 1-month post vaccination

Measurement of hSBA titres was a secondary endpoint in Study MenACWY-TT-087. Although similar responses to groups A and C were observed with both dosing schedules, a single primary dose in infants at 6 months was associated with lower hSBA titres to groups W-135 and Y as measured by the percentage of subjects with hSBA titres ≥8 [87.2% (95% CI: 74.3; 95.2) and 92.3% (95% CI: 81.5; 97.9), respectively] compared with three primary doses at 2, 4, and 6 months of age [100% (95% CI: 96.6; 100) and 100% (95% CI: 97.1; 100), respectively] (see section 4.4). After a booster dose, hSBA titres to all four meningococcal groups were comparable between the two dosing schedules (Table 4).

Immunogenicity in toddlers aged 12-23 months

In clinical studies MenACWY-TT-039 and MenACWY-TT-040, a single dose of **Nimenrix™** elicited SBA titres against the four meningococcal groups, with group C rSBA titres that were comparable to those elicited by a licensed MenC-CRM vaccine in terms of the percentage of subjects with rSBA titres ≥8. In Study MenACWY-TT-039, hSBA was also measured as a secondary endpoint. Results are shown in Table 5.

Table 5: SBA* titres following a single dose of Nimenrix™ (or MenC-CRM) in toddlers aged 12-23 months (Studies MenACWY-TT-039/040)

Mening-ococcal group	Vaccine group	Study MenACWY-TT-039[(1)]						Study MenACWY-TT-040[(2)]		
		rSBA*			hSBA*			rSBA*		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix™	354	99.7% (98.4; 100)	2205 (2008; 2422)	338	77.2% (72.4; 81.6)	19.0 (16.4; 22.1)	183	98.4% (95.3; 99.7)	3170 (2577; 3899)
C	Nimenrix™	354	99.7% (98.4; 100)	478 (437; 522)	341	98.5% (96.6; 99.5)	196 (175; 219)	183	97.3% (93.7; 99.1)	829 (672; 1021)
	MenC-CRM vaccine	121	97.5% (92.9; 99.5)	212 (170; 265)	116	81.9% (73.7; 88.4)	40.3 (29.5; 55.1)	114	98.2% (93.8; 99.8)	691 (521; 918)
W-135	Nimenrix™	354	100% (99.0; 100)	2682 (2453; 2932)	336	87.5% (83.5; 90.8)	48.9 (41.2; 58.0)	186	98.4% (95.4; 99.7)	4022 (3269; 4949)
Y	Nimenrix™	354	100% (99.0; 100)	2729 (2473; 3013)	329	79.3% (74.5; 83.6)	30.9 (25.8; 37.1)	185	97.3% (93.8; 99.1)	3168 (2522; 3979)

The analysis of immunogenicity was conducted on the ATP cohorts.
(1) blood sampling performed 42 to 56 days post vaccination
(2) blood sampling performed 30 to 42 days post vaccination
* SBA analyses performed at GSK laboratories

Long term immunogenicity in toddlers

Study MenACWY-TT-104 evaluated the immunogenicity after 1 month and the persistence of the response up to 5 years following 1 or 2 doses (given 2 months apart) of **Nimenrix™** in toddlers aged 12 to 14 months. One month following one or two doses administered 2 months apart **Nimenrix™** elicited rSBA titres against all four meningococcal groups that were similar in terms of the percentage of subjects with rSBA titre ≥8 and GMT. As a secondary endpoint hSBA titres were measured. In terms of the percentage of subjects with hSBA titres ≥8, at 1 month post vaccination, hSBA titres against groups W-135 and Y were higher after two doses of **Nimenrix™** than after one dose, while the hSBA titres against groups A and C were similar in the two dose groups. At Year 5 only a small difference in antibody persistence between one and two doses was observed, in terms of percentages of subjects with hSBA titres ≥8 against all groups. Antibody persistence was observed at Year 5 against groups C, W-135 and Y. After one and two doses the percentages of subjects with hSBA titres ≥8 for group C were 60.7% and 67.8%, group W-135 were 58.9% and 63.6% and group Y were 61.5% and 54.2%, respectively. For group A, 27.9% and 17.9% of subjects receiving one or two doses, respectively, had hSBA titres ≥8 (Table 6).

Table 6: rSBA and hSBA titres following one or two doses of Nimenrix™ with the first dose administered to toddlers aged 12-14 months and persistence up to 5 years (Study MenACWY-TT-104)

Meningococcal group	Nimenrix™ dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	1 dose	1 Month Post dose 1	180	97.8% (94.4; 99.4)	1437 (1118; 1847)	74	95.9% (88.6; 99.2)	118 (86.8; 161)
		1 Year Post dose 1	167	63.5% (55.7; 70.8)	62.7 (42.6; 92.2)	70	35.7% (24.6; 48.1)	6.1 (4.1; 8.9)

Meningococcal group	Nimenrix™ dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		3 Years Post dose 1	147	46.9% (38.7; 55.3)	29.7 (19.8; 44.5)	55	36.4% (23.8; 50.4)	5.8 (3.8; 8.9)
		5 Years Post dose 1	133	58.6% (49.8; 67.1)	46.8 (30.7; 71.5)	61	27.9% (17.1; 40.8)	4.4 (3.1; 6.2)
	2 doses	1 Month Post dose 1	158	96.8% (92.8; 99.0)	1275 (970; 1675)	66	97.0% (89.5; 99.6)	133 (98.1; 180)
		1 Month Post dose 2	150	98.0% (94.3; 99.6)	1176 (922; 1501)	66	97.0% (89.5; 99.6)	170 (126; 230)
		1 Year Post dose 2	143	70.6% (62.4; 77.9)	76.6 (50.7; 116)	62	35.5% (23.7; 48.7)	6.4 (4.2; 10.0)
		3 Years Post dose 2	121	54.5% (45.2; 63.6)	28.5 (18.7; 43.6)	50	36.0% (22.9; 50.8)	5.4 (3.6; 8.0)
		5 Years Post dose 2	117	65.8% (56.5; 74.3)	69.9 (44.7; 109.3)	56	17.9% (8.9; 30.4)	3.1 (2.4; 4.0)
C	**1 dose**	1 Month Post dose 1	179	95.0% (90.7; 97.7)	452 (346; 592)	78	98.7% (93.1; 100)	152 (105; 220)
		1 Year Post dose 1	167	49.1% (41.3; 56.9)	16.2 (12.4; 21.1)	71	80.3% (69.1; 88.8)	35.2 (22.5; 55.2)
		3 Years Post dose 1	147	35.4% (27.7; 43.7)	9.8 (7.6; 12.7)	61	65.6% (52.3; 77.3)	23.6 (13.9; 40.2)
		5 Years Post dose 1	132	20.5% (13.9; 28.3)	6.6 (5.3; 8.2)	61	60.7% (47.3; 72.9)	18.1 (10.9; 30.0)
	2 doses	1 Month Post dose 1	157	95.5% (91.0; 98.2)	369 (281; 486)	70	95.7% (88.0; 99.1)	161 (110; 236)
		1 Month Post dose 2	150	98.7% (95.3; 99.8)	639 (522; 783)	69	100% (94.8; 100)	1753 (1278; 2404)
		1 Year Post dose 2	143	55.2% (46.7; 63.6)	21.2 (15.6; 28.9)	63	90.5% (80.4; 96.4)	73.4 (47.5; 113)
		3 Years Post dose 2	121	33.9% (25.5; 43.0)	11.5 (8.4; 15.8)	56	67.9% (54.0; 79.7)	27 (15.6; 46.8)
		5 Years Post dose 2	116	28.4% (20.5; 37.6)	8.5 (6.4; 11.2)	59	67.8% (54.4; 79.4)	29.4 (16.3; 52.9)
W-135	**1 dose**	1 Month Post dose 1	180	95.0% (90.8; 97.7)	2120 (1601; 2808)	72	62.5% (50.3; 73.6)	27.5 (16.1; 46.8)
		1 Year Post dose 1	167	65.3% (57.5; 72.5)	57.2 (39.9; 82.0)	72	95.8% (88.3; 99.1)	209 (150; 291)
		3 Years Post dose 1	147	59.2% (50.8; 67.2)	42.5 (29.2; 61.8)	67	71.6% (59.3; 82.0)	30.5 (18.7; 49.6)
		5 Years Post dose 1	133	44.4% (35.8; 53.2)	25 (16.7; 37.6)	56	58.9% (45.0; 71.9)	20.8 (11.6; 37.1)
	2 doses	1 Month Post dose 1	158	94.9% (90.3; 97.8)	2030 (1511; 2728)	61	68.9% (55.7; 80.1)	26.2 (16.0; 43.0)
		1 Month Post dose 2	150	100% (97.6; 100)	3533 (2914; 4283)	70	97.1% (90.1; 99.7)	757 (550; 1041)
		1 Year Post dose 2	143	77.6% (69.9; 84.2)	123 (82.7; 183)	65	98.5% (91.7; 100)	233 (168; 321)
		3 Years Post dose 2	121	72.7% (63.9; 80.4)	92.9 (59.9; 144)	54	87.0% (75.1; 94.6)	55.5 (35.3; 87.1)
		5 Years Post dose 2	117	50.4% (41.0; 59.8)	37.1 (23.3; 59.0)	44	63.6% (47.8; 77.6)	19.5 (10.7; 35.2)
Y	**1 dose**	1 Month Post dose 1	180	92.8% (88.0; 96.1)	952 (705; 1285)	71	67.6% (55.5; 78.2)	41.2 (23.7; 71.5)
		1 Year Post dose 1	167	73.1% (65.7; 79.6)	76.8 (54.2; 109)	62	91.9% (82.2; 97.3)	144 (97.2; 215)
		3 Years Post dose 1	147	61.9% (53.5; 69.8)	58 (39.1; 86.0)	64	53.1% (40.2; 65.7)	17.3 (10.1; 29.6)
		5 Years Post dose 1	133	47.4% (38.7; 56.2)	36.5 (23.6; 56.2)	65	61.5% (48.6; 73.3)	24.3 (14.3; 41.1)
	2 doses	1 Month Post dose 1	157	93.6% (88.6; 96.9)	933 (692; 1258)	56	64.3% (50.4; 76.6)	31.9 (17.6; 57.9)
		1 Month	150	99.3%	1134	64	95.3%	513

