ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Nimenrix powder and solvent for solution for injection in pre-filled syringe
Meningococcal groups A, C, W-135 and Y conjugate vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

Neisseria meningitidis group A polysaccharide[1]	5 micrograms
Neisseria meningitidis group C polysaccharide[1]	5 micrograms
Neisseria meningitidis group W-135 polysaccharide[1]	5 micrograms
Neisseria meningitidis group Y polysaccharide[1]	5 micrograms
[1]conjugated to tetanus toxoid carrier protein	44 micrograms

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
The powder or cake is white.
The solvent is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

Nimenrix should be used in accordance with available official recommendations.

Primary immunisation
Infants from 6 weeks to less than 6 months of age: two doses, each of 0.5 ml, should be administered with an interval of 2 months between doses.

Infants from 6 months of age, children, adolescents and adults: a single 0.5 mL dose should be administered.
An additional primary dose of Nimenrix may be considered appropriate for some individuals (see section 4.4).

Booster doses
Long-term antibody persistence data following vaccination with Nimenrix are available up to 10 years after vaccination (see sections 4.4 and 5.1).

After completion of the primary immunisation course in infants 6 weeks to less than 12 months of age, a booster dose should be given at 12 months of age with an interval of at least 2 months after the last Nimenrix vaccination (see section 5.1).

In previously vaccinated individuals 12 months of age and older, Nimenrix may be given as a booster dose if they have received primary vaccination with a conjugated or plain polysaccharide meningococcal vaccine (see sections 4.4 and 5.1).

Method of administration

Immunisation 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

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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.

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

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 especially in adolescents 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.

Thrombocytopenia and coagulation disorders

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 familial complement deficiencies (for example, C5 or C3 deficiencies) and persons receiving treatments that inhibit 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.

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 any other *Neisseria meningitidis* groups.

A protective immune response may not be elicited in all vaccinees.

Effect of prior vaccination with plain polysaccharide meningococcal vaccine
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 a serum bactericidal assay using rabbit complement (rSBA) than subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years (see section 5.1). The clinical relevance of this observation is unknown.

Effect of pre-vaccination antibody to tetanus toxoid
The safety and immunogenicity of Nimenrix was evaluated when it was sequentially administered or co-administered with a vaccine containing, diphtheria and tetanus toxoids, acellular pertussis, inactivated polioviruses (1, 2 and 3), hepatitis B surface antigen and *Haemophilus influenzae* type b polyribosyl ribose phosphate conjugated to tetanus toxoid (DTaP-HBV-IPV/Hib) in the second year of life. The administration of Nimenrix one month after the DTaP-HBV-IPV/Hib vaccine resulted in lower rSBA GMTs against groups A, C and W-135 compared with co-administration (see section 4.5). The clinical relevance of this observation is unknown.

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 particular 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
Toddlers aged 12-14 months had similar rSBA titres to groups A, C, W-135 and Y at one month after one dose of Nimenrix or at one month after two doses of Nimenrix given two months apart.

A single dose was associated with lower hSBA titres to groups W-135 and Y compared with two doses given two months apart. Similar responses to groups A and C were observed after one or two doses (see section 5.1). The clinical relevance of this observation is unknown. If a toddler is expected to be at particular risk of invasive meningococcal disease due to exposure to groups W-135 and/or Y, consideration may be given to administering a second dose of Nimenrix after an interval of 2 months. 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

Following administration of Nimenrix there is a waning of serum bactericidal antibody titres against group A when using 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 one year previously, consideration may be given to administering a booster dose.

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

Effect of Nimenrix on anti-tetanus antibody concentrations

Although an increase of the anti-tetanus toxoid (TT) antibody concentrations was observed following vaccination with Nimenrix, Nimenrix does not substitute for tetanus immunisation.

Giving Nimenrix with or one month before a TT-containing vaccine in the second year of life does not impair the response to TT or significantly affect safety. No data are available beyond the age of 2 years.

Sodium content

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

In infants, Nimenrix can be given concomitantly with combined DTaP-HBV-IPV/Hib vaccines and with 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.

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

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

Whenever possible, Nimenrix and a TT containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should be co-administered or Nimenrix should be administered at least one month before the TT containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine, 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 immune responses to the other nine pneumococcal serotypes.

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.

It may be expected that in patients receiving immunosuppressive treatment, an adequate response may not be elicited.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Animal studies do not indicate direct or indirect harmful effects with respect to 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.

Breast-feeding

It is unknown whether Nimenrix is excreted in human milk.

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

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

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. However, some of the effects mentioned under section 4.8 “Undesirable effects” may affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of Nimenrix presented in the table below is based on two clinical study datasets as follows:

- A pooled analysis of data from 9,621 subjects administered a single dose of Nimenrix. This total included 3,079 toddlers (12 months to 23 months), 909 children between 2 and 5 years of age, 990 children between 6 and 10 years of age, 2,317 adolescents (11 to 17 years) and 2,326 adults (18 to 55 years).
- Data from a study in infants aged 6 to 12 weeks at the time of the first dose (Study MenACWY-TT-083), 1,052 subjects received at least one dose of a primary series of 2 or 3 doses of Nimenrix and 1,008 received a booster dose at approximately 12 months of age.

Safety data have also been evaluated in a separate study, in which a single dose of Nimenrix was administered to 274 individuals aged 56 years and older.

Local and general adverse reactions
In the 6-12 weeks and in the 12-14 months age groups who received 2 doses of Nimenrix given 2 months apart, the first and second doses were associated with similar local and systemic reactogenicity.

The local and general adverse reaction profile of a booster dose of Nimenrix given to subjects from 12 months through 30 years 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 for gastrointestinal symptoms (including diarrhoea, vomiting, and nausea), which were very common among subjects 6 years of age and older.

Tabulated list of adverse reactions

Adverse reactions reported 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)
Not known (cannot be estimated from available data)

Table 1 shows the adverse reactions reported from the studies in subjects aged from 6 weeks up to 55 years of age and post-marketing experience. Adverse reactions reported in subjects aged >55 years were similar to those observed in younger adults.

Table 1: Tabulated summary of adverse reactions by system organ class

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Not known***	Lymphadenopathy
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
	Uncommon	Insomnia Crying
Nervous system disorders	Very common	Drowsiness Headache
	Uncommon	Hypoaesthesia Dizziness
	Rare	Febrile convulsion
Gastrointestinal disorders	Common	Diarrhoea Vomiting Nausea*
Skin and subcutaneous tissue disorders	Uncommon	Pruritus Urticaria Rash**
Musculoskeletal and connective tissue disorders	Uncommon	Myalgia Pain in extremity
General disorders and administration site conditions	Very common	Fever Swelling at injection site Pain at injection site Redness at injection site Fatigue
	Common	Injection site haematoma*
	Uncommon	Malaise Injection site induration Injection site pruritus Injection site warmth Injection site anaesthesia
	Not known***	Extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb

*Nausea and Injection site haematoma occurred at a frequency of Uncommon in infants
**Rash occurred at a frequency of Common in infants
***ADR identified post-marketing

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, meningococcal vaccines, ATC code: J07AH08

Mechanism of action

Anti-capsular meningococcal antibodies protect against meningococcal disease via complement mediated bactericidal activity. 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.

Immunogenicity in infants

In Study MenACWY-TT-083, the first dose was administered at 6 to 12 weeks of age, the second after an interval of 2 months, and a third (booster) dose administered at approximately 12 months of age. DTaP-HBV-IPV/Hib and a 10-valent pneumococcal vaccine were co-administered. Nimenrix elicited rSBA and hSBA titres against the four meningococcal groups as shown in Table 2. The response against group C was non-inferior to the one elicited by licensed MenC-CRM and MenC-TT vaccines in terms of percentages with rSBA titres ≥8 at 1 month after the second dose.

Data from this study support the extrapolation of the immunogenicity data and posology to infants from 12 weeks to less than 6 months of age.

