

5.06 MENINGOCOCCAL POLYSACCHARIDE CONJUGATE VACCINE SEROGROUPS A, C, W-135 and Y, Pre-filled syringe, 0.5mL, Nimenrix[®], Pfizer Australia Pty Ltd.

1 Purpose of Application

- 1.1 NIP listing for a meningococcal polysaccharide serogroups A, C, W₁₃₅ and Y conjugate vaccine (MenACWY-TT) for the prevention of invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* serogroups A, C, W₁₃₅, and Y (MenA, MenC, MenW₁₃₅ and MenY, respectively) in infants. The PBAC has not previously considered this vaccine.
- 1.2 The submission requested the MenACWY-TT vaccine to be listed on the basis of non-inferior in terms of effectiveness compared to the combined haemophilus influenzae Type B and MenC (Hib-MenC) vaccine, and on a cost-minimisation basis compared to the assumed price of the meningococcal C component of the Hib-MenC vaccine (p129 of the submission).

2 Requested listing

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Approved ex-manufacturer price	Proprietary Name and Manufacturer
MENINGOCOCCAL POLYSACCHARIDE CONJUGATE VACCINE, SEROGROUPS A, C, W-135 AND Y	1	0	\$████	Nimenrix Pfizer Australia Pty Ltd
Category/Program:	NIP			
NIP indication:	A single dose of Nimenrix (MenACWY-TT) for infants at 12 months old.			

- 2.1 The submission proposed an ex-manufacturer price of \$████ (p27 of the submission). In Section 3 the submission stated that the proposed price of the MenACWY-TT vaccine was equivalent to the assumed price of the meningococcal C component of the Hib-MenC vaccine (p129 of the submission).
- 2.2 The submission proposed that a monovalent haemophilus influenzae Type B (Hib) vaccine given at 18 months will also need to be listed on the NIP to replace the displaced Hib component of the Hib-MenC vaccination currently given at 12 months of age (p24 of the submission).

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Background

Registration status

- 3.1 The MenACWY-TT vaccine was registered on the ARTG on 29 August 2013 for: active immunisation of individuals from the age of 12 months through 55 years against IMDs caused by *Neisseria meningitidis* serogroups A, C, W₁₃₅ and Y.

4 Population and disease

- 4.1 IMD is a rare disease caused by the bacterium *Neisseria meningitidis*. IMD can also cause meningitis and sepsis, leading to long-term sequelae including: sensorineural hearing loss, cognitive problems, physical or neurological disability, major amputations, very low IQ, and seizures (p14-15 of the submission).¹ About 10 – 30% of survivors of meningococcal disease have permanent sequelae (p14 of the submission).² Incidence is bimodal, with peaks in incidence for infants and adolescents. The case fatality rate for all cases of IMD is around 4.7%³, however may be higher for MenW.

¹ Viner et al (2012). Outcomes of invasive meningococcal serogroup B disease in children and adolescents (MOSAIC): a case-control study.

² Granoff et al (2013). Ch 21 – Meningococcal vaccines. In: Vaccines (6th Edition).

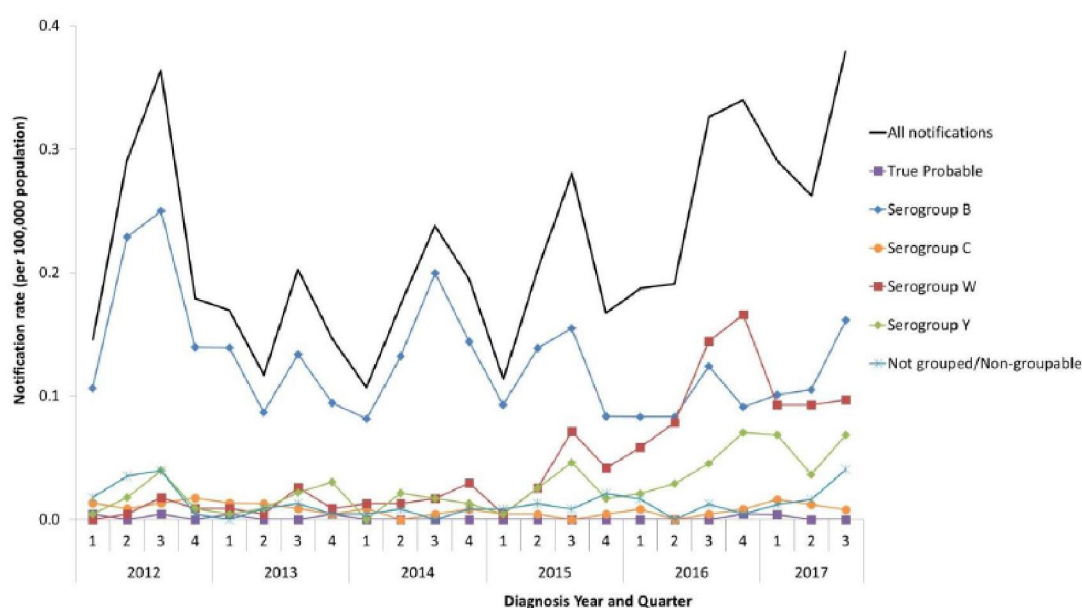
Stoof et al (2015). Disease burden of invasive meningococcal disease in the Netherlands between June 1999 and June 2011: A subjective role for serogroup and clonal complex.

Vyse et al (2013). The burden and impact of severe and long-term sequelae of meningococcal disease.

³ Australian Government Department of Health (2016) Summary of National Surveillance Data on Vaccine Preventable Diseases in Australia, 2008–2011, Communicable Diseases Intelligence, Volume 40

- 4.2 There has been an increase in the number of cases caused by MenW and MenY in recent years (see Figure 1).

Figure 1: Notifications and rates of IMD in Australia (2012 - 2017)*, by serogroup



* Data shown is for 1 January 2012 to 11 September 2017. Rates for Q3 2017 were not adjusted for the incomplete observation period of Q3.

Source: Figure 1.1-1, p16 of the submission and Figure 2, p4 of ATAGI pre-submission advice.

- 4.3 There have been 337 cases of IMD in 2017 (National Notifiable Diseases Surveillance System, NNDSS) to date, of which around 40 cases were caused by MenACWY in infants, of which three died⁴.

5 Comparator

- 5.1 The submission nominated the Hib-MenC vaccine (Menitorix) as the main comparator (p19 of the submission). The main arguments provided in support of this nomination were it is the only meningococcal vaccine listed on the NIP (p19 of the submission). This is reasonable.