Meningococcal group	Nimenrix™ dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		Post dose 2		(96.3; 100)	(945; 1360)		(86.9; 99.0)	(339; 775)
		1 Year Post dose 2	143	79.7% (72.2; 86.0)	112 (77.5; 163)	58	87.9% (76.7; 95.0)	144 (88.5; 234)
		3 Years Post dose 2	121	68.6% (59.5; 76.7)	75.1 (48.7; 115.9)	52	61.5% (47.0; 74.7)	24.1 (13.3; 43.8)
		5 Years Post dose 2	117	58.1% (48.6; 67.2)	55.8 (35.7; 87.5)	48	54.2% (39.2; 68.6)	16.8 (9.0; 31.3)

The analysis of immunogenicity was conducted on the ATP cohort
(1) blood sampling performed 21 to 48 days post vaccination and 44 to 60 weeks post vaccination
* rSBA analysis performed at Public Health England laboratories
** hSBA analysis performed at GSK laboratories

In children vaccinated at toddler age, the persistence of rSBA and hSBA titres was evaluated up to 4 years in Study MenACWY-TT-048. Results are shown in Table 7.

Table 7: rSBA and hSBA titres up to 4 years following Nimenrix™ (or MenC-CRM) in toddlers aged 12-23 months (Study MenACWY-TT-048)

Mening-ococcal group	Vaccine group	Time point (Years)	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix™	3	262	59.9% (53.7; 65.9)	19.3 (15.7; 23.6)	251	35.9% (29.9; 42.1)	5.8 (4.8; 7.0)
		4	224	74.1% (67.9; 79.7)	107 (77.6; 148)	198	28.8% (22.6; 35.6)	4.9 (4.0; 6.0)
C	Nimenrix™	3	262	35.9% (30.1; 42.0)	9.8 (8.1; 11.7)	253	78.3% (72.7; 83.2)	37.8 (29.4; 48.6)
		4	225	40.4% (34.0; 47.2)	12.3 (9.8; 15.3)	209	73.2% (66.7; 79.1)	32.0 (23.8; 43.0)
	MenC-CRM vaccine	3	46	13.0% (4.9; 26.3)	5.7 (4.2; 7.7)	31	41.9% (24.5; 60.9)	6.2 (3.7; 10.3)
		4	45	35.6% (21.9; 51.2)	13.5 (7.4; 24.5)	32	46.9% (29.1; 65.3)	11.3 (4.9; 25.6)
W-135	Nimenrix™	3	261	49.8% (43.6; 56.0)	24.9 (19.2; 32.4)	254	82.3% (77.0; 86.8)	52.0 (41.4; 65.2)
		4	225	49.3% (42.6; 56.1)	30.5 (22.4; 41.5)	165	80.6% (73.7; 86.3)	47.1 (35.7; 62.2)
Y	Nimenrix™	3	262	53.8% (47.6; 60.0)	22.3 (17.6; 28.4)	250	72.0% (66.0; 77.5)	33.2 (25.9; 42.5)
		4	225	58.2% (51.5; 64.7)	36.2 (27.1; 48.4)	130	65.4% (56.5; 73.5)	29.8 (20.2; 44.1)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time point.
* rSBA analysis performed at PHE laboratories in UK
** hSBA analysis performed at GSK laboratories

rSBA and hSBA titres were determined over a period of 10 years in children initially vaccinated with one dose of **Nimenrix™** or MenC-CRM at 12 to 23 months of age in Study MenACWY-TT-027. Persistence of SBA titres was evaluated in two extension studies: MenACWY-TT-032 (up to 5 years) and MenACWY-TT-100 (up to 10 years). Study MenACWY-TT-100 also evaluated the response to a single booster dose of **Nimenrix™** administered 10 years following the initial vaccination with **Nimenrix™** or MenC-CRM. Results are shown in Table 8 (see section 4.4).

Table 8: rSBA and hSBA titres following a single dose of Nimenrix™ (or MenC-CRM) in toddlers aged 12-23 months, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-027/032/100)