Table 2: 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	Post-dose 2[(1)]	456	97.4% (95.4; 98.6)	203 (182; 227)	202	96.5% (93.0; 98.6)	157 (131; 188)
		Post-booster[(1)]	462	99.6% (98.4; 99.9)	1561 (1412; 1725)	214	99.5% (97.4;100)	1007 (836;1214)
C	Nimenrix	Post-dose 2[(1)]	456	98.7% (97.2; 99.5)	612 (540; 693)	218	98.6% (96.0; 99.7)	1308 (1052; 1627)
		Post-booster[(1)]	463	99.8% (98.8; 100)	1177 (1059; 1308)	221	99.5% (97.5; 100)	4992 (4086; 6100)
	MenC-CRM vaccine	Post-dose 2[(1)]	455	99.6% (98.4; 99.9)	958 (850; 1079)	202	100% (98.2; 100)	3188 (2646; 3841)
		Post-booster[(1)]	446	98.4% (96.8; 99.4)	1051 (920; 1202)	216	100% (98.3; 100)	5438 (4412; 6702)
	MenC-TT vaccine	Post-dose 2[(1)]	457	100% (99.2; 100)	1188 (1080; 1307)	226	100% (98.4; 100)	2626 (2219; 3109)
		Post-booster[(1)]	459	100% (99.2; 100)	1960 (1776; 2163)	219	100% (98.3; 100)	5542 (4765; 6446)
W	Nimenrix	Post-dose 2[(1)]	455	99.1% (97.8; 99.8)	1605 (1383; 1862)	217	100% (98.3; 100)	753 (644; 882)
		Post-booster[(1)]	462	99.8% (98.8; 100)	2777 (2485; 3104)	218	100% (98.3; 100)	5123 (4504; 5826)
Y	Nimenrix	Post-dose 2[(1)]	456	98.2% (96.6; 99.2)	483 (419; 558)	214	97.7% (94.6; 99.2)	328 (276; 390)
		Post-booster[(1)]	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

[(1)] blood sampling performed 21 to 48 days post vaccination

In Study MenACWY-TT-087, infants received either a single primary dose at 6 months followed by a booster dose at 15-18 months (DTaP-IPV/Hib and 10-valent pneumococcal conjugate vaccine was co-administered at both vaccination time points) or three primary doses at 2, 4, and 6 months followed by a booster dose at 15-18 months. 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 3.

Table 3: 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)

Meningo-coccal 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	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 in 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. Results are shown in Table 3.

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 4.

Table 4: SBA* titres following a single dose of Nimenrix (or MenC-CRM) in toddlers aged 12-23 months (Studies MenACWY-TT-039/040)

Meningo-coccal 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 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. One month post dose one or two Nimenrix elicited hSBA titres against groups W-135 and Y that were higher in terms of the percentage of subjects with hSBA titre ≥8 when two doses were given compared with one (see section 4.4). Nimenrix elicited hSBA titres against groups A and C that were similar in terms of the percentage of subjects with hSBA titre ≥8 when two doses were given compared with one. 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. Results are shown in Table 5.

Table 5: 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)

Meningo-coccal 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	Post dose 1	180	97.8% (94.4; 99.4)	1437 (1118; 1847)	74	95.9% (88.6; 99.2)	118 (86.8; 161)
		Year 1	167	63.5% (55.7; 70.8)	62.7 (42.6; 92.2)	70	35.1% (25.9; 49.5)	6.1 (4.1; 8.9)
		Year 3	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)
		Year 5	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	Post dose 1	158	96.8% (92.8; 99.0)	1275 (970; 1675)	66	97.0% (89.5; 99.6)	133 (98.1; 180)
		Post dose 2	150	98.0% (94.3; 99.6)	1176 (922; 1501)	66	97.0% (89.5; 99.6)	170 (126; 230)
		Year 1	143	70.6% (62.4; 77.9)	76.6 (50.7; 115.7)	62	35.5% (23.7; 48.7)	6.4 (4.2; 10.0)
		Year 3	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)
		Year 5	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	Post dose 1	179	95.0% (90.7; 97.7)	452 (346; 592)	78	98.7% (93.1; 100)	152 (105; 220)
		Year 1	167	49.1% (41.3; 56.9)	16.2 (12.4; 21.1)	71	81.7% (70.7; 89.9)	35.2 (22.5; 55.2)
		Year 3	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)
		Year 5	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	Post dose 1	157	95.5% (91.0; 98.2)	369 (281; 485)	70	95.7% (88.0; 99.1)	161 (110; 236)
		Post dose 2	150	98.7% (95.3; 99.8)	639 (522; 783)	69	100% (94.8; 100)	1753 (1278; 2404)
		Year 1	143	55.2% (46.7; 63.6)	21.2 (15.6; 28.9)	63	93.7% (84.5; 98.2)	73.4 (47.5; 113.4)
		Year 3	121	33.9% (25.5; 43.0)	11.5 (8.4; 15.8)	56	67.9% (54.0; 79.7)	27.0 (15.6; 46.8)

Meningo-coccal group	Nimenrix dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		Year 5	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	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)
		Year 1	167	65.3% (57.5; 72.5)	57.2 (39.9; 82.0)	72	95.8% (88.3; 99.1)	209.0 (149.9; 291.4)
		Year 3	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)
		Year 5	133	44.4% (35.8; 53.2)	25.0 (16.7; 37.6)	56	58.9% (45.0; 71.9)	20.8 (11.6; 37.1)
	2 doses	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)
		Post dose 2	150	100% (97.6; 100)	3533 (2914; 4283)	70	97.1% (90.1; 99.7)	757 (550; 1041)
		Year 1	143	77.6% (69.9; 84.2)	123 (82.7; 183)	65	98.5% (91.7; 100.0)	232.6 (168.3; 321.4)
		Year 3	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)
		Year 5	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	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)
		Year 1	167	73.1% (65.7; 79.6)	76.8 (54.2; 109.0)	62	91.9% (82.2; 97.3)	144 (97.2; 214.5)
		Year 3	147	61.9% (53.5; 69.8)	58.0 (39.1; 86.0)	64	53.1% (40.2; 65.7)	17.3 (10.1; 29.6)
		Year 5	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	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)
		Post dose 2	150	99.3% (96.3; 100)	1134 (944; 1360)	64	95.3% (86.9; 99.0)	513 (339; 775)
		Year 1	143	79.7% (72.2; 86.0)	112.3 (77.5; 162.8)	58	87.9% (76.7; 95.0)	143.9 (88.5; 233.8)
		Year 3	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)

Meningo-coccal group	Nimenrix dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		Year 5	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
*rSBA analysis performed at PHE laboratories
**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 6 (see section 4.4).

Table 6: 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)

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)]	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)

Table 6: 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)

Meningococcal group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		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] (Pre-booster)	62	45.2% (32.5; 58.3)	27.4 (14.7; 51.0)	56	42.9% (29.7; 56.8)	9.1 (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. Subjects with a suboptimal response to meningococcal group C (defined as SBA titre below the pre-defined assay cut-off) were to receive an additional dose of MenC vaccine before Year 6. These subjects were excluded from the analysis at Years 4 and 5 but included in the analysis at Year 10.

(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 7 (see section 4.4).

Table 7: 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)

Table 7: 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)
		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.

Immunogenicity in children aged 2-10 years

In Study MenACWY-TT-081, a single dose of Nimenrix was demonstrated to be non-inferior to another licensed MenC-CRM vaccine 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]. The GMT was lower for the Nimenrix group [2795 (95% CI: 2393; 3263)] versus the MenC-CRM vaccine [5292 (95% CI: 3815; 7340)].

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 8.

Table 8: 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

Persistence of SBA titres was evaluated in children initially vaccinated in Study MenACWY-TT-081 as shown in Table 9 (see section 4.4).

Table 9: rSBA and hSBA titres up to 44 months following Nimenrix (or MenC-CRM) in children aged 2-10 years at time of vaccination (Study MenACWY-TT-088)

Meningo coccal 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)
		44	189	85.7% (79.9; 90.4)	307 (224; 423)	89	25.8% (17.1; 36.2)	4.8 (3.4; 6.7)
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)
		44	189	37.0% (30.1; 44.3)	14.5 (10.9; 19.2)	82	76.8% (66.2; 85.4)	36.4 (23.1; 57.2)
	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)
		44	66	45.5% (33.1; 58.2)	31.0 (16.6; 58.0)	31	64.5% (45.4; 80.8)	38.8 (13.3; 113)
W-135	**Nimenrix**	32	193	77.2%	214	86	84.9%	69.9

				(70.6; 82.9)	(149; 307)		(75.5; 91.7)	(48.2; 101)
		44	189	68.3% (61.1; 74.8)	103 (72.5; 148)	87	80.5% (70.6; 88.2)	64.3 (42.7; 96.8)
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)
		44	189	62.4% (55.1; 69.4)	78.9 (54.6; 114)	76	82.9% (72.5; 90.6)	127 (78.0; 206)

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

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 (Table 10) (see section 4.4).