For more detail on PBAC's view, see section 7 PBAC outcome.

⁴ Assuming around 38% were MenB, 4% were MenC, 30% were MenW, 19% were MenY, and 8% were other or unknown strains, and 22% of cases were aged less than five years old in 2017. Sources: Australian Government Department of Health (2017) Notifications of a selected disease by age group, sex and year, Available: http://www9.health.gov.au/cda/source/rpt_5_sel.cfm. Accessed 16 November 2017.

Australian Government Department of Health (14 August 2017) Invasive Meningococcal disease national surveillance report.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (2) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described the complications that can arise out of infant onset of meningococcal disease and were supportive of the requested listing.

Clinical trials

6.3 No head-to head RCTs of the MenACWY-TT vaccine and a Hib-MenC vaccine were identified.

6.4 The submission was based on four RCTs of the MenACWY-TT vaccine versus a MenC vaccine:

- Trial MenACWY-TT-013 + one extension study (MenACWY-TT-014)
- Trial MenACWY-TT-027 + five extension studies (MenACWY-TT-028 to 32)
- Trial MenACWY-TT-039
- Trial MenACWY-TT-040

6.5 One RCT of a Hib-MenC plus a MMR vaccine versus a MenC vaccine plus a Hib vaccine plus a MMR vaccine:

- Trial Hib-MenC-TT-016 + four extension studies (Hib-MenC-TT-017 to 20)

6.6 A meta-analysis of the trials comparing the MenACWY-TT vaccine versus a MenC vaccine was conducted, which was used in an indirect comparison of the MenACWY-TT vaccine with a Hib-MenC vaccine, using a MenC vaccine as the common comparator.

6.7 Details of the trials presented in the submission are provided in the table below.

Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
MenACWY-TT-013	A Phase II, open (partially double-blind), randomised, controlled dose-range study to evaluate the immunogenicity, reactogenicity and safety of four different formulations of GlaxoSmithKline (GSK) Biologicals' new generations meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine versus MenC or other MenACWY vaccine (Mencevax) ACWY when given as one dose to children aged 12 to 14 months and 3 to 5 years old.	2009
Trial 1	Knuf et al 2010. A dose-range study assessing immunogenicity and safety of one dose of a new candidate meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine administered in the second year of life and in young children.	<i>Vaccine</i> . 28(3):744-53.
MenACWY-TT-027	A phase IIb, open, randomized, controlled primary vaccination study to evaluate the noninferiority and the persistence of the immune response of GSK Biologicals' meningococcal serogroup ACWY conjugate vaccine given intramuscularly versus MenC or Other MenACWY vaccine (Mencevax) [™] ACWY to healthy subjects aged 1 through 10 years of age. Vesikari et al 2012. Randomised trial to assess the immunogenicity, safety and antibody persistence up to three years after a single dose of a tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine in toddlers.	2007 <i>Human vaccines & Immunotherapeutics</i> . 8(12):1892-903.
MenACWY-TT-039	Immunogenicity & safety study of GSK Biologicals' meningococcal vaccine GSK134612 when co-administered with GSK Biologicals' MMRV vaccine (Priorix-Tetra [™]) in healthy 12 to 23-month-old children. Vesikari et al 2011. Tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine is well tolerated and immunogenic when co-administered with measles-mumps-rubella-varicella vaccine during the second year of life: An open, randomized controlled trial.	2011 <i>Vaccine</i> . 29(25):4274-84.
MenACWY-TT-040	Co-administration of GSK Biologicals' meningococcal vaccine GSK134612 with Infanrix-hexa [™] , compared to individual administration of each vaccine, in healthy 12- through 23-month-old children. Knuf et al 2011. An investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine co-administered with Infanrix [™] hexa is immunogenic, with an acceptable safety profile in 12-23-month-old children.	2009 <i>Vaccine</i> . 29(25):4264-73.
Hib-MenC-TT-016	A phase III, open, randomized, controlled, multi-centre study to demonstrate the non-inferiority of the meningococcal serogroup C and the Haemophilus influenzae type b immune response of GlaxoSmithKline (GSK) Biologicals' conjugate Hib-MenC vaccine co-administered with GSK Biologicals' measles-mumps-rubella vaccine, Priorix, versus MenC-CRM197 conjugate vaccine co-administered with GSK Biologicals' Hib vaccine, Hiberix, and Priorix in 12- to 18-month-old toddlers primed in infancy with a Hib vaccine but not with a meningococcal serogroup C vaccine; and to evaluate the long-term antibody persistence up to 5 years after the administration of the Hib-MenC vaccine. Booy et al 2011. Immediate and longer term immunogenicity of a single dose of the combined haemophilus influenzae Type B-neisseria meningitidis serogroup C-tetanus toxoid conjugate vaccine in primed toddlers 12 to 18 months of age.	2008 <i>The Paediatric Infectious Disease Journal</i> . 30(4):340-342.

Source: Table2.2-2, p38-39 of the submission.

6.8 The key features of the direct randomised trials are summarised in the table below.

Table 2: Key features of the included evidence – indirect comparison

Trial	N (in relevant arms)	Design/ duration	Risk of bias	Patient population	Outcomes
MenACWY-TT vs. MenC					
MenACWY-TT-013	MenACWY-TT [^] :48 MenC [^] : 48	R, OL 15 months**	Low	Healthy subjects aged 12-14 months and 3-5 years	Immunogenicity Safety
MenACWY-TT-027	MenACWY-TT: 229 MenC: 75	R, OL 5 years**	Unclear	Healthy subjects aged 12-23 months	Immunogenicity Safety Persistence
MenACWY-TT-039	MenACWY-TT: 374 ^{^^} MenC ^{^^} : 125	R, OL 1 month	Unclear	Healthy subjects aged 12-23 months	Immunogenicity Safety
Men-ACWY-TT-040	MenACWY-TT#: 220 MenC#: 127	R, OL 1 month	Low	Healthy subjects aged 12-23 months	Immunogenicity Safety
Meta-analysis	Included MenACWY-TT-013, MenACWY-TT-027, MenACWY-TT-039 and MenACWY-TT-040				
Hib-MenC-TT vaccine vs. MenC					
Hib-MenC-016	Hib-MenC + MMR: 324 MenC + Hib + MMR: 109	R, OL 4 years**	Unclear	Health subjects aged 12-18 months	Immunogenicity Safety Persistence

DTPa-HBV-IPV/Hib: diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis and haemophilus influenzae type b; MenACWY-TT: Meningococcal serogroups ACWY tetanus toxoid vaccine, MenC: Meningococcal C, MMRV: measles, mumps, rubella and varicella; OL: open label; R: randomised.