Mening-ococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix™	Month 1[1]	222	100% (98.4; 100)	3707 (3327; 4129)	217	91.2% (86.7; 94.6)	59.0 (49.3; 70.6)
		Year 4[2]	45	64.4% (48.8; 78.1)	35.1 (19.4; 63.4)	44	52.3% (36.7; 67.5)	8.8 (5.4; 14.2)
		Year 5[2]	49	73.5% (58.9; 85.1)	37.4 (22.1; 63.2)	45	35.6% (21.9; 51.2)	5.2 (3.4; 7.8)
		Year 10[3] (Pre-booster)	62	66.1% (53.0; 77.7)	28.9 (16.4; 51.0)	59	25.4% (15.0; 38.4)	4.2 (3.0; 5.9)
		(Post-booster)[3,4]	62	98.4% (91.3; 100)	5122 (3726; 7043)	62	100% (94.2; 100)	1534 (1112; 2117)
C	Nimenrix™	Month 1[1]	220	100% (98.3; 100)	879 (779; 991)	221	99.1% (96.8; 99.9)	190 (165; 219)
		Year 4[2]	45	97.8% (88.2; 99.9)	110 (62.7; 192)	45	97.8% (88.2; 99.9)	370 (214; 640)
		Year 5[2]	49	77.6% (63.4; 88.2)	48.9 (28.5; 84.0)	48	91.7% (80.0; 97.7)	216 (124; 379)
		Year 10[3] (Pre-booster)	62	82.3% (70.5; 90.8)	128 (71.1; 231)	60	91.7% (81.6; 97.2)	349 (197; 619)
		(Post-booster)[3,4]	62	100% (94.2; 100)	7164 (5478; 9368)	59	100% (93.9; 100)	33960 (23890; 48274)
	MenC-CRM vaccine	Month 1[1]	68	98.5% (92.1; 100)	415 (297; 580)	68	72.1% (59.9; 82.3)	21.2 (13.9; 32.3)
		Year 4[2]	10	80.0% (44.4; 97.5)	137 (22.6; 832)	10	70.0% (34.8; 93.3)	91.9 (9.8; 859)
		Year 5[2]	11	63.6% (30.8; 89.1)	26.5 (6.5; 107)	11	90.9% (58.7; 99.8)	109 (21.2; 557)
		Year 10[3] (Pre-booster)	16	87.5% (61.7; 98.4)	86.7 (29.0; 259)	15	93.3% (68.1; 99.8)	117 (40.0; 344)
		(Post-booster)[3,4]	16	100% (79.4; 100)	5793 (3631; 9242)	15	100% (78.2; 100)	42559 (20106; 90086)
W-135	Nimenrix™	Month 1[1]	222	100% (98.4; 100)	5395 (4870; 5976)	177	79.7% (73.0; 85.3)	38.8 (29.7; 50.6)
		Year 4[2]	45	60.0% (44.3; 74.3)	50.8 (24.0; 108)	45	84.4% (70.5; 93.5)	76.9 (44.0; 134)
		Year 5[2]	49	34.7% (21.7; 49.6)	18.2 (9.3; 35.3)	46	82.6% (68.6; 92.2)	59.7 (35.1; 101)
		Year 10[3] (Pre-booster)	62	30.6% (19.6; 43.7)	15.8 (9.1; 27.6)	52	44.2% (30.5; 58.7)	7.7 (4.9; 12.2)
		(Post-booster)[3,4]	62	100% (94.2; 100)	25911 (19120; 35115)	62	100% (94.2; 100)	11925 (8716; 16316)
Y	Nimenrix™	Month 1[1]	222	100% (98.4; 100)	2824 (2529; 3153)	201	66.7% (59.7; 73.1)	24.4 (18.6; 32.1)
		Year 4[2]	45	62.2% (46.5; 76.2)	44.9 (22.6; 89.3)	41	87.8% (73.8; 95.9)	74.6 (44.5; 125)
		Year 5[2]	49	42.9% (28.8; 57.8)	20.6 (10.9; 39.2)	45	80.0% (65.4; 90.4)	70.6 (38.7; 129)
		Year 10[3]	62	45.2%	27.4	56	42.9%	9.1

Mening-ococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		(Pre-booster)		(32.5; 58.3)	(14.7; 51.0)		(29.7; 56.8)	(5.5; 15.1)
		(Post-booster)[3,4]	62	98.4% (91.3; 100)	7661 (5263; 11150)	61	100% (94.1; 100)	12154 (9661; 15291)

The analysis of immunogenicity was conducted on the ATP cohorts for 1 month and 5 years post vaccination and the booster ATP cohort.

[1] Study MenACWY-TT-027

[2] Study MenACWY-TT-032

[3] Study MenACWY-TT-100

[4] Blood sampling was performed 1 month after a booster dose at Year 10.

* rSBA analysis performed at GSK laboratories for 1 month post-primary vaccination samples and at PHE laboratories in UK for subsequent sampling time points.

** hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT-100.

Persistence of booster response

Study MenACWY-TT-102 evaluated the persistence of SBA titres up to 6 years after a booster dose of **Nimenrix™** or MenC-CRM$_{197}$ administered in Study MenACWY-TT-048 to children who initially received the same vaccine at 12 to 23 months of age in Study MenACWY-TT-039. A single booster dose was administered 4 years after the initial vaccination. Results are shown in Table 9 (see section 4.4).

Table 9: rSBA and hSBA titres following a single dose of Nimenrix™ (or MenC-CRM) in toddlers aged 12-23 months, persistence at 4 years and response following a booster 4 years after initial vaccination, and persistence up to 6 years following booster vaccination (Studies MenACWY-TT-039/048/102)

Meningo-coccal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix™	Month 1[1]	354	99.7% (98.4; 100)	2205 (2008; 2422)	338	77.2% (72.4; 81.6)	19.0 (16.4; 22.1)
		Year 4[2] (Pre-Nimenrix™ booster)	212	74.5% (68.1; 80.2)	112 (80.3; 156)	187	28.9% (22.5; 35.9)	4.8 (3.9; 5.9)
		(Post-booster)[2,3]	214	100% (98.3; 100)	7173 (6389; 8054)	202	99.5% (97.3; 100)	1343 (1119; 1612)
		5 years after booster dose[4]	137	89.8% (83.4; 94.3)	229 (163; 322)	135	53.3% (44.6; 62.0)	13.2 (9.6; 18.3)
		6 years after booster dose[4]	134	92.5% (86.7; 96.4)	297 (214; 413)	130	58.5% (49.5; 67.0)	14.4 (10.5; 19.7)
C	Nimenrix™	Month 1[1]	354	99.7% (98.4; 100)	478 (437; 522)	341	98.5% (96.6; 99.5)	196 (175; 219)
		Year 4[2] (Pre-Nimenrix™ booster)	213	39.9% (33.3; 46.8)	12.1 (9.6; 15.2)	200	73.0% (66.3; 79.0)	31.2 (23.0; 42.2)

		(Post-booster)[2,3]	215	100% (98.3; 100)	4512 (3936; 5172)	209	100% (98.3; 100)	15831 (13626; 18394)
		5 years after booster dose[4]	137	80.3% (72.6; 86.6)	66.0 (48.1; 90.5)	136	99.3% (96.0; 100)	337 (261; 435)
		6 years after booster dose[4]	134	71.6% (63.2; 79.1)	39.6 (28.6; 54.6)	130	97.7% (93.4; 99.5)	259 (195; 345)
	MenC-CRM vaccine	Month 1[1]	121	97.5% (92.9; 99.5)	212 (170; 265)	116	81.9% (73.7; 88.4)	40.3 (29.5; 55.1)
		Year 4[2] (Pre-MenC-CRM_{197} booster)	43	37.2% (23.0; 53.3)	14.3 (7.7; 26.5)	31	48.4% (30.2; 66.9)	11.9 (5.1; 27.6)
		(Post-booster)[2,3]	43	100% (91.8; 100)	3718 (2596; 5326)	33	100% (89.4; 100)	8646 (5887; 12699)
		5 years after booster dose[4]	23	78.3% (56.3; 92.5)	47.3 (19.0; 118)	23	100% (85.2; 100)	241 (139; 420)
		6 years after booster dose[4]	23	65.2% (42.7; 83.6)	33.0 (14.7; 74.2)	23	95.7% (78.1; 99.9)	169 (94.1; 305)
W-135	**Nimenrix™**	Month 1[1]	354	100% (99.0; 100)	2682 (2453; 2932)	336	87.5% (83.5; 90.8)	48.9 (41.2; 58.0)
		Year 4[2] (Pre-**Nimenrix™** booster)	213	48.8% (41.9; 55.7)	30.2 (21.9; 41.5)	158	81.6% (74.7; 87.3)	48.3 (36.5; 63.9)
		(Post-booster)[2,3]	215	100% (98.3; 100)	10950 (9531; 12579)	192	100% (98.1; 100)	14411 (12972; 16010)
		5 years after booster dose[4]	137	88.3% (81.7; 93.2)	184 (130; 261)	136	100% (97.3; 100)	327 (276; 388)
		6 years after booster dose[4]	134	85.8% (78.7; 91.2)	172 (118; 251)	133	98.5% (94.7; 99.8)	314 (255; 388)
Y	**Nimenrix™**	Month 1[1]	354	100% (99.0; 100)	2729 (2473; 3013)	329	79.3% (74.5; 83.6)	30.9 (25.8; 37.1)
		Year 4[2] (Pre-**Nimenrix™** booster)	213	58.2% (51.3; 64.9)	37.3 (27.6; 50.4)	123	65.9% (56.8; 74.2)	30.2 (20.2; 45.0)
		(Post-booster)[2,3]	215	100% (98.3; 100)	4585 (4129; 5093)	173	100% (97.9; 100)	6776 (5961; 7701)
		5 years after booster dose[4]	137	92.7% (87.0; 96.4)	265 (191; 368)	137	97.8% (93.7; 99.5)	399 (321; 495)

		6 years after booster dose[4]	134	94.0% (88.6; 97.4)	260 (189; 359)	131	97.7% (93.5; 99.5)	316 (253; 394)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

(1) Study MenACWY-TT-039

(2) Study MenACWY-TT-048

(3) Blood sampling was performed 1 month after a booster dose at Year 4.