Table 10: 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)

Meningococcal group	Vaccine group	1 month post-vaccination (Study MenACWY-TT-027)			1 year persistence (Study MenACWY-TT-028)		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	**Nimenrix**	105	80.0 % (71.1; 87.2)	53.4 (37.3; 76.2)	104	16.3% (9.8; 24.9)	3.5 (2.7; 4.4)
	ACWY-PS vaccine	35	25.7% (12.5; 43.3)	4.1 (2.6; 6.5)	35	5.7% (0.7; 19.2)	2.5 (1.9; 3.3)
C	**Nimenrix**	101	89.1% (81.3; 94.4)	156 (99.3; 244)	105	95.2% (89.2; 98.4)	129 (95.4; 176)
	ACWY-PS vaccine	38	39.5% (24.0; 56.6)	13.1 (5.4; 32.0)	31	32.3% (16.7; 51.4)	7.7 (3.5; 17.3)
W-135	**Nimenrix**	103	95.1% (89.0; 98.4)	133 (99.9; 178)	103	100% (96.5; 100)	257 (218; 302)
	ACWY-PS vaccine	35	34.3% (19.1; 52.2)	5.8 (3.3; 9.9)	31	12.9% (3.6; 29.8)	3.4 (2.0; 5.8)
Y	**Nimenrix**	89	83.1% (73.7;90.2)	95.1 (62.4; 145)	106	99.1% (94.9; 100)	265 (213; 330)
	ACWY-PS vaccine	32	43.8% (26.4; 62.3)	12.5 (5.6; 27.7)	36	33.3% (18.6; 51.0)	9.3 (4.3; 19.9)

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 11 (see section 4.4).

Table 11: 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 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)]	225	100% (98.4; 100)	7301 (6586; 8093)	111[(5)]	81.1% (72.5; 87.9)	57.0 (40.3; 80.6)

Table 11: 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 group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		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% (2.7; 32.4)	7.6 (3.7; 15.6)	23	30.4% (13.2; 52.9)	7.0 (2.9; 16.9)

Table 11: 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 group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		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. Subjects with a suboptimal response to meningococcal group C (defined as SBA titre below the pre-defined assay cut-off) were to receive an additional dose of MenC vaccine before Year 6. These subjects were excluded from the analysis at Year 5 but included in the analyses at Years 6 and 10.

(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.

Nimenrix was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine in terms of vaccine response as shown in Table 12.

Table 12: 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 group	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 13.

Table 13: 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)

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)	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)

Table 13: 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)

Meningo-coccal group	Time point	Nimenrix			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
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% (83.8; 92.3)	249 (194; 318)	85	87.1% (78.0; 93.4)	366 (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[(2)]	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[(2)]	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.

hSBA persistence was evaluated up to 5 years after vaccination in adolescents and adults initially vaccinated in Study MenACWY-TT-052 as shown in Table 14 (see section 4.4).

Table 14: hSBA* titres following a single dose of Nimenrix in adolescents and adults aged 11-25 years and persistence up to 5 years following vaccination (Studies MenACWY-TT-052/059)

Meningococcal group	Time point	N	≥8 (95% CI)	GMT (95% CI)
A	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)
	Year 5[(2)]	141	48.9% (40.4; 57.5)	8.9 (6.8; 11.8)
C	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)
W-135	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)
Y	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)

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 15.

Table 15: 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)

Table 15: 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)
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 separate study (MenACWY-TT-085), a single dose of Nimenrix was administered to 194 Lebanese adults aged 56 years and older (including 133 aged 56-65 years and 61 aged >65 years). The percentage of subjects with rSBA titres (measured at GSK's laboratories) ≥128 before vaccination ranged from 45% (group C) to 62% (group Y). Overall, at 1 month post-vaccination the percentage of vaccines with rSBA titres ≥128 ranged from 93% (group C) to 97% (group Y). In the subgroup aged >65 years the percentage of vaccines with rSBA titres ≥128 at 1 month post-vaccination ranged from 90% (group A) to 97% (group Y).

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 6, 7, 11, 13, and 15).

Response to Nimenrix in subjects previously vaccinated with a plain polysaccharide 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. An immune response (rSBA titre ≥8) was observed against all four meningococcal groups in all subjects regardless of the

meningococcal vaccine history. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to Nimenrix, however 100% of subjects achieved rSBA titres ≥8 for all four meningococcal groups (A, C, W-135, Y) (see section 4.4).

Children (2-17 years) with anatomical or functional asplenia

Study MenACWY-TT-084 compared immune responses to two doses of Nimenrix given 2 months apart between 43 subjects aged 2-17 years with anatomic or functional asplenia subjects and 43 age-matched subjects with normal splenic function. One month after the first vaccine dose and 1 month after the second dose similar percentages of subjects in the two groups had rSBA titres ≥8 and ≥128 and hSBA titres ≥4 and ≥8.

Impact of a single dose of Nimenrix

In 2018, the Netherlands added Nimenrix to the national immunisation programme as a single dose for toddlers at 14 months of age to replace the meningococcal C conjugate vaccine. A catch-up campaign with a single dose of Nimenrix for adolescents 14-18 years of age also initiated in 2018, and it became routine in 2020 leading to a toddler and adolescent national immunisation programme. 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). The impact of Nimenrix was primarily driven by a reduction in group W disease.

5.2 Pharmacokinetic properties

Not applicable.

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

4 years

After reconstitution:

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.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Store in the original package in order to protect from light.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

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

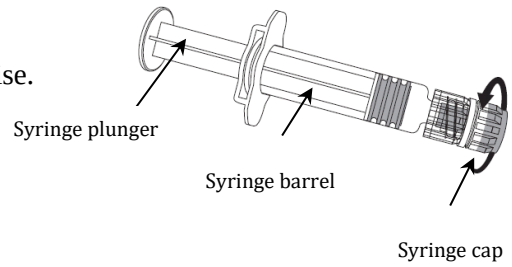
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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 (without screw thread) than the syringe described in the picture. In that case, the needle should be attached without screwing.

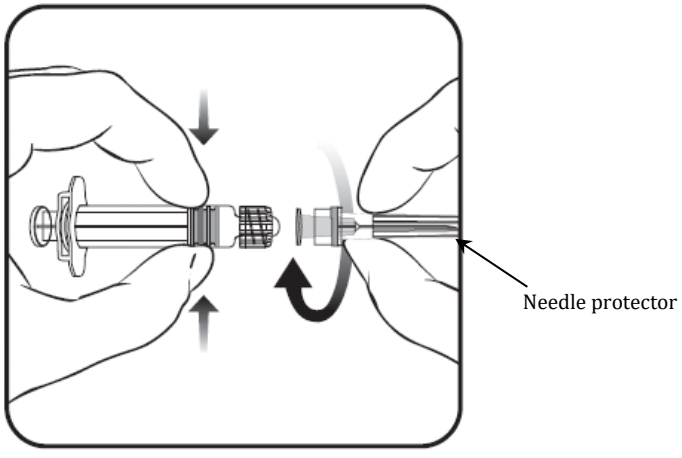
1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.



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.

4. 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.



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.

A new needle should be used to administer the vaccine.

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

7. MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/12/767/001
EU/1/12/767/002
EU/1/12/767/003
EU/1/12/767/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 April 2012
Date of latest renewal: 16 February 2017

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Nimenrix powder and solvent for solution for injection in vials
Meningococcal groups A, C, W-135 and Y conjugate vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

Neisseria meningitidis group A polysaccharide[1]	5 micrograms
Neisseria meningitidis group C polysaccharide[1]	5 micrograms
Neisseria meningitidis group W-135 polysaccharide[1]	5 micrograms
Neisseria meningitidis group Y polysaccharide[1]	5 micrograms
[1]conjugated to tetanus toxoid carrier protein	44 micrograms

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
The powder or cake is white.
The solvent is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

Nimenrix should be used in accordance with available official recommendations.