* MenACWY-TT-013 contained 4 different formulations of the MenACWY-TT vaccine as the intervention. The MenACWY-TT vaccine used in the submission is Form 3.

** Including extension studies

[^] Subjects also received a DTPa-HBV-IPV/Hib vaccine (Infanrix hexa) at visit 2.

^{^^} Subjects received a MMRV vaccine (Priorix-Tetra) 42 and 84 days later.

Subjects in the MenACWY-TT arm received a DTPa-HBV-IPV/Hib vaccine (Infanrix hexa) at visit 2. Subjects in the Hib-MenC arm were given the option of not receiving the vaccine.

Source: Compiled during the evaluation from Table 2.3-1 p44, Table 2.3-3 p51, Table 2.3-4 p52, Table 2.4-2 p59 of the submission.

6.9 In the MenACWY-TT-027, MenACWY-TT-039 and Hib-MenC-016 trials blinding of laboratory personnel was not specified, which introduces uncertainty into the risk of detection bias in the immunogenicity results.

6.10 All of the trials were open-label, which increases the risk of bias in the safety results as the subjects were aware of the vaccines received. This could lead to over-reporting or under-reporting of the self-reported adverse events.

6.11 No vaccines were co-administered at the time of administration of the vaccine of interest in the MenACWY-TT trials, however subjects in trials MenACWY-TT-013, MenACWY-TT-039 and MenACWY-TT-040 received concomitant vaccinations at the second visit after outcomes were measured. A MMR vaccine was co-administered with each of the Hib-MenC and MenC + Hib vaccine arms in trial Hib-MenC-016, which introduces uncertainty into the indirect comparison of the safety outcomes.

Comparative effectiveness

- 6.12 No direct evidence was presented regarding vaccine efficacy against infection or disease caused by serogroups A, C, W or Y. The submission argued that pre-registration clinical effectiveness studies were not feasible due to the relatively low incidence of meningococcal disease (p61 of the submission). Consequently, the submission presented immunogenicity results as a surrogate outcome. This increases uncertainty in the results. This approach has been previously accepted by the PBAC.⁵
- 6.13 The PBAC has previously accepted the use of serum bactericidal antibodies (SBA) titres as a surrogate outcome for clinical efficacy in its consideration of the Hib-MenC vaccine, which used rSBA titres > 1:8 to estimate vaccine efficacy.⁶ This level was based on a study from the 1960s assessing the bactericidal activity of an Army recruit population for susceptibility to meningococcal disease, which found that hSBA <1:4 was correlated with the development of MenC.⁷ In addition, another study found that hSBA ≥1:4 were correlated with clinical protection against MenA, MenB and MenC.⁸
- 6.14 There is no established surrogate serological correlate of protection for non-MenC serogroups. The PBAC previously questioned the applicability of the hSBA ≥1:4 to bacterial proteins, as used in the 4CMenB vaccine, rather than polysaccharide capsule.⁹
- 6.15 ATAGI considered that rSBA titre ≥ 1:8 is an appropriate serological correlation of protection against serogroups A, C, W and Y in the short term (p10 of ATAGI pre-submission advice).
- 6.16 The submission nominated a non-inferiority margin of -10% in respect to rSBA-MenC ≥ 1:8 titres (p72 of the submission). This is reasonable. The PBAC submission for Menitorix (November 2010) used a non-inferiority margin of -10%.¹⁰
- 6.17 Table 3 presents a summary of the key immunogenicity results across the trials.

⁵ PBAC (November 2010) Public summary document: Multicomponent Meningococcal Group B Vaccine, 0.5mL, injection, prefilled syringe, Bexsero.

⁶ PBAC (November 2010) Public summary document: Haemophilus influenzae type b and group c meningococcal polysaccharide conjugate vaccine, lyophilised powder for injection, 1 vial with 0.5 mL pre-filled syringe diluent, 10 vials with 10 0.5 mL pre-filled syringe diluent, Menitorix.

⁷ Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. I. The role of humoral antibodies. *Journal of Experimental Medicine*, 1969, 129:1307–1326.

⁸ Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. II. Development of natural immunity. *Journal of Experimental Medicine*, 1969, 129:1327–1348.

⁹ PBAC (November 2013) Public summary document: multicomponent meningococcal group B vaccine, 0.5mL, injection, prefilled syringe, Bexsero.

¹⁰ PBAC (November 2010) Public summary document: Haemophilus influenzae type b and group C meningococcal polysaccharide conjugate vaccine, commentary on the major submission.

Table 3: Proportion of subjects with rSBA-Men titres $\geq 1:8$ (ATP immunogenicity cohort)