(4) Study MenACWY-TT-102

* rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

** hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT-102.

Immune memory

In Study MenACWY-TT-014, the induction of immune memory was assessed 1 month after the administration of a fifth of the dose of ACWY-PS vaccine (10 µg of each polysaccharide) to children in the third year of life initially vaccinated in Study MenACWY-TT-013 with **Nimenrix™** or a licensed MenC-CRM vaccine at the age of 12 to 14 months.

One month after the challenge dose, the GMTs elicited by the initial vaccination with **Nimenrix™** increased by 6.5 to 8 fold for groups A, C, W-135, and Y, indicating that **Nimenrix™** induces immune memory to all four meningococcal groups. The post-challenge rSBA-MenC GMT was similar in both study groups, indicating that **Nimenrix™** induces an analogous immune memory to group C as the licensed MenC-CRM vaccine. Results are shown in Table 10.

Table 10: rSBA* titres 1 month after a challenge vaccination in subjects initially vaccinated with Nimenrix™ or a MenC-CRM vaccine at the age of 12 to 14 months (Study MenACWY-TT-014)

Meningococcal group	Vaccine group	Pre-challenge		Post-challenge	
		N	GMT (95% CI)	N	GMT (95% CI)
A	**Nimenrix™**	32	544 (325; 911)	25	3322 (2294; 4810)
C	**Nimenrix™**	31	174 (105; 289)	32	5966 (4128; 8621)
	MenC-CRM vaccine	28	34.4 (15.8; 75.3)	30	5265 (3437; 8065)
W-135	**Nimenrix™**	32	644 (394; 1052)	32	11058 (8587; 14240)
Y	**Nimenrix™**	32	440 (274; 706)	32	5737 (4216; 7806)

The analysis of immunogenicity was conducted on the ATP cohort.

* rSBA analysis performed at GSK laboratories

Immunogenicity in children aged 2-10 years

In two comparative studies conducted in subjects aged 2-10 years, one group of subjects received a dose of **Nimenrix™** and a second group a dose of either a licensed MenC-CRM vaccine (Study MenACWY-TT-081) or the licensed ACWY-PS vaccine (Study MenACWY-TT-038) as comparator.

In Study MenACWY-TT-038, a single dose of **Nimenrix™** was demonstrated to be non-inferior to the licensed ACWY-PS vaccine in terms of vaccine response to the four meningococcal groups as shown in Table 11.

Table 11: rSBA* titres following a single dose of Nimenrix™ (or ACWY-PS) in children aged 2-10 years (Study MenACWY-TT-038)

Meningo-coccal group	Nimenrix™[(1)]			ACWY-PS vaccine[(1)]		
	N	VR (95% CI)	GMT (95% CI)	N	VR (95% CI)	GMT (95% CI)
A	594	89.1% (86.3; 91.5)	6343 (5998; 6708)	192	64.6% (57.4; 71.3)	2283 (2023; 2577)
C	691	96.1% (94.4; 97.4)	4813 (4342; 5335)	234	89.7% (85.1; 93.3)	1317 (1043; 1663)
W-135	691	97.4% (95.9; 98.4)	11543 (10873; 12255)	236	82.6% (77.2; 87.2)	2158 (1815; 2565)
Y	723	92.7% (90.5; 94.5)	10825 (10233; 11452)	240	68.8% (62.5; 74.6)	2613 (2237; 3052)

The analysis of immunogenicity was conducted on the ATP cohort.

(1) Blood sampling performed 1 month post vaccination

VR: vaccine response defined as the proportion of subjects with:

- rSBA titres ≥32 for initially seronegative subjects (i.e., pre-vaccination rSBA titre <8)
- at least a 4-fold increase in rSBA titres from pre- to post vaccination for initially seropositive subjects (i.e., pre-vaccination rSBA titre ≥8)

* rSBA analysis performed at GSK laboratories

In Study MenACWY-TT-081, a single dose of **Nimenrix™** (N = 268) was demonstrated to be non-inferior to another licensed MenC-CRM vaccine (N = 92) in terms of vaccine response to group C [94.8% (95% CI: 91.4; 97.1) and 95.7% (95% CI: 89.2; 98.8), respectively]. GMTs were lower for the **Nimenrix™** group [2795 (95% CI: 2393; 3263)] versus the MenC-CRM vaccine [5292 (95% CI: 3815; 7340)].

In Study MenACWY-TT-088, the persistence of SBA titres was evaluated up to 68 months after vaccination in children 2-10 years of age initially vaccinated in Study MenACWY-TT-081. Results are shown in Table 12 (see section 4.4).

Table 12: rSBA and hSBA titres up to 68 months following Nimenrix™ (or MenC-CRM) in children aged 2-10 years at time of vaccination (Study MenACWY-TT-088)

Mening-ococcal group	Vaccine group	Time-point (months)	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N***	≥8 (95% CI)	GMT (95% CI)
A	**Nimenrix™**	32	193	86.5% (80.9; 91.0)	196 (144; 267)	90	25.6% (16.9; 35.8)	4.6 (3.3; 6.3)
		68	178	86.5% (80.6; 91.2)	129 (93.5; 179)	170	40.6% (33.1; 48.4)	6.9 (5.4; 8.9)
C	**Nimenrix™**	32	192	64.6% (57.4; 71.3)	34.8 (26.0; 46.4)	90	95.6% (89.0; 98.8)	75.9 (53.4; 108)
		68	178	39.9% (32.6; 47.5)	14.2 (10.8; 18.7)	172	75.6% (68.5; 81.8)	28.4 (21.2; 37.9)
	MenC-CRM vaccine	32	69	76.8% (65.1; 86.1)	86.5 (47.3; 158)	33	90.9% (75.7; 98.1)	82.2 (34.6; 196)
		68	61	62.3% (49.0; 74.4)	44.5 (23.7; 83.6)	57	75.4% (62.2; 85.9)	34.3 (19.0; 61.9)
W-135	**Nimenrix™**	32	193	77.2% (70.6; 82.9)	214 (149; 307)	86	84.9% (75.5; 91.7)	69.9 (48.2; 101)

Mening-ococcal group	Vaccine group	Time-point (months)	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N***	≥8 (95% CI)	GMT (95% CI)
		68	178	52.8% (45.2; 60.3)	59.2 (39.3; 89.2)	159	78.6% (71.4; 84.7)	56.7 (41.5; 77.3)
Y	Nimenrix™	32	193	81.3% (75.1; 86.6)	227 (165; 314)	91	81.3% (71.8; 88.7)	79.2 (52.5; 119)
		68	178	71.3% (64.1; 77.9)	139 (96.0; 202)	159	73.0% (65.3; 79.7)	56.3 (39.5; 80.3)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time point.
* rSBA analysis performed at PHE laboratories in UK
** hSBA analysis performed at GSK laboratories
*** at Month 32, a subset of subjects has been tested for hSBA

In Study MenACWY-TT-028, the persistence of hSBA titres was evaluated 1 year after vaccination in children aged 6-10 years who were initially vaccinated in Study MenACWY-TT-027. Results are shown in Table 13.