Primary immunisation
Infants from 6 weeks to less than 6 months of age: two doses, each of 0.5 ml, should be administered with an interval of 2 months between doses.

Infants from 6 months of age, children, adolescents and adults: a single 0.5 mL dose should be administered.
An additional primary dose of Nimenrix may be considered appropriate for some individuals (see section 4.4).

Booster doses
Long-term antibody persistence data following vaccination with Nimenrix are available up to 10 years after vaccination (see sections 4.4 and 5.1).

After completion of the primary immunisation course in infants 6 weeks to less than 12 months of age, a booster dose should be given at 12 months of age with an interval of at least 2 months after the last Nimenrix vaccination (see section 5.1).

In previously vaccinated individuals 12 months of age and older, Nimenrix may be given as a booster dose if they have received primary vaccination with a conjugated or plain polysaccharide meningococcal vaccine (see sections 4.4 and 5.1).

Method of administration

Immunisation 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

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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.

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

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 especially in adolescents 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.

Thrombocytopenia and coagulation disorders

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 familial complement deficiencies (for example, C5 or C3 deficiencies) and persons receiving treatments that inhibit 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.

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 any other *Neisseria meningitidis* groups.

A protective immune response may not be elicited in all vaccinees.

Effect of prior vaccination with plain polysaccharide meningococcal vaccine
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 a serum bactericidal assay using rabbit complement (rSBA) than subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years (see section 5.1). The clinical relevance of this observation is unknown.

Effect of pre-vaccination antibody to tetanus toxoid
The safety and immunogenicity of Nimenrix was evaluated when it was sequentially administered or co-administered with a vaccine containing, diphtheria and tetanus toxoids, acellular pertussis, inactivated polioviruses (1, 2 and 3), hepatitis B surface antigen and *Haemophilus influenzae* type b polyribosyl ribose phosphate conjugated to tetanus toxoid (DTaP-HBV-IPV/Hib) in the second year of life. The administration of Nimenrix one month after the DTaP-HBV-IPV/Hib vaccine resulted in lower rSBA GMTs against groups A, C and W-135 compared with co-administration (see section 4.5). The clinical relevance of this observation is unknown.

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 particular 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
Toddlers aged 12-14 months had similar rSBA titres to groups A, C, W-135 and Y at one month after one dose of Nimenrix or at one month after two doses of Nimenrix given two months apart.

A single dose was associated with lower hSBA titres to groups W-135 and Y compared with two doses given two months apart. Similar responses to groups A and C were observed after one or two doses (see section 5.1). The clinical relevance of this observation is unknown. If a toddler is expected to be at particular risk of invasive meningococcal disease due to exposure to groups W-135 and/or Y, consideration may be given to administering a second dose of Nimenrix after an interval of 2 months. 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

Following administration of Nimenrix there is a waning of serum bactericidal antibody titres against group A when using 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 one year previously, consideration may be given to administering a booster dose.

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

Effect of Nimenrix on anti-tetanus antibody concentrations

Although an increase of the anti-tetanus toxoid (TT) antibody concentrations was observed following vaccination with Nimenrix, Nimenrix does not substitute for tetanus immunisation.

Giving Nimenrix with or one month before a TT-containing vaccine in the second year of life does not impair the response to TT or significantly affect safety. No data are available beyond the age of 2 years.

Sodium content

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

In infants, Nimenrix can be given concomitantly with combined DTaP-HBV-IPV/Hib vaccines and with 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.

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

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

Whenever possible, Nimenrix and a TT containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should be co-administered or Nimenrix should be administered at least one month before the TT containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine, 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 immune responses to the other nine pneumococcal serotypes.

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.

It may be expected that in patients receiving immunosuppressive treatment, an adequate response may not be elicited.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Animal studies do not indicate direct or indirect harmful effects with respect to 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.

Breast-feeding

It is unknown whether Nimenrix is excreted in human milk.

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

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

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. However, some of the effects mentioned under section 4.8 “Undesirable effects” may affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of Nimenrix presented in the table below is based on two clinical study datasets as follows:

- A pooled analysis of data from 9,621 subjects administered a single dose of Nimenrix. This total included 3,079 toddlers (12 months to 23 months), 909 children between 2 and 5 years of age, 990 children between 6 and 10 years of age, 2,317 adolescents (11 to 17 years) and 2,326 adults (18 to 55 years).
- Data from a study in infants aged 6 to 12 weeks at the time of the first dose (Study MenACWY-TT-083), 1,052 subjects received at least one dose of a primary series of 2 or 3 doses of Nimenrix and 1,008 received a booster dose at approximately 12 months of age.

Safety data have also been evaluated in a separate study, in which a single dose of Nimenrix was administered to 274 individuals aged 56 years and older.

Local and general adverse reactions
In the 6-12 weeks and in the 12-14 months age groups who received 2 doses of Nimenrix given 2 months apart, the first and second doses were associated with similar local and systemic reactogenicity.

The local and general adverse reaction profile of a booster dose of Nimenrix given to subjects from 12 months through 30 years 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 for gastrointestinal symptoms (including diarrhoea, vomiting, and nausea), which were very common among subjects 6 years of age and older.

Tabulated list of adverse reactions

Adverse reactions reported 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)
Not known (cannot be estimated from available data)

Table 1 shows the adverse reactions reported from the studies in subjects aged from 6 weeks up to 55 years of age and post-marketing experience. Adverse reactions reported in subjects aged >55 years were similar to those observed in younger adults.

Table 1: Tabulated summary of adverse reactions by system organ class

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Not known***	Lymphadenopathy
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
	Uncommon	Insomnia Crying
Nervous system disorders	Very common	Drowsiness Headache
	Uncommon	Hypoaesthesia Dizziness
	Rare	Febrile convulsion
Gastrointestinal disorders	Common	Diarrhoea Vomiting Nausea*
Skin and subcutaneous tissue disorders	Uncommon	Pruritus Urticaria Rash**
Musculoskeletal and connective tissue disorders	Uncommon	Myalgia Pain in extremity

Table 1: Tabulated summary of adverse reactions by system organ class

System Organ Class	Frequency	Adverse reactions
General disorders and administration site conditions	Very common	Fever Swelling at injection site Pain at injection site Redness at injection site Fatigue
	Common	Injection site haematoma*
	Uncommon	Malaise Injection site induration Injection site pruritus Injection site warmth Injection site anaesthesia
	Not known***	Extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb

*Nausea and Injection site haematoma occurred at a frequency of Uncommon in infants
**Rash occurred at a frequency of Common in infants
***ADR identified post-marketing

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, meningococcal vaccines, ATC code: J07AH08

Mechanism of action

Anti-capsular meningococcal antibodies protect against meningococcal disease via complement mediated bactericidal activity. 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.

Immunogenicity in infants

In Study MenACWY-TT-083, the first dose was administered at 6 to 12 weeks of age, the second after an interval of 2 months, and a third (booster) dose administered at approximately 12 months of age. DTaP-HBV-IPV/Hib and a 10-valent pneumococcal vaccine were co-administered. Nimenrix elicited rSBA and hSBA titres against the four meningococcal groups as shown in Table 2. The response against group C was non-inferior to the one elicited by licensed MenC-CRM and MenC-TT vaccines in terms of percentages with rSBA titres ≥8 at 1 month after the second dose.

Data from this study support the extrapolation of the immunogenicity data and posology to infants from 12 weeks to less than 6 months of age.