Trial ID	MenACWY-TT n/N (%)	MenC n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
MenACWY-TT clinical trials				
Serogroup A				
MenACWY-TT-013 <i>Pre-vaccination</i> 1 month post vaccination	19/37 (51.4) 42/42 (100)	7/37 (18.9) 14/39 (35.9)	2.73 (1.81, 4.12)*	64.10 (48.86, 79.34)*
MenACWY-TT-027 <i>Pre-vaccination</i> 1 month post vaccination	81/191 (42.4) 222/222 (100)	26/65 (40.0) 22/63 (34.9)	2.84 (2.03, 3.96)*	65.08 (53.37, 76.79)*
MenACWY-TT-039 # <i>Pre-vaccination</i> 1 month post vaccination	77/171 (45) 353/354 (99.7)	18/53 (34.0) 23/51 (45.1)	2.21 (1.63, 2.99)*	54.62 (40.95, 68.29)*
MenACWY-TT-040 <i>Pre-vaccination</i> 1 month post vaccination	32/77 (41.6) 180/183 (98.4)	18/46 (39.1) 43/100 (43.0)	2.29 (1.82, 2.87)*	55.36 (45.48, 65.24)*
Serogroup C				
MenACWY-TT-013 <i>Pre-vaccination</i> 1 month post vaccination	3/42 (7.1) 42/42 (100)	4/45 (8.9) 45/46 (97.8)	1.02 (0.96, 1.09)	2.17 (-3.79, 8.13)
MenACWY-TT-027 <i>Pre-vaccination</i> 1 month post vaccination	80/203 (39.4) 220/220 (100)	19/61 (31.1) 67/68 (98.5)	1.02 (0.98, 1.06)	1.47 (-2.03, 4.97)
MenACWY-TT-039 # <i>Pre-vaccination</i> 1 month post vaccination	77/171 (45.0) 353/354 (99.7)	13/60 (21.7) 118/121 (97.5)	1.02 (0.99, 1.05)	2.20 (-0.63, 5.02)
MenACWY-TT-040 <i>Pre-vaccination</i> 1 month post vaccination	25/91 (27.5) 178/183 (97.3)	11/54 (20.4) 112/114 (98.2)	0.99 (0.96, 1.02)	-0.98 (-4.35, 2.40)
Serogroup W₁₃₅				
MenACWY-TT-013 <i>Pre-vaccination</i> 1 month post vaccination	15/42 (35.7) 43/43 (100)	14/45 (31.3) 15/45 (33.3)	2.93 (1.95, 4.41)*	66.67 (52.65, 80.68)*
MenACWY-TT-027 <i>Pre-vaccination</i> 1 month post vaccination	59/208 (28.4) 222/222 (100)	24/26 (38.7) 27/63 (42.9)	2.32 (1.75, 3.08)*	57.14 (45.00, 69.29)*
MenACWY-TT-039 # <i>Pre-vaccination</i> 1 month post vaccination	81/177 (45.8) 354/354 (100)	30/61 (49.2) 29/58 (50.0)	2.00 (1.55, 2.58)*	50.00 (37.24, 62.76)*
MenACWY-TT-040 <i>Pre-vaccination</i> 1 month post vaccination	42/84 (50) 183/186 (98.4)	22/55 (40) 41/112 (36.6)	2.69 (2.10, 3.43)*	61.78 (52.68, 70.88)*
Serogroup Y				
MenACWY-TT-013 <i>Pre-vaccination</i> 1 month post vaccination	24/41 (58.5) 42/42 (100)	20/45 (44.4) 21/45 (46.7)	2.11 (1.55, 2.88)*	53.33 (38.56, 68.10)*
MenACWY-TT-027 <i>Pre-vaccination</i> 1 month post vaccination	115/208 (55.3) 222/222 (100)	41/67 (61.2) 49/66 (74.2)	1.35 (1.17, 1.56)*	25.76 (15.22, 36.29)*
MenACWY-TT-039 # <i>Pre-vaccination</i> 1 month post vaccination	112/181 (61.9) 354/354 (100)	34/62 (54.8) 32/59 (54.2)	1.84 (1.46, 2.33)*	45.76 (33.15, 58.38)*
MenACWY-TT-040				

Trial ID	MenACWY-TT n/N (%)	MenC n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
<i>Pre-vaccination</i> 1 month post vaccination	53/87 (60.9) 180/185 (97.3)	30/55 (54.5) 71/110 (64.5)	1.51 (1.31, 1.73)*	32.75 (23.51, 41.99)*
Trial ID	Hib-MenC + MMR n/N (%)	MenC + Hib + MMR n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
Hib-MenC clinical trial				
Hib-MenC-016 <i>Pre-vaccination</i> 1 month post vaccination	37/255 (14.5) 280/281 (99.6)	7/83 (8.4) 98/98 (100)	1.00 (0.98, 1.02)	-0.36 (-1.99, 1.28)

CI: confidence interval; Hib: monovalent haemophilus influenza type B vaccine; Hib-MenC: haemophilus influenza type B & meningococcal C vaccine; MenC: monovalent meningococcal C vaccine; MMR: measles, mumps & rubella vaccine; MenACWY-TT: Meningococcal serogroups ACWY tetanus toxoid vaccine; MenC: monovalent meningococcal C vaccine; n: number of participants with event; N: total participants in group

#Outcome measurements taken at day 42 in trial MenACWY-TT-039

*Statistically significant result

Source: Table 2.5-3, p76 of the submission and Table 19, p.101 of MenACWY-TT-013 CSR; Table 22, p.86 of MenACWY-TT-027 CSR; Table 20, p.101 of MenACWY-TT-039 CSR; Table 21, p.105 of MenACWY-TT-040 CSR and Table 2.5-10, p84 of the submission; Table 16, p.65 of Hib-MenC CSR.

- 6.18 The submission claimed that the three non-inferiority trials (MenACWY-TT-027, 039 and 040) all demonstrated non-inferiority of the MenACWY-TT vaccine compared to the monovalent MenC vaccine since the lower limit of the 95% confidence interval was above the pre-specified non-inferiority limit of -10% (-15% in MenACWY-TT-027) in the trials (p75 of the submission). This is reasonable.
- 6.19 The submission claimed that the MenACWY-TT vaccine elicited a protective bactericidal antibody response against the four serogroups in each of the MenACWY TT trials (p75 of the submission). Based on the relative risks, the MenACWY TT vaccine may be more beneficial at protecting against serogroups A and W than it is against serogroup Y.
- 6.20 The submission also claimed that the Hib-MenC + MMR arm was non-inferior to the MenC + Hib + MMR arm in terms of rSBA \geq 1:8 titre against meningococcal C (p83 to 84 of the submission). The concomitant administration of the Hib and MMR vaccines may, but is unlikely to, affect the immunogenicity results against MenC.
- 6.21 Table 4 presents the results of the persistence studies conducted by the submission.