Table 13: hSBA* titres following a single dose of Nimenrix™ (or ACWY-PS) in children aged 6-10 years and persistence 1 year following vaccination (Studies MenACWY-TT-027/028)

Mening-ococcal group	Vaccine group	1 month post vaccination (Study MenACWY-TT-027)			1 year persistence (Study MenACWY-TT-028)		
		N	≥8	GMT	N	≥8	GMT
A	Nimenrix™	105	80.0%	53.4	104	16.3%	3.5
	ACWY-PS Vaccine	35	25.7%	4.1	35	5.7%	2.5
C	Nimenrix™	101	89.1%	156	105	95.2%	129
	ACWY-PS Vaccine	38	39.5%	13.1	31	32.3%	7.7
W-135	Nimenrix™	103	95.1%	133	103	100%	257
	ACWY-PS Vaccine	35	34.3%	5.8	31	12.9%	3.4
Y	Nimenrix™	89	83.1%	95.1	106	99.1%	265
	ACWY-PS Vaccine	32	43.8%	12.5	36	33.3%	9.3

The analysis of immunogenicity was conducted on the ATP cohort for persistence at Year 1.
hSBA analysis was not performed for children aged 2 to <6 years (at time of vaccination).
* hSBA analysis performed at GSK laboratories

SBA titres were determined over a period of 10 years in children initially vaccinated with one dose of **Nimenrix™** or ACWY-PS at 2 to 10 years of age in Study MenACWY-TT-027. Persistence of SBA titres was evaluated in two extension studies: MenACWY-TT-032 (up to 5 years) and MenACWY-TT-100 (up to 10 years).

Study MenACWY-TT-100 also evaluated the response to a single booster dose of **Nimenrix™** administered 10 years following the initial vaccination with **Nimenrix™** or ACWY-PS. Results are shown in Table 14 (see section 4.4).

Table 14: rSBA and hSBA titres following a single dose of Nimenrix™ (or ACWY-PS) in children aged 2-10 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-027/032/100)

Meningo-coccal	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8	GMT	N	≥8	GMT

group				(95% CI)	(95% CI)		(95% CI)	(95% CI)
A	Nimenrix™	Month 1[1]	225	100% (98.4; 100)	7301 (6586; 8093)	111[5]	81.1% (72.5; 87.9)	57.0 (40.3; 80.6)
		Year 5[2]	98	90.8% (83.3; 95.7)	141 (98.2; 203)	n/a[6]	--	--
		Year 6[3]	98	79.6% (70.3; 87.1)	107 (66.0; 174)	90	41.1% (30.8; 52.0)	6.5 (4.8; 8.8)
		Year 10[3] (Pre-booster)	73	89.0% (79.5; 95.1)	96.3 (57.1; 163)	62	33.9% (22.3; 47.0)	4.5 (3.3; 6.2)
		(Post-booster)[3,4]	74	95.9% (88.6; 99.2)	4626 (3041; 7039)	73	100% (95.1; 100)	1213 (994; 1481)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	2033 (1667; 2480)	35[5]	25.7% (12.5; 43.3)	4.1 (2.6; 6.5)
		Year 5[2]	13	15.4% (1.9; 45.4)	4.7 (3.7; 6.0)	n/a[6]	--	--
		Year 6[3]	24	12.5% (2.7; 32.4)	5.8 (3.5; 9.6)	21	33.3% (14.6; 57.0)	5.9 (3.0; 11.7)
		Year 10[3] (Pre-booster)	17	23.5% (6.8; 49.9)	8.0 (3.3; 19.3)	17	29.4% (10.3; 56.0)	6.2 (2.4; 15.7)
		(Post-booster)[3,4]	17	100% (80.5; 100)	6414 (3879; 10608)	17	100% (80.5; 100)	211 (131; 340)
C	Nimenrix™	Month 1[1]	225	100% (98.4; 100)	2435 (2106; 2816)	107[5]	89.7% (82.3; 94.8)	155 (101; 237)
		Year 5[2]	98	90.8% (83.3; 95.7)	79.7 (56.0; 113)	n/a[6]	--	--
		Year 6[3]	98	82.7% (73.7; 89.6)	193 (121; 308)	97	93.8% (87.0; 97.7)	427 (261; 700)
		Year 10[3] (Pre-booster)	74	85.1% (75.0; 92.3)	181 (106; 310)	73	91.8% (83.0; 96.9)	222 (129; 380)
		(Post-booster)[3,4]	74	100% (95.1; 100)	4020 (3319; 4869)	71	100% (94.9; 100)	15544 (11735; 20588)
	ACWY-PS vaccine	Month 1[1]	74	100% (95.1; 100)	750 (555; 1014)	38[5]	39.5% (24.0; 56.6)	13.1 (5.4; 32.0)
		Year 5[2]	13	100% (75.3; 100)	128 (56.4; 291)	n/a[6]	--	--
		Year 6[3]	24	79.2% (57.8; 92.9)	98.7 (42.2; 231)	24	100% (85.8; 100)	235 (122; 451)
		Year 10[3] (Pre-booster)	17	76.5% (50.1; 93.2)	96.2 (28.9; 320)	17	100% (80.5; 100)	99.1 (35.8; 274)
		(Post-booster)[3,4]	17	100% (80.5; 100)	15101 (7099; 32122)	17	94.1 (71.3; 99.9)	44794 (10112; 198440)
W-135	Nimenrix™	Month 1[1]	225	100% (98.4; 100)	11777 (10666; 13004)	107[5]	95.3% (89.4; 98.5)	134 (101; 178)
		Year 5[2]	98	78.6% (69.1; 86.2)	209 (128; 340)	n/a[6]	--	--
		Year 6[3]	98	73.5% (63.6; 81.9)	265 (155; 454)	92	81.5% (72.1; 88.9)	62.5 (42.0; 93.1)
		Year 10[3] (Pre-booster)	74	68.9% (57.1; 79.2)	206 (109; 392)	59	61.0% (47.4; 73.5)	17.5 (10.5; 29.2)
		(Post-booster)[3,4]	74	100% (95.1; 100)	27944 (22214; 35153)	74	100% (95.1; 100)	6965 (5274; 9198)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	2186 (1723; 2774)	35[5]	34.3% (19.1; 52.2)	5.8 (3.3, 9.9)
		Year 5[2]	13	0% (0.0; 24.7)	4.0 (4.0; 4.0)	n/a[6]	--	--
		Year 6[3]	24	12.5%	7.6	23	30.4%	7.0

				(2.7; 32.4)	(3.7; 15.6)		(13.2; 52.9)	(2.9; 16.9)
		Year 10[3] (Pre-booster)	17	23.5% (6.8; 49.9)	15.4 (4.2; 56.4)	15	26.7% (7.8; 55.1)	4.1 (2.0; 8.5)
		(Post-booster)[3,4]	17	94.1% (71.3; 99.9)	10463 (3254; 33646)	15	100% (78.2; 100)	200 (101; 395)
Y	**Nimenrix™**	Month 1[1]	225	100% (98.4; 100)	6641 (6044; 7297)	94[5]	83.0% (73.8; 89.9)	93.7 (62.1; 141)
		Year 5[2]	98	78.6% (69.1; 86.2)	143 (88.0; 233)	n/a[6]	--	--
		Year 6[3]	98	71.4% (61.4; 80.1)	136 (82.6; 225)	89	65.2% (54.3; 75.0)	40.3 (23.9; 68.1)
		Year 10[3] (Pre-booster)	74	67.6% (55.7; 78.0)	98.5 (54.3; 179)	65	72.3% (59.8; 82.7)	35.7 (21.0; 60.6)
		(Post-booster)[3,4]	74	100% (95.1; 100)	7530 (5828; 9729)	74	100% (95.1; 100)	11127 (8909; 13898)
	ACWY-PS vaccine	Month 1[1]	75	100% (95.2; 100)	1410 (1086; 1831)	32[5]	43.8% (26.4; 62.3)	12.5 (5.6; 27.7)
		Year 5[2]	13	7.7% (0.2; 36.0)	5.5 (2.7; 11.1)	n/a[6]	--	--
		Year 6[3]	24	20.8% (7.1; 42.2)	11.6 (4.7; 28.7)	24	25.0% (9.8; 46.7)	7.3 (2.7; 19.8)
		Year 10[3] (Pre-booster)	17	17.6% (3.8; 43.4)	10.2 (3.5; 30.2)	14	35.7% (12.8; 64.9)	7.8 (2.5; 24.4)
		(Post-booster)[3,4]	17	100% (80.5; 100)	6959 (3637; 13317)	17	100% (80.5; 100)	454 (215; 960)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

[1] Study MenACWY-TT-027

[2] Study MenACWY-TT-032

[3] Study MenACWY-TT-100

[4] Blood sampling was performed 1 month after a booster dose at Year 10.