Table 2: 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	Post-dose 2[(1)]	456	97.4% (95.4; 98.6)	203 (182; 227)	202	96.5% (93.0; 98.6)	157 (131; 188)
		Post-booster[(1)]	462	99.6% (98.4; 99.9)	1561 (1412; 1725)	214	99.5% (97.4;100)	1007 (836;1214)
C	Nimenrix	Post-dose 2[(1)]	456	98.7% (97.2; 99.5)	612 (540; 693)	218	98.6% (96.0; 99.7)	1308 (1052; 1627)
		Post-booster[(1)]	463	99.8% (98.8; 100)	1177 (1059; 1308)	221	99.5% (97.5; 100)	4992 (4086; 6100)
	MenC-CRM vaccine	Post-dose 2[(1)]	455	99.6% (98.4; 99.9)	958 (850; 1079)	202	100% (98.2; 100)	3188 (2646; 3841)
		Post-booster[(1)]	446	98.4% (96.8; 99.4)	1051 (920; 1202)	216	100% (98.3; 100)	5438 (4412; 6702)
	MenC-TT vaccine	Post-dose 2[(1)]	457	100% (99.2; 100)	1188 (1080; 1307)	226	100% (98.4; 100)	2626 (2219; 3109)
		Post-booster[(1)]	459	100% (99.2; 100)	1960 (1776; 2163)	219	100% (98.3; 100)	5542 (4765; 6446)
W	Nimenrix	Post-dose 2[(1)]	455	99.1% (97.8; 99.8)	1605 (1383; 1862)	217	100% (98.3; 100)	753 (644; 882)
		Post-booster[(1)]	462	99.8% (98.8; 100)	2777 (2485; 3104)	218	100% (98.3; 100)	5123 (4504; 5826)
Y	Nimenrix	Post-dose 2[(1)]	456	98.2% (96.6; 99.2)	483 (419; 558)	214	97.7% (94.6; 99.2)	328 (276; 390)
		Post-booster[(1)]	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
[(1)] blood sampling performed 21 to 48 days post vaccination

In Study MenACWY-TT-087, infants received either a single primary dose at 6 months followed by a booster dose at 15-18 months (DTaP-IPV/Hib and 10-valent pneumococcal conjugate vaccine was co-administered at both vaccination time points) or three primary doses at 2, 4, and 6 months followed by a booster dose at 15-18 months. 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 3.

Table 3: 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)

Meningo-coccal 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	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 in 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. Results are shown in Table 3.

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 4.

Table 4: SBA* titres following a single dose of Nimenrix (or MenC-CRM) in toddlers aged 12-23 months (Studies MenACWY-TT-039/040)

Meningo-coccal 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 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. One month post dose one or two Nimenrix elicited hSBA titres against groups W-135 and Y that were higher in terms of the percentage of subjects with hSBA titre ≥8 when two doses were given compared with one (see section 4.4). Nimenrix elicited hSBA titres against groups A and C that were similar in terms of the percentage of subjects with hSBA titre ≥8 when two doses were given compared with one. 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. Results are shown in Table 5.

Table 5: 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)

Meningo-coccal 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	Post dose 1	180	97.8% (94.4; 99.4)	1437 (1118; 1847)	74	95.9% (88.6, 99.2)	118 (86.8; 161)
		Year 1	167	63.5% (55.7; 70.8)	62.7 (42.6; 92.2)	70	35.1% (25.9; 49.5)	6.1 (4.1; 8.9)
		Year 3	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)
		Year 5	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	Post dose 1	158	96.8% (92.8; 99.0)	1275 (970; 1675)	66	97.0% (89.5; 99.6)	133 (98.1; 180)
		Post dose 2	150	98.0% (94.3; 99.6)	1176 (922; 1501)	66	97.0% (89.5; 99.6)	170 (126; 230)
		Year 1	143	70.6% (62.4; 77.9)	76.6 (50.7; 115.7)	62	35.5% (23.7; 48.7)	6.4 (4.2; 10.0)
		Year 3	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)
		Year 5	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	Post dose 1	179	95.0% (90.7; 97.7)	452 (346; 592)	78	98.7% (93.1; 100)	152 (105; 220)
		Year 1	167	49.1% (41.3; 56.9)	16.2 (12.4; 21.1)	71	81.7% (70.7; 89.9)	35.2 (22.5; 55.2)
		Year 3	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)
		Year 5	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	Post dose 1	157	95.5% (91.0; 98.2)	369 (281; 485)	70	95.7% (88.0; 99.1)	161 (110; 236)
		Post dose 2	150	98.7% (95.3; 99.8)	639 (522; 783)	69	100% (94.8; 100)	1753 (1278; 2404)
		Year 1	143	55.2% (46.7; 63.6)	21.2 (15.6; 28.9)	63	93.7% (84.5; 98.2)	73.4 (47.5; 113.4)
		Year 3	121	33.9% (25.5; 43.0)	11.5 (8.4; 15.8)	56	67.9% (54.0; 79.7)	27.0 (15.6; 46.8)
		Year 5	116	28.4%	8.5	59	67.8%	29.4

Meningo-coccal Group	Nimenrix dose group	Time point[(1)]	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
				(20.5; 37.6)	(6.4; 11.2)		(54.4; 79.4)	(16.3; 52.9)
W-135	1 dose	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)
		Year 1	167	65.3% (57.5; 72.5)	57.2 (39.9; 82.0)	72	95.8% (88.3; 99.1)	209.0 (149.9; 291.4)
		Year 3	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)
		Year 5	133	44.4% (35.8; 53.2)	25.0 (16.7; 37.6)	56	58.9% (45.0; 71.9)	20.8 (11.6; 37.1)
	2 doses	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)
		Post dose 2	150	100% (97.6; 100)	3533 (2914; 4283)	70	97.1% (90.1; 99.7)	757 (550; 1041)
		Year 1	143	77.6% (69.9; 84.2)	123 (82.7; 183)	65	98.5% (91.7; 100.0)	232.6 (168.3; 321.4)
		Year 3	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)
		Year 5	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	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)
		Year 1	167	73.1% (65.7; 79.6)	76.8 (54.2; 109.0)	62	91.9% (82.2; 97.3)	144 (97.2; 214.5)
		Year 3	147	61.9% (53.5; 69.8)	58.0 (39.1; 86.0)	64	53.1% (40.2; 65.7)	17.3 (10.1; 29.6)
		Year 5	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	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)
		Post dose 2	150	99.3% (96.3; 100)	1134 (944; 1360)	64	95.3% (86.9; 99.0)	513 (339; 775)
		Year 1	143	79.7% (72.2; 86.0)	112.3 (77.5; 162.8)	58	87.9% (76.7; 95.0)	143.9 (88.5; 233.8)
		Year 3	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)
		Year 5	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
*rSBA analysis performed at PHE laboratories
**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 6 (see section 4.4).

Table 6: 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)

Meningococcal 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)

Table 6: 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)

Meningococcal group	Vaccine Group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		Year 10[3] (Pre-booster)	62	45.2% (32.5; 58.3)	27.4 (14.7; 51.0)	56	42.9% (29.7; 56.8)	9.1 (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. Subjects with a suboptimal response to meningococcal group C (defined as SBA titre below the pre-defined assay cut-off) were to receive an additional dose of MenC vaccine before Year 6. These subjects were excluded from the analysis at Years 4 and 5 but included in the analysis at Year 10.

(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 7 (see section 4.4).

Table 7: 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)

Table 7: 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)
	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.

Immunogenicity in children aged 2-10 years

In Study MenACWY-TT-081, a single dose of Nimenrix was demonstrated to be non-inferior to another licensed MenC-CRM vaccine 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]. The GMT was lower for the Nimenrix group [2795 (95% CI: 2393; 3263)] versus the MenC-CRM vaccine [5292 (95% CI: 3815; 7340)].

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 8.

Table 8: 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

Persistence of SBA titres was evaluated in children initially vaccinated in Study MenACWY-TT-081 as shown in Table 9 (see section 4.4).

Table 9: rSBA and hSBA titres up to 44 months following Nimenrix (or MenC-CRM) in children aged 2-10 years at time of vaccination (Study MenACWY-TT-088)

Meningo coccal 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)
		44	189	85.7% (79.9; 90.4)	307 (224; 423)	89	25.8% (17.1; 36.2)	4.8 (3.4; 6.7)
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)
		44	189	37.0% (30.1; 44.3)	14.5 (10.9; 19.2)	82	76.8% (66.2; 85.4)	36.4 (23.1; 57.2)
	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)
		44	66	45.5% (33.1; 58.2)	31.0 (16.6; 58.0)	31	64.5% (45.4; 80.8)	38.8 (13.3; 113)
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)
		44	189	68.3% (61.1; 74.8)	103 (72.5; 148)	87	80.5% (70.6; 88.2)	64.3 (42.7; 96.8)
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)
		44	189	62.4% (55.1; 69.4)	78.9 (54.6; 114)	76	82.9% (72.5; 90.6)	127 (78.0; 206)

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

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 (Table 10) (see section 4.4).