Table 4: Proportion of subjects with rSBA-Men titres $\geq 1:8$ during the persistence stage (ATP immunogenicity cohort)

Year	Trial ID	MenACWY-TT n/N (%)	MenC n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
MenACWY-TT clinical trials					
Serogroup A					
1	Study 014#	39/40 (97.5)	11/36 (30.6)	3.19 (1.95, 5.23)*	0.67 (0.51, 0.83)*
	Study 028	210/212 (99.1)	16/49 (32.7)	3.03 (2.03, 4.54)*	0.66 (0.53, 0.80)*
2	Study 029	188/190 (98.9)	30/45 (66.7)	1.48 (1.21, 1.83)*	0.32 (0.18, 0.46)*
3	Study 030	168/170 (98.8)	27/32 (84.4)	1.17 (1.01, 1.36)*	0.14 (0.02, 0.27)*
4	Study 031	133/136 (97.8)	21/24 (87.5)	1.12 (0.96, 1.30)	0.10 (-0.03, 0.24)
5	Study 032 [^]	36/49 (73.5)	0/11 (0)	17.52 (1.16, 265.61)*	0.73 (0.57, 0.90)*
Serogroup C					
1	Study 014#	36/39 (92.3)	24/40 (60.0)	1.54 (1.18, 2.01)*	0.32 (0.15, 0.50)*
	Study 028	203/207 (98.1)	50/63 (79.4)	1.24 (1.09, 1.40)*	0.19 (0.09, 0.29)*
2	Study 029	185/197 (93.9)	38/52 (73.1)	1.29 (1.09, 1.52)*	0.21 (0.08, 0.33)*
3	Study 030	158/174 (90.8)	36/37 (97.3)	0.93 (0.87, 1.00)	-0.06 (-0.13, 0.00)
4	Study 031	125/137 (91.2)	27/30 (90.0)	1.01 (0.89, 1.15)	0.01 (-0.10, 0.13)
5	Study 032 [^]	38/49 (77.6)	7/11 (63.6)	1.22 (0.76, 1.95)	0.14 (-0.17, 0.45)
Serogroup W₁₃₅					
1	Study 014#	39/40 (97.5)	17/41 (41.5)	2.35 (1.63, 3.39)*	0.56 (0.40, 0.72)*
	Study 028	216/216 (100)	38/64 (59.4)	1.68 (1.38, 2.06)*	0.41 (0.29, 0.53)*
2	Study 029	198/199 (99.5)	24/44 (54.5)	1.82 (1.39, 2.39)*	0.45 (0.30, 0.60)*
3	Study 030	172/174 (98.9)	24/33 (72.7)	1.36 (1.10, 1.68)*	0.26 (0.11, 0.41)*
4	Study 031	133/138 (96.4)	18/27 (66.7)	1.45 (1.11, 1.89)*	0.30 (0.12, 0.48)*
5	Study 032 [^]	17/49 (34.7)	2/11 (18.2)	1.91 (0.51, 7.08)	0.17 (-0.10, 0.43)
Serogroup Y					
1	Study 014#	39/40 (97.5)	30/40 (75.0)	1.30 (1.08, 1.57)*	0.22 (0.08, 0.37)*
	Study 028	214/216 (99.1)	42/66 (63.6)	1.56 (1.30, 1.87)*	0.41 (0.29, 0.53)*
2	Study 029	193/197 (98.0)	37/50 (74.0)	1.32 (1.12, 1.56)*	0.45 (0.30, 0.60)*
3	Study 030	174/177 (98.3)	33/36 (91.7)	1.07 (0.97, 1.19)	0.26 (0.11, 0.41)*
4	Study 031	134/138 (97.1)	23/29 (79.3)	1.22 (1.01, 1.48)*	0.30 (0.12, 0.48)*
5	Study 032 [^]	21/49 (42.9)	2/11 (18.2)	2.36 (0.65, 8.60)	0.17 (-0.10, 0.43)
Hib-MenC clinical trial					
Year	Trial ID	Hib-MenC + MMR n/N (%)	MenC + Hib + MMR n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
1	Hib-MenC-017	216/249 (86.7)	68/89 (76.4)	1.14 (1.00, 1.29)*	0.1034 (0.0057, 0.2012)*
2	Hib-MenC-018	164/235 (69.8)	52/86 (60.5)	1.15 (0.95, 1.40)	0.0932 (-0.0256, 0.2121)
3	Hib-MenC-019	145/266 (64.2)	41/77 (53.2)	1.02 (0.81, 1.30)	0.0126 (-0.1138, 0.1391)
4 ^{^^}	Hib-MenC-020	26/208 (12.5)	9/73 (12.3)	1.01 (0.50, 2.06)	0.0017 (-0.0861, 0.0895)
5 ^{^^}	Hib-MenC-020	37/195 (19.0)	17/68 (25.0)	0.76 (0.46, 1.26)	-0.0603 (-0.1770, 0.0565)

CI: confidence interval; Hib: monovalent haemophilus influenza type B vaccine; Hib-MenC: haemophilus influenza type B & meningococcal C vaccine; MenC: monovalent meningococcal C vaccine; MMR: measles, mumps & rubella vaccine; MenACWY-TT: Meningococcal serogroups ACWY tetanus toxoid vaccine; MenC: monovalent meningococcal C vaccine; n: number of participants with event; N: total participants in group

Month 15

[^] Serological assays for Year 5 data in Study 032 were performed at the Health Protection Agency (HPA) in the United Kingdom where titres were expressed as the reciprocal of the last dilution resulting in at least 50% inhibition (rather than GSK Biologicals' central laboratory where titres were expressed as the reciprocal of the dilution resulting in 50% inhibition).

^{^^} Serological assays for Year 4 and Year 5 data in Study 016 were performed at Public Health England (PHE) where titres were expressed as the reciprocal of the last dilution resulting in at least 50% inhibition (rather than GSK Biologicals' central laboratory where titres were expressed as the reciprocal of the dilution resulting in 50% inhibition).

* P < 0.05

Source: Table 2.5.9, p82 and Table 2.5-12, p85 of the submission

- 6.22 The proportion of subjects with rSBA antibody titres $\geq 1:8$ for Years 1 to 5 were higher for each of the four meningococcal serogroups with the MenACWY-TT vaccine compared to the MenC vaccine (p79 of the submission). For each of the serogroups, the proportion of subjects with rSBA antibody titres $\geq 1:8$ in the MenACWY-TT arm remained relatively stable over Years 1 to 4, while the proportion of subjects with rSBA antibody titres $\geq 1:8$ in the MenC arm increased (p79 of the submission). The high rate of withdrawal may bias these results.
- 6.23 The proportion of subjects with rSBA-MenC titres $\geq 1:8$ was higher with the Hib-MenC + MMR arm compared with the MenC + Hib + MMR arm for Year 1 to Year 4. The proportion of subjects with rSBA-MenC titres $\geq 1:8$ declined over time in both arms (p85 of the submission). The concomitant administration of the Hib and MMR vaccines may, but is unlikely to, affect the immunogenicity results against MenC.
- 6.24 Table 5 presents the results of the key indirect comparison conducted by the submission.