[5] Includes children aged 6 to <11 years. hSBA analysis was not performed for children aged 2 to <6 years (at time of vaccination).

[6] Per the protocol for Study MenACWY-TT-032, hSBA was not measured for this age group at Year 5.

* rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for subsequent sampling time points.

** hSBA analysis performed at GSK laboratories and at Neomed in Canada for time points in Study MenACWY-TT-100.

Immunogenicity in adolescents aged 11-17 years and adults aged ≥18 years

In two clinical studies, conducted in adolescents aged 11-17 years (Study MenACWY-TT-036) and in adults aged 18-55 years (Study MenACWY-TT-035), either one dose of **Nimenrix™** or one dose of the ACWY-PS vaccine was administered.

In both adolescents and adults, **Nimenrix™** was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine in terms of vaccine response. rSBA titres to the four meningococcal groups elicited by **Nimenrix™** were either similar to or higher than those elicited by the ACWY-PS vaccine as shown in Table 15.

Table 15: rSBA* titres following a single dose of Nimenrix™ (or ACWY-PS) in adolescents aged 11-17 years and adults aged 18-55 years (Studies MenACWY-TT-035/036)

Meningo-coccal	Vaccine group	Study MenACWY-TT-036 (11-17 years)[1]	Study MenACWY-TT-035 (18-55 years)[1]

		N	VR (95% CI)	GMT (95% CI)	N	VR (95% CI)	GMT (95% CI)
A	**Nimenrix**	553	85.4% (82.1; 88.2)	5928 (5557; 6324)	743	80.1% (77.0; 82.9)	3625 (3372; 3897)
	ACWY-PS vaccine	191	77.5% (70.9; 83.2)	2947 (2612; 3326)	252	69.8% (63.8; 75.4)	2127 (1909; 2370)
C	**Nimenrix**	642	97.4% (95.8; 98.5)	13110 (11939; 14395)	849	91.5% (89.4; 93.3)	8866 (8011; 9812)
	ACWY-PS vaccine	211	96.7% (93.3; 98.7)	8222 (6807; 9930)	288	92.0% (88.3; 94.9)	7371 (6297; 8628)
W-135	**Nimenrix**	639	96.4% (94.6; 97.7)	8247 (7639; 8903)	860	90.2% (88.1; 92.1)	5136 (4699; 5614)
	ACWY-PS vaccine	216	87.5% (82.3; 91.6)	2633 (2299; 3014)	283	85.5% (80.9; 89.4)	2461 (2081; 2911)
Y	**Nimenrix**	657	93.8% (91.6; 95.5)	14086 (13168; 15069)	862	87.0% (84.6; 89.2)	7711 (7100; 8374)
	ACWY-PS vaccine	219	78.5% (72.5; 83.8)	5066 (4463; 5751)	288	78.8% (73.6; 83.4)	4314 (3782; 4921)

The analysis of immunogenicity was conducted on the ATP cohorts.

(1) Blood sampling performed 1 month post vaccination

VR: vaccine response defined as the proportion of subjects with:

- rSBA titres ≥32 for initially seronegative subjects (i.e., pre-vaccination rSBA titre <8)
- at least a 4-fold increase in rSBA titres from pre- to post vaccination for initially seropositive subjects (i.e., pre-vaccination rSBA titre ≥8)

* rSBA analysis performed at GSK laboratories

rSBA titres were determined over a period of 10 years in subjects initially vaccinated with one dose of **Nimenrix™** or ACWY-PS at 11 to 17 years of age in Study MenACWY-TT-036. Persistence of rSBA titres was evaluated in two extension studies: MenACWY-TT-043 (up to 5 years) and MenACWY-TT-101 (at 10 years). Study MenACWY-TT-101 also evaluated the response to a single booster dose of **Nimenrix™** administered 10 years following the initial vaccination with **Nimenrix™** or ACWY-PS. Results are shown in Table 16.

Table 16: rSBA* titres following a single dose of Nimenrix™ (or ACWY-PS) in adolescents aged 11-17 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-036/043/101)

Mening-ococcal group	Time point	Nimenrix™			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Month 1(1)	674	100% (99.5; 100)	5929 (5557; 6324)	224	99.6% (97.5; 100)	2947 (2612; 3326)
	Year 3(2)	449	92.9% (90.1; 95.1)	448 (381; 527)	150	82.7% (75.6; 88.4)	206 (147; 288)
	Year 5(2)	236	97.5% (94.5; 99.1)	644 (531; 781)	86	93.0% (85.4; 97.4)	296 (202; 433)
	Year 10(3) (Pre-booster)	162	85.2% (78.8; 90.3)	248 (181; 340)	51	80.4% (66.9; 90.2)	143 (80.5; 253)
	(Post-booster)(3,4)	162	100% (97.7; 100)	3760 (3268; 4326)	51	100% (93.0; 100)	2956 (2041; 4282)
C	Month 1(1)	673	100% (99.5; 100)	13110 (11939; 14395)	224	100% (98.4; 100)	8222 (6808; 9930)
	Year 3(2)	449	91.1% (88.1; 93.6)	371 (309; 446)	150	86.0% (79.4; 91.1)	390 (262; 580)
	Year 5(2)	236	88.6%	249	85	87.1	366

Mening-ococcal group	Time point	Nimenrix™			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
			(83.8; 92.3)	(194; 318)		(78.0; 93.4)	(224; 599)
	Year 10[3] (Pre-booster)	162	90.1% (84.5; 94.2)	244 (182; 329)	51	82.4% (69.1; 91.6)	177 (86.1; 365)
	(Post-booster)[3,4]	162	100% (97.7; 100)	8698 (7391; 10235)	51	100% (93.0; 100)	3879 (2715; 5544)
W-135	Month 1[1]	678	99.9% (99.2; 100)	8247 (7639; 8903)	224	100% (98.4; 100)	2633 (2299; 3014)
	Year 3	449	82.0% (78.1; 85.4)	338 (268; 426)	150	30.0% (22.8; 38.0)	16.0 (10.9; 23.6)
	Year 5	236	86.0% (80.9; 90.2)	437 (324; 588)	86	34.9% (24.9; 45.9)	19.7 (11.8; 32.9)
	Year 10[3] (Pre-booster)	162	71.6% (64.0; 78.4)	146 (97.6; 217)	51	43.1% (29.3; 57.8)	16.4 (9.2; 29.4)
	(Post-booster)[3,4]	162	100% (97.7; 100)	11243 (9367; 13496)	51	100% (93.0; 100)	3674 (2354; 5734)
Y	Month 1[1]	677	100% (99.5; 100)	14087 (13168; 15069)	224	100% (98.4; 100)	5066 (4463; 5751)
	Year 3[2]	449	93.1% (90.3; 95.3)	740 (620; 884)	150	58.0% (49.7; 66.0)	69.6 (44.6; 109)
	Year 5[2]	236	96.6% (93.4; 98.5)	1000 (824; 1214)	86	66.3% (55.3; 76.1)	125 (71.2; 219)
	Year 10[3] (Pre-booster)	162	90.7% (85.2; 94.7)	447 (333; 599)	51	49.0% (34.8; 63.4)	32.9 (17.1; 63.3)
	(Post-booster)[3,4]	162	100% (97.7; 100)	7585 (6748; 8525)	51	98.0% (89.6; 100)	3296 (1999; 5434)

The analysis of immunogenicity was conducted on the ATP cohort for each time point.

[1] Study MenACWY-TT-036

[2] Study MenACWY-TT-043

[3] Study MenACWY-TT-101

[4] Blood sampling was performed 1 month after a booster dose at Year 10.

* rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

In Study MenACWY-TT-059, hSBA persistence was evaluated up to 5 years after vaccination in adolescents and adults aged 11-25 years initially vaccinated in Study MenACWY-TT-052.