Table 10: 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)

Meningococcal Group	Vaccine group	1 month post-vaccination (Study MenACWY-TT-027)			1 year persistence (Study MenACWY-TT-028)		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
A	Nimenrix	105	80.0 % (71.1; 87.2)	53.4 (37.3; 76.2)	104	16.3% (9.8; 24.9)	3.5 (2.7; 4.4)
	ACWY-PS vaccine	35	25.7% (12.5; 43.3)	4.1 (2.6; 6.5)	35	5.7% (0.7; 19.2)	2.5 (1.9; 3.3)
C	Nimenrix	101	89.1% (81.3; 94.4)	156 (99.3; 244)	105	95.2% (89.2; 98.4)	129 (95.4; 176)
	ACWY-PS vaccine	38	39.5% (24.0; 56.6)	13.1 (5.4; 32.0)	31	32.3% (16.7; 51.4)	7.7 (3.5; 17.3)
W-135	Nimenrix	103	95.1% (89.0; 98.4)	133 (99.9; 178)	103	100% (96.5; 100)	257 (218; 302)
	ACWY-PS vaccine	35	34.3% (19.1; 52.2)	5.8 (3.3; 9.9)	31	12.9% (3.6; 29.8)	3.4 (2.0; 5.8)
Y	Nimenrix	89	83.1% (73.7; 90.2)	95.1 (62.4; 145)	106	99.1% (94.9; 100)	265 (213; 330)
	ACWY-PS vaccine	32	43.8% (26.4; 62.3)	12.5 (5.6; 27.7)	36	33.3% (18.6; 51.0)	9.3 (4.3; 19.9)

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 11 (see section 4.4).

Table 11: 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 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)]	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)

Table 11: 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 group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
		(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% (2.7; 32.4)	7.6 (3.7; 15.6)	23	30.4% (13.2; 52.9)	7.0 (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)

Table 11: 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 group	Vaccine group	Time point	rSBA*			hSBA**		
			N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
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. Subjects with a suboptimal response to meningococcal group C (defined as SBA titre below the pre-defined assay cut-off) were to receive an additional dose of MenC vaccine before Year 6. These subjects were excluded from the analysis at Year 5 but included in the analyses at Years 6 and 10.

(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.

Nimenrix was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine in terms of vaccine response as shown in Table 12.

Table 12: 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 group	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 13.

Table 13: 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)

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)	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)

Table 13: 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)

Meningo-coccal group	Time point	Nimenrix			ACWY-PS vaccine		
		N	≥8 (95% CI)	GMT (95% CI)	N	≥8 (95% CI)	GMT (95% CI)
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% (83.8; 92.3)	249 (194; 318)	85	87.1% (78.0; 93.4)	366 (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[(2)]	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[(2)]	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.

hSBA persistence was evaluated up to 5 years after vaccination in adolescents and adults initially vaccinated in Study MenACWY-TT-052 as shown in Table 14 (see section 4.4).

Table 14: hSBA* titres following a single dose of Nimenrix in adolescents and adults aged 11-25 years and persistence up to 5 years following vaccination (Studies MenACWY-TT-052/059)

Meningococcalgroup	Time point	N	≥8 (95% CI)	GMT (95% CI)
A	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)
	Year 5[(2)]	141	48.9% (40.4; 57.5)	8.9 (6.8; 11.8)
C	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)
W-135	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)
Y	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)

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 15.

Table 15: 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)

Table 15: 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)
	(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 separate study (MenACWY-TT-085), a single dose of Nimenrix was administered to 194 Lebanese adults aged 56 years and older (including 133 aged 56-65 years and 61 aged >65 years). The percentage of subjects with rSBA titres (measured at GSK's laboratories) ≥128 before vaccination ranged from 45% (group C) to 62% (group Y). Overall, at 1 month post-vaccination the percentage of vaccines with rSBA titres ≥128 ranged from 93% (group C) to 97% (group Y). In the subgroup aged >65 years the percentage of vaccines with rSBA titres ≥128 at 1 month post-vaccination ranged from 90% (group A) to 97% (group Y).

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 6, 7, 11, 13, and 15).

Response to Nimenrix in subjects previously vaccinated with a plain polysaccharide 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. An immune response (rSBA titre ≥8) was observed against all four meningococcal groups in all subjects regardless of the meningococcal vaccine history. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to Nimenrix, however 100% of subjects achieved rSBA titres ≥8 for all four meningococcal groups (A, C, W-135, Y) (see section 4.4).

Children (2-17 years) with anatomical or functional asplenia

Study MenACWY-TT-084 compared immune responses to two doses of Nimenrix given 2 months apart between 43 subjects aged 2-17 years with anatomic or functional asplenia subjects and 43 age-matched subjects with normal splenic function. One month after the first vaccine dose and 1 month after the second dose similar percentages of subjects in the two groups had rSBA titres ≥8 and ≥128 and hSBA titres ≥4 and ≥8.

Impact of a single dose of Nimenrix

In 2018, the Netherlands added Nimenrix to the national immunisation programme as a single dose for toddlers at 14 months of age to replace the meningococcal C conjugate vaccine. A catch-up campaign with a single dose of Nimenrix for adolescents 14-18 years of age also initiated in 2018, and it became routine in 2020 leading to a toddler and adolescent national immunisation programme. 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). The impact of Nimenrix was primarily driven by a reduction in group W disease.

5.2 Pharmacokinetic properties

Not applicable.

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

4 years

After reconstitution:

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.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Store in the original package in order to protect from light.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Powder in a vial (type I glass) with a stopper (butyl rubber) and solvent in a vial (type I glass) with a stopper (butyl rubber).
Pack size of 50.

6.6 Special precautions for disposal and other handling

Instructions for reconstitution of the vaccine with the solvent presented in vials

Nimenrix must be reconstituted by adding the entire contents of the solvent vial to the vial containing the powder.
1. Withdraw the entire contents of the solvent vial and add the solvent to the powder vial.
2. The mixture should be well shaken until the powder is completely dissolved in the solvent.

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.

A new needle should be used to administer the vaccine.

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

7. MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/12/767/008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 April 2012
Date of latest renewal: 16 February 2017

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Pfizer Ireland Pharmaceuticals
Grange Castle Business Park
Clondalkin
Dublin 22
Ireland

Name and address of the manufacturer responsible for batch release

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2. of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency.
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change in the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
1 VIAL AND 1 PRE-FILLED SYRINGE WITHOUT NEEDLE
1 VIAL AND 1 PRE-FILLED SYRINGE WITH 2 NEEDLES
10 VIALS AND 10 PRE-FILLED SYRINGES WITHOUT NEEDLE
10 VIALS AND 10 PRE-FILLED SYRINGES WITH 20 NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

Nimenrix powder and solvent for solution for injection in pre-filled syringe
Meningococcal groups A, C, W-135 and Y conjugate vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains 5 micrograms of *Neisseria meningitidis* groups A, C, W-135 and Y polysaccharides.

3. LIST OF EXCIPIENTS

Excipients:
Sucrose
Trometamol
Sodium chloride
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection in a pre-filled syringe

1 vial: powder
1 pre-filled syringe: solvent
1 dose (0.5 ml)

10 vials: powder
10 pre-filled syringes: solvent
10 x 1 dose (0.5 ml)

1 vial: powder
1 pre-filled syringe: solvent
2 needles
1 dose (0.5 ml)

10 vials: powder
10 pre-filled syringes: solvent
20 needles
10 x 1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intramuscular use.
Shake well before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.
After reconstitution, use promptly.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local regulations.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/12/767/001 – pack of 1 without needle
EU/1/12/767/002 – pack of 10 without needle
EU/1/12/767/003 – pack of 1 with 2 needles
EU/1/12/767/004 – pack of 10 with 20 needles

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
50 POWDER VIALS AND 50 SOLVENT VIALS

1. NAME OF THE MEDICINAL PRODUCT

Nimenrix powder and solvent for solution for injection in vials
Meningococcal groups A, C, W-135 and Y conjugate vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains 5 micrograms of *Neisseria meningitidis* groups A, C, W-135 and Y polysaccharides.