Table 5: Summary of results of the indirect comparison for rSBA-MenC $\geq 1:8$ at one month

Trial type or estimate	Trial ID	n with event/N (%)	MenC n with event/N (%)	Treatment effect (RR)	Treatment effect (RD)
MenACWY-TT vs. MenC trials	MenACWY-TT-013	42/42 (100)	45/46 (97.8)	1.02 (0.96, 1.09)	2.17 (-3.79, 8.13)
	MenACWY-TT-027	220/220 (100)	67/68 (98.5)	1.02 (0.98, 1.06)	1.47 (-2.03, 4.97)
	MenACWY-TT-039	353/354 (99.7)	118/121 (97.5)	1.02 (0.99, 1.05)	2.20 (-0.63, 5.02)
	MenACWY-TT-040	178/183 (97.3)	112/114 (98.2)	0.99 (0.96, 1.02)	-0.98 (-4.35, 2.40)
	Pooled	793/799 (99.2)	342/349 (98.0)	1.01 (0.99, 1.03)	1.15 (-0.61, 2.91)
Hib-MenC vs. MenC (+Hib + MMR) trial	Hib-MenC-016	280/281 (99.6)	98/98 (100)	1.00 (0.98, 1.02)	-0.36 (-1.99, 1.28)
Indirect estimate of effect adjusted for MenC	–	–	–	1.01 (0.99, 1.04)	1.50 (-0.90, 3.91)

CI: confidence interval; n = number of participants with event; N = total number of participants in group.
Source: Table 2.6-3, p101 of the submission.

- 6.25 The submission claimed that there was no statistically significant difference between the MenACWY-TT vaccine and the Hib-MenC vaccine (via the MenC vaccine as the common reference) for rSBA-MenC $\geq 1:8$ at one month with an indirect relative risk of 1.01 (95% CI: 0.99; 1.04), although numerically the relative risk slightly favoured the MenACWY-TT vaccine. Therefore, the submission considered MenACWY-TT to be non-inferior to the Hib-MenC vaccine in terms of rSBA-MenC $\geq 1:8$ at one month (p101 of the submission).
- 6.26 The submission also claimed that the MenACWY-TT vaccine was associated with a higher proportion of subjects achieving rSBA-MenC $\geq 1:128$ titres (relative risk =

1.21, 95% CI: 1.04, 1.41) and GMT ratios (2.51, 95% CI: 1.63, 3.88) compared with the Hib-MenC vaccine (p102 of the submission).

- 6.27 Conducting an indirect comparison of non-inferiority trials introduces uncertainty as finding a non-statistically significant result does not mean that the vaccines are non-inferior.
- 6.28 There was a higher proportion of subjects with rSBA-Men titres $\geq 1:8$ in MenACWY-TT clinical trials pre-vaccination (7.1 – 45.0%) compared to the Hib-MenC trials pre-vaccination (8.4 - 14.5%). However, the proportion of subjects achieving rSBA-MenC $\geq 1:8$ titre with the common reference (the MenC vaccine) was consistent across the trials (98.0% vs. 100%).
- 6.29 The submission did not conduct an indirect comparison using the persistence data.

Comparative harms

- 6.30 Table 6 presents a summary of the safety results across the MenACWY-TT trials.

Table 6: Summary of adverse events in the randomised trials

Trial ID	MenACWY-TT n/N (%)	MenC n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
Any symptoms at day 4				
MenACWY-TT-013#	39/48 (81.3)	37/48 (77.1)	1.05 (0.86, 1.29)	0.04 (-0.12, 0.20)
MenACWY-TT-027	186/229 (81.2)	63/75 (84.0)	0.97 (0.86, 1.09)	-0.03 (-0.12, 0.07)
MenACWY-TT-039	306/374 (81.8)	108/125 (86.4)	0.95 (0.87, 1.03)	-0.05 (-0.12, 0.03)
MenACWY-TT-040	147/220 (66.8)	69/127 (54.3)	1.23 (1.02, 1.48)*	0.12 (0.02, 0.23)*
Severity Grade 3 at day 4 any symptoms				
MenACWY-TT-013#	3/48 (6.3)	3/48 (6.3)	1.00 (0.21, 4.71)	0.00 (-0.10, 0.10)
MenACWY-TT-027	22/229 (9.6)	4/75 (5.3)	1.80 (0.64, 5.06)	0.04 (-0.02, 0.11)
MenACWY-TT-039	31/374 (8.3)	2/125 (1.6)	5.18 (1.26, 21.34)*	0.07 (0.03, 0.10)*
MenACWY-TT-040	15/220 (6.8)	4/127 (3.1)	2.16 (0.73, 6.38)	0.04 (-0.01, 0.08)
Treatment related AEs at day 4 any symptoms				
MenACWY-TT-013#	35/48 (72.9)	31/48 (64.6)	1.13 (0.86, 1.48)	0.02 (-0.05, 0.10)
MenACWY-TT-027	176/229 (76.9)	61/75 (81.3)	0.94 (0.83, 1.08)	-0.04 (-0.15, 0.06)
MenACWY-TT-039	291/374 (77.8)	102/125 (81.6)	0.95 (0.86, 1.05)	-0.04 (-0.12, 0.04)
MenACWY-TT-040	123/220 (55.9)	58/127 (45.7)	1.22 (0.98, 1.53)	0.10 (-0.01, 0.21)
Severity Grade 3 local symptoms at day 4				
MenACWY-TT-013#	2/48 (4.2)	0/48 (0)	5.00 (0.25, 101.48)	0.04 (-0.03, 0.11)
MenACWY-TT-027	11/229 (4.8)	1/75 (1.3)	3.60 (0.47, 27.44)	0.03 (-0.00, 0.07)
MenACWY-TT-039	26/374 (7.0)	1/125 (0.8)	8.69 (1.19, 63.38)*	0.06 (0.03, 0.09)*
MenACWY-TT-040	9/220 (4.1)	3/127 (2.4)	1.73 (0.48, 6.28)	0.02 (-0.02, 0.05)
Severity Grade 3 general symptoms at day 4				
Study 013#	1/48 (2.1)	3/48 (6.3)	0.33 (0.04, 3.09)	-0.04 (-0.12, 0.04)
Study 027	11/229 (4.8)	3/75 (4.0)	1.20 (0.34, 4.19)	0.01 (-0.04, 0.06)
Study 039	6/374 (1.6)	1/125 (0.8)	2.01 (0.24, 16.50)	0.01 (-0.01, 0.03)
Study 040	7/220 (3.2)	1/127 (0.8)	4.04 (0.50, 32.47)	0.02 (-0.00, 0.05)
Severity Grade 3 unsolicited AEs at day 31				
Study 013	0/48 (0)	0/48 (0)	Not estimable	0.00 (-0.04, 0.04)
Study 027	26/229 (11.4)	11/75 (14.7)	0.77 (0.40, 1.49)	-0.03 (-0.12, 0.06)
Study 039 #	38/374 (10.2)	12/125 (9.6)	1.06 (0.57, 1.96)	0.01 (-0.05, 0.07)
Study 040	5/220 (2.3)	0/127 (0)	6.37 (0.36, 114.28)	0.02 (-0.00, 0.05)