For all meningococcal groups, the persistence of hSBA titres elicited by **Nimenrix™** was similar to or higher than those induced by the licensed quadrivalent meningococcal diphtheria toxoid (DT) conjugate (ACWY-DT) vaccine as shown in Table 17.

Table 17: hSBA* titres following a single dose of Nimenrix™ (or ACWY-DT) in adolescents and adults aged 11-25 years and persistence up to 5 years following vaccination (Studies MenACWY-TT-052/059)

Meningococcal group	Vaccine group	Time point	N	≥8 (95% CI)	GMT (95% CI)
A	**Nimenrix™**	Month 1[1]	356	82.0% (77.6; 85.9)	58.7 (48.6; 70.9)
		Year 1[2]	350	29.1% (24.4; 34.2)	5.4 (4.5; 6.4)

Meningococcal group	Vaccine group	Time point	N	≥8 (95% CI)	GMT (95% CI)
		Year 5[2]	141	48.9% (40.4; 57.5)	8.9 (6.8; 11.8)
	ACWY-DT	Month 1[1]	107	73.8% (64.4; 81.9)	42.5 (28.5; 63.3)
		Year 1[2]	111	31.5% (23.0; 41.0)	6.0 (4.3; 8.5)
		Year 5[2]	45	44.4% (29.6; 60.0)	7.9 (4.8; 13.2)
C	Nimenrix™	Month 1[1]	359	96.1% (93.5; 97.9)	532 (424; 668)
		Year 1[2]	336	94.9% (92.0; 97.0)	172 (142; 207)
		Year 5[2]	140	92.9% (87.3; 96.5)	94.6 (65.9; 136)
	ACWY-DT	Month 1[1]	113	99.1% (95.2; 100)	317 (217; 462)
		Year 1[2]	105	73.3% (63.8; 81.5)	46.7 (30.2; 72.1)
		Year 5[2]	44	79.5% (64.7; 90.2)	30.6 (17.3; 54.4)
W-135	Nimenrix™	Month 1[1]	334	91.0% (87.4; 93.9)	117 (96.8; 141)
		Year 1[2]	327	98.5% (96.5; 99.5)	197 (173; 225)
		Year 5[2]	138	87.0% (80.2; 92.1)	103 (76.3; 140)
	ACWY-DT	Month 1[1]	96	75.0% (65.1; 83.3)	70.4 (43.7; 113)
		Year 1[2]	107	75.7% (66.5; 83.5)	48.9 (32.5; 73.8)
		Year 5[2]	44	84.1% (69.9; 93.4)	70.4 (37.2; 133)
Y	Nimenrix™	Month 1[1]	364	95.1% (92.3; 97.0)	246 (208; 291)
		Year 1[2]	356	97.8% (95.6; 99.0)	272 (237; 311)
		Year 5[2]	142	94.4% (89.2; 97.5)	225 (174; 290)
	ACWY-DT	Month 1[1]	111	81.1% (72.5; 87.9)	103 (67.5; 159)
		Year 1[2]	112	86.6% (78.9; 92.3)	101 (69.6; 146)
		Year 5[2]	44	90.9% (78.3; 97.5)	129 (77.4; 216)

The analysis of immunogenicity was conducted on the ATP cohort for persistence adapted for each time-point.

[1] Study MenACWY-TT-052

[2] Study MenACWY-TT-059

* hSBA analysis performed at GSK laboratories

rSBA titres were determined over a period of 10 years in subjects initially vaccinated with one dose of **Nimenrix™** or ACWY-PS at 11 to 55 years of age in Study MenACWY-TT-015. Persistence of rSBA titres was evaluated in two extension studies: MenACWY-TT-020 (up to 5 years) and MenACWY-TT-099 (up to 10 years). Study MenACWY-TT-099 also evaluated the response to a single booster dose of **Nimenrix™** administered 10 years following the initial vaccination with **Nimenrix™** or ACWY-PS. Results are shown in Table 18.

Table 18: rSBA* titres following a single dose of Nimenrix™ (or ACWY-PS) in adolescents and adults aged 11-55 years, persistence up to 10 years, and post-booster administered 10 years following initial vaccination (Studies MenACWY-TT-015/020/099)

Meningo-coccal group	Time point	Nimenrix™			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)

A	Month 1[(1)]	323	100% (98.9; 100)	4945 (4452; 5493)	112	100% (96.8; 100)	2190 (1858; 2582)
	Year 4[(2)]	43	95.3% (84.2; 99.4)	365 (226; 590)	17	76.5% (50.1; 93.2)	104 (31.0; 351)
	Year 5[(2)]	51	84.3% (71.4; 93.0)	190 (108; 335)	19	57.9% (33.5; 79.7)	37.0 (12.6; 109)
	Year 10[(3)] (Pre-booster)	155	78.1% (70.7; 84.3)	154 (108; 219)	52	71.2% (56.9; 82.9)	75.1 (41.4; 136)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	4060 (3384; 4870)	52	100% (93.2; 100)	3585 (2751; 4672)
C	Month 1[(1)]	341	99.7% (98.4; 100)	10074 (8700, 11665)	114	100% (96.8; 100)	6546 (5048; 8488)
	Year 4[(2)]	43	76.7% (61.4; 88.2)	126 (61.6; 258)	17	41.2% (18.4; 67.1)	16.7 (5.7; 48.7)
	Year 5[(2)]	51	72.5% (58.3; 84.1)	78.5 (41.8; 147)	18	38.9% (17.3; 64.3)	17.3 (6.0; 49.7)
	Year 10[(3)] (Pre-booster)	154	90.9% (85.2; 94.9)	193 (141; 264)	52	88.5% (76.6; 95.6)	212 (110; 412)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	13824 (10840; 17629)	52	98.1% (89.7; 100)	3444 (1999; 5936)
W-135	Month 1[(1)]	340	99.7% (98.4; 100)	8577 (7615; 9660)	114	100% (96.8; 100)	2970 (2439; 3615)
	Year 4[(2)]	43	90.7% (77.9; 97.4)	240 (128; 450)	17	17.6% (3.8; 43.4)	8.3 (3.6; 19.5)
	Year 5[(2)]	51	86.3% (73.7; 94.3)	282 (146; 543)	19	31.6% (12.6; 56.6)	15.4 (5.7; 41.9)
	Year 10[(3)] (Pre-booster)	154	71.4% (63.6; 78.4)	166 (107; 258)	52	21.2% (11.1; 34.7)	10.9 (6.1; 19.3)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	23431 (17351; 31641)	52	98.1% (89.7; 100)	5793 (3586; 9357)
Y	Month 1[(1)]	340	100% (98.9; 100)	10315 (9317; 11420)	114	100% (96.8; 100)	4574 (3864; 5414)
	Year 4[(2)]	43	86.0% (72.1; 94.7)	443 (230; 853)	17	47.1% (23.0; 72.2)	30.7 (9.0; 105)
	Year 5[(2)]	51	92.2% (81.1; 97.8)	770 (439; 1351)	19	63.2% (38.4; 83.7)	74.1 (21.9; 250)
	Year 10[(3)] (Pre-booster)	154	86.4% (79.9; 91.4)	364 (255; 519)	52	61.5% (47.0; 74.7)	56.0 (28.8; 109)
	(Post-booster)[(3,4)]	155	100% (97.6; 100)	8958 (7602; 10558)	52	100% (93.2; 100)	5138 (3528; 7482)

The analysis of immunogenicity was conducted on the ATP cohorts for 1 month and 5 years post vaccination and the booster ATP cohort.

[(1)] Study MenACWY-TT-015

[(2)] Study MenACWY-TT-020

[(3)] Study MenACWY-TT-099

[(4)] Blood sampling was performed 1 month after a booster dose at Year 10.

* rSBA analysis performed at GSK laboratories for 1 month post primary vaccination samples and at PHE laboratories in UK for the subsequent sampling time points.

In a descriptive study conducted in 194 adults aged 56 years and older (Study MenACWY-TT-085), **Nimenrix™** was immunogenic, with a vaccine response rate ≥63.4% and with ≥97.4% of subjects with rSBA titres ≥8 against all four meningococcal groups. Moreover, at least 93.2% of subjects achieved the more conservative threshold of protection of rSBA titres ≥128.