3. LIST OF EXCIPIENTS

Excipients:
Sucrose
Trometamol
Sodium chloride
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection in vials
50 vials: powder
50 vials: solvent
50 x 1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intramuscular use.
Shake well before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.
After reconstitution, use promptly.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local regulations.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/12/767/008 – pack of 50

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
PRE-FILLED SYRINGE WITH SOLVENT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for Nimenrix
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
VIAL WITH SOLVENT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for Nimenrix
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
VIAL WITH MEN ACWY CONJUGATE POWDER

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Powder for Nimenrix
MenACWY Conjugate
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Nimenrix powder and solvent for solution for injection in pre-filled syringe

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

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you or your child. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

This leaflet has been written assuming the person receiving the vaccine is reading it, but it can be given to adults and children so you may be reading it for your child.

What is in this leaflet

1. What Nimenrix is and what it is used for

What Nimenrix is and what it is used for
Nimenrix is a vaccine which helps protect against infections caused by bacteria (germs) called "*Neisseria meningitidis"* types A, C, W-135 and Y.
"Neisseria meningitidis" types A, C, W-135 and Y bacteria can cause serious illnesses such as:
- meningitis - an infection of the tissue that lines the brain and spinal cord.
- septicaemia - an infection of the blood.

These infections are passed easily from person to person and can cause death if not treated.
Nimenrix may be given to adults, adolescents, children and infants over the age of 6 weeks.

How Nimenrix works
Nimenrix helps your body to produce its own protection (antibodies) against the bacteria. These antibodies help protect you against the diseases.

Nimenrix will only protect against infections caused by the bacteria "*Neisseria meningitidis"* types A, C, W-135 and Y.

2. What you need to know before you receive Nimenrix

Nimenrix should not be given if:
- you are allergic to the active substances or any of the other ingredients in this vaccine (listed in section 6).
  Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue. **See your doctor immediately if you notice any of these**.

If you are not sure, talk to your doctor or nurse before you receive Nimenrix.

Warnings and precautions:
Check with your doctor or nurse before you receive this vaccine if:

- you have an infection with a high temperature (over 38°C). If this applies to you, the vaccination will not be given until you are feeling better. A minor infection such as a cold should not be a problem. However, talk to your doctor or nurse first.
- you have a bleeding problem or you bruise easily.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you receive Nimenrix.

Nimenrix may not fully protect everyone who is vaccinated. If you have a weak immune system (such as due to HIV infection or medicines that affect the immune system) you may not get a full benefit from Nimenrix.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore tell the doctor or nurse if you or your child fainted with a previous injection.

Other medicines and Nimenrix
Tell your doctor or nurse if you are taking or have recently taken any other medicines, including other vaccines and medicines obtained without a prescription.

Nimenrix may not work as well if you are taking medicines that affect your immune system.

In infants, Nimenrix can be given concomitantly with combined diphtheria - tetanus - acellular pertussis (DTaP) vaccines, including combination DTaP vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b (HBV, IPV or Hib) such as DTaP-HBV-IPV/Hib vaccine, and with 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.

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

In individuals aged 9 to 25 years, Nimenrix can be given concomitantly with human papillomavirus vaccine [Types 16, 18] and a combined diphtheria (reduced antigen content), tetanus and acellular pertussis vaccine.

Whenever possible, Nimenrix and a TT containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should be co-administered or Nimenrix should be administered at least one month before the TT containing vaccine.

A different injection site will be used for each vaccine.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant, plan to become pregnant or are breast-feeding, you must tell your doctor before receiving Nimenrix.

Driving and using machines
Nimenrix is not likely to affect your ability to drive or use machines. However, do not drive or use any machines if you are feeling unwell.

Nimenrix contains sodium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How Nimenrix is given

Nimenrix will be given to you by a doctor or nurse.
Nimenrix is always injected into a muscle, usually in the upper arm or thigh.

Primary immunisation

Infants from 6 weeks to less than 6 months of age
Two injections given 2 months apart at e.g. 2 and 4 months of age (the first injection may be given from the age of 6 weeks).

Infants from 6 months of age, children, adolescents and adults
One injection.

Booster doses

Infants from 6 weeks to less than 12 months of age:
One booster dose at 12 months of age, at least 2 months after the last dose of Nimenrix.

Previously vaccinated individuals 12 months of age and older:
Please tell your doctor if you have received a previous injection with another meningococcal vaccine than Nimenrix.
Your doctor will tell you if and when you need an additional dose of Nimenrix, especially if you or your child:

- received your first dose at age 6-14 months and could be at particular risk of infection caused by *Neisseria meningitidis* types W-135 and Y
- received your dose more than approximately one year ago and could be at risk of infection caused by *Neisseria meningitidis* type A
- received your first dose at age 12-23 months and could be at particular risk of infection caused by *Neisseria meningitidis* types A, C, W-135 and Y

You will be informed when you or your child should come back for the next injection. If you or your child misses a scheduled injection, it is important that you make another appointment.

Make sure you or your child finishes the complete vaccination course.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Very common (these may occur with more than 1 in 10 doses of the vaccine):

- fever
- tiredness (fatigue)
- headache
- feeling drowsy
- loss of appetite

- feeling irritable
- swelling, pain and redness where the injection is given.

Common (these may occur with up to 1 in 10 doses of the vaccine):
- bruising (haematoma) where the injection is given
- stomach and digestion problems such as diarrhoea, vomiting and nausea
- rash (infants).

Uncommon (these may occur with up to 1 in 100 doses of the vaccine):
- rash
- hives
- itching
- crying
- feeling dizzy
- aching muscles
- pain in the arms or legs
- generally feeling unwell
- difficulty sleeping
- decreased feeling or sensitivity, especially in the skin
- reactions where the injection is given such as itching, a feeling of warmth or numbness or a hard lump.

Rare (these may occur up to 1 in 1,000 doses of the vaccine):
- fits (seizures) associated with a high temperature

Not known: frequency cannot be estimated from the available data
- injection site swelling and redness; this may affect a large area of the vaccinated limb
- enlarged lymph nodes

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nimenrix

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C).
- Store in the original package in order to protect from light.
- Do not freeze.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Nimenrix contains
- The active substances are:
  - After reconstitution, 1 dose (0.5 ml) contains:
  - Neisseria meningitidis group A polysaccharide1 5 micrograms

- Neisseria meningitidis group C polysaccharide1 5 micrograms
- Neisseria meningitidis group W-135 polysaccharide1 5 micrograms
- Neisseria meningitidis group Y polysaccharide1 5 micrograms
- 1conjugated to tetanus toxoid carrier protein 44 micrograms

- The other ingredients are:
  - In the powder: sucrose and trometamol
  - In the solvent: sodium chloride (see section 2 “Nimenrix contains sodium”) and water for injections

What Nimenrix looks like and contents of the pack
Nimenrix is a powder and a solvent for solution for injection.
Nimenrix is supplied as a white powder or cake in a single dose glass vial and a clear and colourless solvent in a pre-filled syringe.
These must be mixed together before use. The mixed vaccine will appear as a clear colourless solution.
Nimenrix is available in packs of 1 or 10 with or without needles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

Manufacturer responsible for batch release:
Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

The vaccine is for intramuscular use only. Do not administer intravascularly, intradermally or subcutaneously.

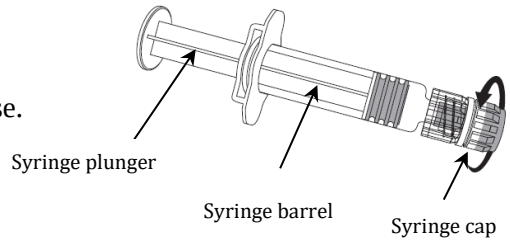
If Nimenrix is co-administered with other vaccines, different injection sites should be used.

Nimenrix should not be mixed with other vaccines.