AE: adverse event; CI: confidence interval; n: number of participants reporting data; MenACWY-TT: Meningococcal serogroups ACWY tetanus toxoid vaccine; MenC: monovalent meningococcal C vaccine; N: total participants in group; RD: risk difference; RR: relative risk. # Adverse events were reported up to day 8 after vaccine administration for trial MenACWY-TT-013

*statistically significant result

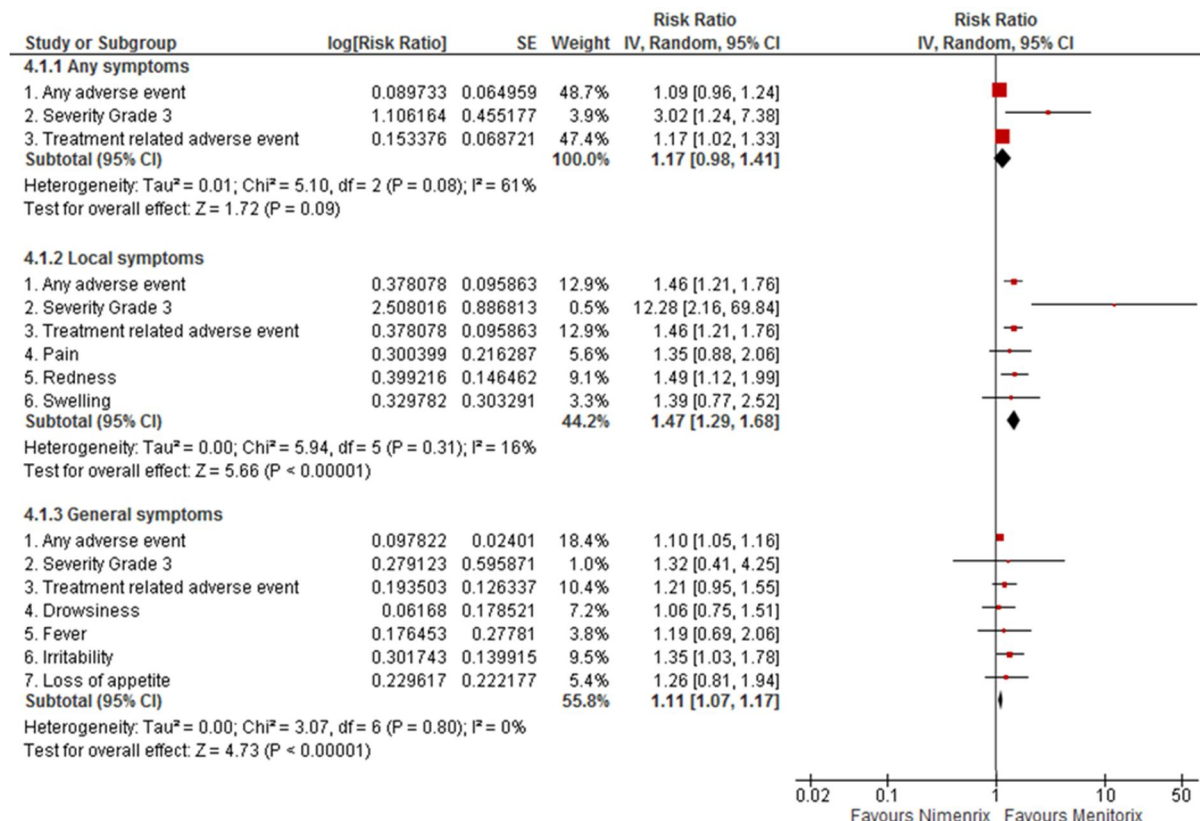
Source: Table 2.5-14 p87, Table 2.5-15, p87-88 and Table 2.5-16, p89 and Table 2.5.17, p90 of the submission

- 6.31 The most commonly reported local symptoms were redness, pain and swelling. The most commonly reported general symptoms were drowsiness, fever and irritability. The most commonly reported unsolicited treatment-related AE was diarrhea.
- 6.32 The submission did not report whether any febrile seizures occurred.
- 6.33 The submission claimed that vaccination with the MenACWY-TT vaccine was well tolerated across the MenACWY-TT trials and that the overall safety profile was similar to that reported in the MenC arms in terms of frequencies, types and severity of events, with limited statistically significant differences occurring across treatment

groups (p86 of the submission). There were some measures where there were statistically significant differences.

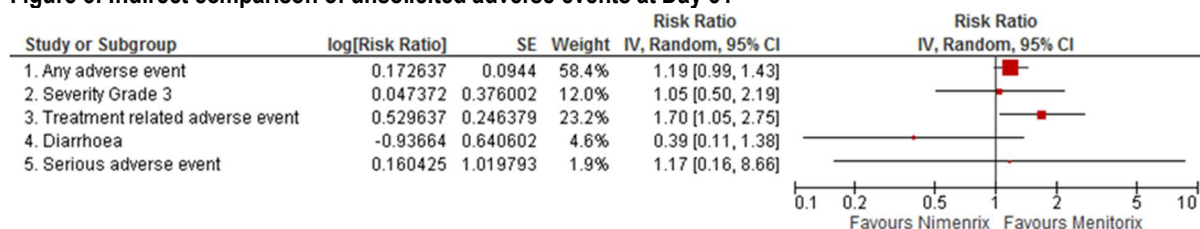
6.34 The indirect comparison of any symptom (local and general) adverse events at day four and unsolicited adverse events at day 31 is presented in Figure 2 and Figure 3.

Figure 2: Indirect comparison of reactogenicity at Day 4



Source: Figure 2.6-24, p115 of the submission.

Figure 3: Indirect comparison of unsolicited adverse events at Day 31



Source: Figure 2.6-25, p116 of the submission.