Booster response for subjects previously vaccinated with a conjugate meningococcal vaccine against *Neisseria meningitidis*

Nimenrix™ booster vaccination in subjects previously primed with a monovalent (MenC-CRM) or a quadrivalent conjugate meningococcal vaccine (MenACWY-TT) was studied in subjects from 12 months of age onwards who received a booster vaccination. Robust anamnestic responses to the antigen(s) in the priming vaccine were observed (see Tables 8, 9, 14, 16, and 18).

Response to **Nimenrix™** in subjects previously vaccinated with a plain polysaccharide meningococcal vaccine against *Neisseria meningitidis*

In Study MenACWY-TT-021 conducted in subjects aged 4.5-34 years, the immunogenicity of **Nimenrix™** administered between 30 and 42 months after vaccination with a ACWY-PS vaccine was compared to the immunogenicity of **Nimenrix™** administered to age-matched subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to **Nimenrix™**. The clinical relevance of this observation is unknown since all subjects achieved rSBA titres ≥8 for all four meningococcal groups. Results are shown in Table 19.

Table 19: rSBA* titres 1 month after Nimenrix™ vaccination in subjects according to their meningococcal vaccine history (Study MenACWY-TT-021)

Meningococcal group	Subjects vaccinated 30 to 42 months previously with ACWY-PS			Subjects who had not received a meningococcal vaccine in the preceding 10 years		
	N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	146	100% (97.5; 100)	6869 (6045; 7805)	69	100% (94.8; 100)	13015 (10722; 15798)
C	169	100% (97.8; 100)	1946 (1583; 2391)	75	100% (95.2; 100)	5495 (4266; 7076)
W-135	169	100% (97.8; 100)	4636 (3942; 5451)	75	100% (95.2; 100)	9078 (7088; 11627)
Y	169	100% (97.8; 100)	7800 (6683; 9104)	75	100% (95.2; 100)	13895 (11186; 17261)

The analysis of immunogenicity was conducted on the ATP cohort.
* rSBA analysis performed at GSK laboratories

Immunogenicity in children aged 2-17 years with anatomical or functional asplenia

Study MenACWY-TT-084 evaluated the immunogenicity of one and two doses of **Nimenrix™** given 2 months apart in 43 at-risk subjects aged 2-17 years (at increased risk for meningococcal disease, i.e., asplenic subjects, and hyposplenic subjects) compared to 43 healthy age-matched subjects.

One month after the first vaccine dose, vaccine response rates (rSBA titre ≥1:32 or a ≥4-fold increase in rSBA titre from baseline) for groups A, C, W-135, and Y, respectively, were 100%, 92.5%, 100% and 97.5% in the at-risk group and were 97.5%, 97.5%, 97.5%, and 100% for healthy subjects. After the second vaccine dose, vaccine response rates in both at-risk and healthy subjects were 100% for each of the four meningococcal groups.

One month after Vaccination 1, hSBA response rates for groups A, C, W-135, and Y, respectively, were 69.7%, 77.1%, 55.6%, and 60.5% in the at-risk group and were 69.7%, 60.6%, 65.5%, and 76.3%, in the healthy group. One month after Vaccination 2, hSBA response rates were 84.8%, 100%, 80.6% and 73.0%, in the at-risk group and 75.0%, 85.3%, 77.4%, and 73.0% in the healthy group.

Impact of a single dose of **Nimenrix™**
The Netherlands introduced **Nimenrix™** into the national immunization program in 2018 as a single dose at 14 months of age. A catch-up campaign for individuals 14-18 years of age initiated in 2018 and in 2020 a single dose of **Nimenrix™** at 14 years of age became routine, resulting in a toddler and adolescent national immunization program. Within two years, the incidence of meningococcal disease caused by groups C, W, and Y was significantly reduced by 100% (95% CI: 14, 100) in individuals 14-18 years of age, 85% (95% CI: 32, 97) in all vaccine eligible ages (direct effect), and 50% (95% CI: 28, 65) in non-vaccine eligible ages (indirect effect). In children 15 to 36 months, there were only 3 cases during the pre-vaccination period and 2 cases in the post vaccination period, resulting in an IRR of 33% (95% CI: -302, 89). The low number of cases among this age group, does not allow for a reliable assessment of vaccine impact as indicated by the wide 95% CIs.

5.2. Pharmacokinetic Properties

Not relevant for vaccines.

5.3. Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on local tolerance, acute toxicity, repeated dose toxicity, developmental/reproductive toxicity and fertility studies.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Powder: sucrose, trometamol.
Solvent: sodium chloride, 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

The expiry date is indicated on the label and packaging.

6.4. Special Precautions for Storage

- Store in a refrigerator (2°C – 8°C)
- The solvent may also be stored at ambient temperature (25°C)
- Do not freeze
- Protect from light

6.5. Nature and Contents of Container

- Powder in a vial containing 1 dose (type I glass) with a stopper (butyl rubber) and 0.5 ml of solvent for 1 dose in a pre-filled syringe with a stopper (butyl rubber).
  Pack sizes of 1 and 10 with or without needles.

- Powder in a vial containing 1 dose (type I glass) with a stopper (butyl rubber) and 0.5 ml of solvent for 1 dose in an ampoule (type I glass).
  Pack sizes of 1, 10 and 100
  The powder is white. The solvent is clear and colourless.

6.6. Special Precautions for Disposal and Other Handling

Before reconstitution

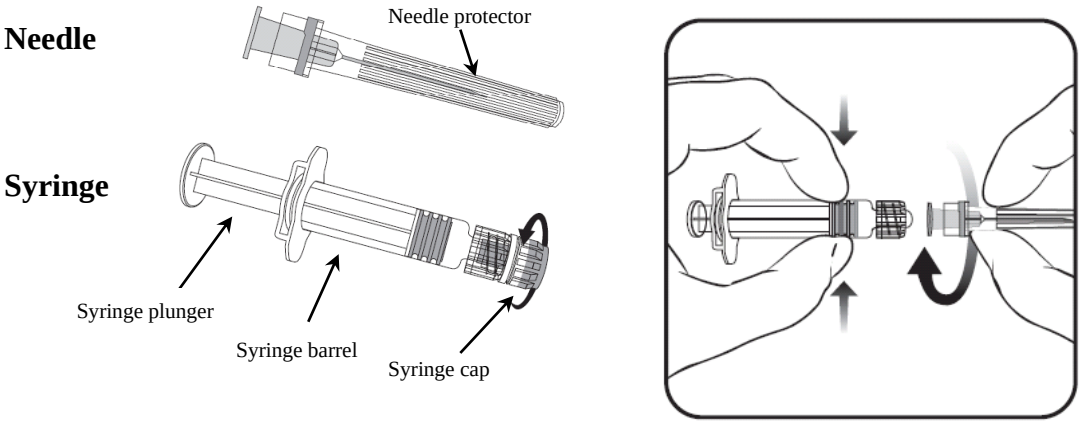
Instructions for reconstitution of the vaccine with solvent presented in ampoules

Nimenrix™ must be reconstituted by adding the entire content of the ampoule of solvent to the vial containing the powder. To do so, break the top of the ampoule, draw up the solvent with a syringe and add the solvent to the powder. The mixture should be well shaken until the powder is completely dissolved in the solvent.

Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe

Nimenrix™ must be reconstituted by adding the entire content of the pre-filled syringe of solvent to the vial containing the powder.

To attach the needle to the syringe, refer to the below picture. However, the syringe provided with **Nimenrix™** might be slightly different than the syringe described in the picture.



1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.

Add the solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

After reconstitution
The reconstituted vaccine is a clear colourless solution.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

After reconstitution, the vaccine should be used promptly. Although delay is not recommended, stability has been demonstrated for 8 hours at 30°C after reconstitution. If not used within 8 hours, do not administer the vaccine.

A new needle should be used to administer the vaccine.

Any unused product or waste material should be disposed of in accordance with local requirements.

Not all presentations are available in every country.

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