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

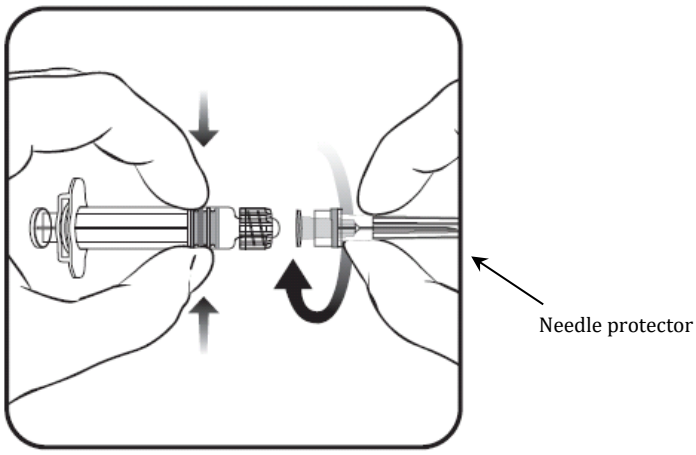
Nimenrix must be reconstituted by adding the entire content of the pre-filled syringe of solvent to the vial containing the powder.
To attach the needle to the syringe, refer to the picture. However, the syringe provided with Nimenrix might be slightly different (without screw thread) than the syringe described in the picture. In that case the needle should be attached without screwing.

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.



4. 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.

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.

A new needle should be used to administer the vaccine.

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

Package leaflet: Information for the user

Nimenrix powder and solvent for solution for injection in vials
Meningococcal groups A, C, W-135 and Y conjugate vaccine

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you or your child. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

This leaflet has been written assuming the person receiving the vaccine is reading it, but it can be given to adults and children so you may be reading it for your child.

What is in this leaflet

1. What Nimenrix is and what it is used for

What Nimenrix is and what it is used for
Nimenrix is a vaccine which helps protect against infections caused by bacteria (germs) called "*Neisseria meningitidis"* types A, C, W-135 and Y.
"Neisseria meningitidis" types A, C, W-135 and Y bacteria can cause serious illnesses such as:
- meningitis - an infection of the tissue that lines the brain and spinal cord.
- septicaemia - an infection of the blood.

These infections are passed easily from person to person and can cause death if not treated.
Nimenrix may be given to adults, adolescents, children and infants over the age of 6 weeks.

How Nimenrix works
Nimenrix helps your body to produce its own protection (antibodies) against the bacteria. These antibodies help protect you against the diseases.
Nimenrix will only protect against infections caused by the bacteria "*Neisseria meningitidis"* types A, C, W-135 and Y.

2. What you need to know before you receive Nimenrix

Nimenrix should not be given if:
- you are allergic to the active substances or any of the other ingredients in this vaccine (listed in section 6).
  Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue. **See your doctor immediately if you notice any of these**.

If you are not sure, talk to your doctor or nurse before you receive Nimenrix.

Warnings and precautions:
Check with your doctor or nurse before you receive this vaccine if:

- you have an infection with a high temperature (over 38°C). If this applies to you, the vaccination will not be given until you are feeling better. A minor infection such as a cold should not be a problem. However, talk to your doctor or nurse first.
- you have a bleeding problem or you bruise easily.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you receive Nimenrix.

Nimenrix may not fully protect everyone who is vaccinated. If you have a weak immune system (such as due to HIV infection or medicines that affect the immune system) you may not get a full benefit from Nimenrix.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore tell the doctor or nurse if you or your child fainted with a previous injection.

Other medicines and Nimenrix
Tell your doctor or nurse if you are taking or have recently taken any other medicines, including other vaccines and medicines obtained without a prescription.

Nimenrix may not work as well if you are taking medicines that affect your immune system.

In infants, Nimenrix can be given concomitantly with combined diphtheria - tetanus - acellular pertussis (DTaP) vaccines, including combination DTaP vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b (HBV, IPV or Hib) such as DTaP-HBV-IPV/Hib vaccine, and with 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.

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

In individuals aged 9 to 25 years, Nimenrix can be given concomitantly with human papillomavirus vaccine [Types 16, 18] and a combined diphtheria (reduced antigen content), tetanus and acellular pertussis vaccine.

Whenever possible, Nimenrix and a TT containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should be co-administered or Nimenrix should be administered at least one month before the TT containing vaccine.

A different injection site will be used for each vaccine.

Pregnancy and breast-feeding
If you are pregnant, think you may be pregnant, plan to become pregnant or are breast-feeding, you must tell your doctor before receiving Nimenrix.

Driving and using machines
Nimenrix is not likely to affect your ability to drive or use machines. However, do not drive or use any machines if you are feeling unwell.

Nimenrix contains sodium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How Nimenrix is given

Nimenrix will be given to you by a doctor or nurse.
Nimenrix is always injected into a muscle, usually in the upper arm or thigh.

Primary immunisation

Infants from 6 weeks to less than 6 months of age
Two injections given 2 months apart at e.g. 2 and 4 months of age (the first injection may be given from the age of 6 weeks).

Infants from 6 months of age, children, adolescents and adults
One injection.

Booster doses

Infants from 6 weeks to less than 12 months of age:
One booster dose at 12 months of age, at least 2 months after the last dose of Nimenrix.

Previously vaccinated individuals 12 months of age and older:
Please tell your doctor if you have received a previous injection with another meningococcal vaccine than Nimenrix. Your doctor will tell you if and when you need an additional dose of Nimenrix, especially if you or your child:

- received your first dose at age 6-14 months and could be at particular risk of infection caused by *Neisseria meningitidis* types W-135 and Y
- received your dose more than approximately one year ago and could be at risk of infection caused by *Neisseria meningitidis* type A
- received your first dose at age 12-23 months and could be at particular risk of infection caused by *Neisseria meningitidis* types A, C, W-135 and Y

You will be informed when you or your child should come back for the next injection. If you or your child misses a scheduled injection, it is important that you make another appointment.
Make sure you or your child finishes the complete vaccination course.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Very common (these may occur with more than 1 in 10 doses of the vaccine):

- fever
- tiredness (fatigue)
- headache
- feeling drowsy
- loss of appetite
- feeling irritable
- swelling, pain and redness where the injection is given.

Common (these may occur with up to 1 in 10 doses of the vaccine):
- bruising (haematoma) where the injection is given
- stomach and digestion problems such as diarrhoea, vomiting and nausea.
- rash (infants).

Uncommon (these may occur with up to 1 in 100 doses of the vaccine):
- rash
- hives
- itching
- crying
- feeling dizzy
- aching muscles
- pain in the arms or legs
- generally feeling unwell
- difficulty sleeping
- decreased feeling or sensitivity, especially in the skin
- reactions where the injection is given such as itching, a feeling of warmth or numbness or a hard lump.

Rare (these may occur up to 1 in 1,000 doses of the vaccine):
- fits (seizures) associated with a high temperature

Not known: frequency cannot be estimated from the available data
- injection site swelling and redness; this may affect a large area of the vaccinated limb
- enlarged lymph nodes

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nimenrix

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C).
- Store in the original package in order to protect from light.
- Do not freeze.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Nimenrix contains
- The active substances are:
  - After reconstitution, 1 dose (0.5 ml) contains:
  - *Neisseria meningitidis* group A polysaccharide[1] 5 micrograms
  - *Neisseria meningitidis* group C polysaccharide[1] 5 micrograms
  - *Neisseria meningitidis* group W-135 polysaccharide[1] 5 micrograms
  - *Neisseria meningitidis* group Y polysaccharide[1] 5 micrograms
  - [1]conjugated to tetanus toxoid carrier protein 44 micrograms

- The other ingredients are:
  - In the powder: sucrose and trometamol
  - In the solvent: sodium chloride (see section 2 “Nimenrix contains sodium”) and water for injections

What Nimenrix looks like and contents of the pack
Nimenrix is a powder and a solvent for solution for injection.
Nimenrix is supplied as a white powder or cake in a single dose glass vial and a clear and colourless solvent in a vial.
These must be mixed together before use. The mixed vaccine will appear as a clear colourless solution.
Nimenrix is available in a pack of 50.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

Manufacturer responsible for batch release:
Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

The following information is intended for healthcare professionals only:

The vaccine is for intramuscular use only. Do not administer intravascularly, intradermally or subcutaneously.

If Nimenrix is co-administered with other vaccines, different injection sites should be used.

Nimenrix should not be mixed with other vaccines.

Instructions for reconstitution of the vaccine with the solvent presented in vials:

Nimenrix must be reconstituted by adding the entire contents of the vial of solvent to the vial containing the powder.

1. Withdraw the entire contents of the solvent vial and add the solvent to the powder vial.
2. The mixture should be well shaken until the powder is completely dissolved in the solvent.

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.

A new needle should be used to administer the vaccine.

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