6.35 The submission claimed that:

- any symptom (local and general symptoms) adverse events were similar across the MenACWY-TT vaccine and the Hib-MenC vaccine (p115 of the submission).

- There were more severity grade 3 adverse events associated with the MenACWY-TT vaccine compared with the Hib-MenC vaccine (p115 of the submission).
- Treatment-related adverse events were statistically significantly more likely to occur with the MenACWY-TT vaccine compared with the Hib-MenC vaccine as shown by the indirect relative risk of 1.70 (95% CI: 1.05, 2.75); $p = 0.03$. However, when comparing the numerical percentages of the individual vaccines there was substantial variation in the MenC common reference (MenACWY-TT 10.6% vs. MenC 7.2% and Hib-MenC 29.3% vs. MenC 43.1%) (p116 of the submission).

6.36 In the comparator trial (trial Hib-MenC-016) subjects were co-administered the MMR vaccine and received Hib vaccination via a combined vaccine (Hib-MenC vaccine) or via separate vaccines (Hib vaccine + MenC vaccine). This may bias the safety outcomes in favour of the MenACWY-TT vaccine.

Benefits/harms

6.37 The naïve indirect comparison presented in the submission did not allow for a quantitative comparison of the benefits and harms of the MenACWY-TT vaccine and the Hib-MenC vaccine. Accordingly, a benefits/harms table has not been presented.

Clinical claim

6.38 The submission described the MenACWY-TT vaccine as non-inferior in terms of effectiveness (based on rSBA-MenC $\geq 1:8$ at one month) and non-inferior in terms of safety compared to the Hib-MenC vaccine (p126 of the submission).

6.39 This claim should be considered with caution.

- The indirect comparison found that the MenACWY-TT vaccine elicited an immune response to serogroup C (rSBA-MenC $\geq 1:8$) that was comparable with the Hib-Men C vaccine. However, the trials included in the submission were all non-inferiority trials. Conducting an indirect comparison of non-inferiority trials introduces uncertainty as the finding of a non-statistically significant result does not mean that the vaccines are non-inferior.
- All of the trials were open-label, which increases the risk of bias in the safety results as the subjects were aware of the vaccines received. Furthermore, in the comparator trial (trial Hib-MenC-016) subjects were co-administered the MMR vaccine and received Hib vaccination via a combined vaccine (Hib-MenC vaccine) or via separate vaccines (Hib vaccine + MenC vaccine). This may bias the safety outcomes in favour of the MenACWY-TT vaccine.

6.40 The PBAC accepted the ATAGI advice that the clinical claim of non-inferiority to the MenC component of the Hib-MenC vaccine based on rSBA-MenC protection at one

month and the added benefit of serogroup A, W135 and Y antibody protection, was reasonable.

- 6.41 The PBAC accepted the ATAGI advice that overall, MenACWY-TT had a similar safety profile to the comparator.

Economic analysis

- 6.42 The submission presented a cost-minimisation analysis of the MenACWY-TT vaccine compared to the Hib-MenC vaccine.

- 6.43 The equi-effective doses were estimated as:

- 5 µg of meningococcal serogroup C component from the MenACWY-TT (Nimenrix) conjugate vaccine, and
- 5 µg of meningococcal serogroup C component of the Hib-MenC (Menitorix) conjugate vaccine.

- 6.44 The equi-effective doses are reasonable if the PBAC accepts the claim that the meningococcal serogroup C component of the MenACWY-TT conjugate vaccine is non-inferior to the meningococcal serogroup C component of the Hib-MenC conjugate vaccine.

- 6.45 The submission proposed the price of the MenACWY-TT vaccine to be equal to the assumed price of the meningococcal C component of the Hib-MenC vaccine (p130 of the submission).

- 6.46 The submission suggested that a monovalent Hib vaccine will also need to be listed on the NIP (p128 of the submission). There is no monovalent Hib vaccine currently supplied in Australia (p19 of the ATAGI pre-submission advice 2017).

- 6.47 The price of a monovalent Hib vaccine for infants aged 18 months was proposed to be the same with the Hib component in the Hib-MenC vaccine. Consequently, the submission claimed that listing the MenACWY-TT vaccine will be cost-neutral (p133 of the submission).

- 6.48 There will be additional costs to the NIP if:

- The monovalent Hib vaccine is not listed on the NIP when the MenACWY-TT is listed on the NIP, and the Hib-MenC vaccine is used as a Hib booster (p19 of the ATAGI pre-submission advice 2017), or
- The monovalent Hib vaccine is listed on the NIP at a higher price than the Hib component of the Hib-MenC vaccine.

Drug cost/patient/course

6.49 \$ [REDACTED], assuming one dose per patient. The price for the monovalent Hib vaccine is unknown.

Estimated PBS usage & financial implications

6.50 This submission was not considered by DUSC.

6.51 The submission employed an epidemiological approach to estimate NIP usage and financial implications. Estimates of the number of eligible target population were taken from the Australian Bureau of Statistics population estimates and the uptake rate of the proposed program was taken from the current Hib-MenC vaccine coverage rate. This is reasonable. The submission claimed that if a monovalent Hib vaccine is also listed on the NIP, then the number of eligible patients and uptake rate of the monovalent Hib vaccine would be the same as the MenACWY-TT vaccine. The uptake rate may differ as the monovalent Hib vaccine is proposed to be implemented at a different time (i.e. at age 18 months).

6.52 Table 7 summarises the estimated use and financial implications with listing MenACWY-TT + a monovalent Hib vaccine on the NIP.

Table 7: Estimated use and financial implications

	Year 1 (Aug-Dec)	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Estimated extent of use							
Number of patients treated	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number of scripts dispensed ^a	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated financial implications of MenACWY-TT vaccine^b							
Cost to NIP	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Copayments	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Estimated financial implications of monovalent Hib vaccine							
Cost to NIP	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Copayments	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Estimated financial implications of removing the MenC component of the Hib-MenC vaccine							
Cost to NIP	-\$ [REDACTED]	-\$ [REDACTED]	\$ [REDACTED]	-\$ [REDACTED]	\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Copayments	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Estimated financial implications of removing the Hib component of the Hib-MenC vaccine							
Cost to NIP	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Copayments	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Net financial implications							
Net cost to NIP	\$0	\$0	\$0	\$0	\$0	\$0	\$0

^a Assuming a single use of vaccine for infants aged 12 months as estimated by the submission.

^b Assuming the price of the MenACWY-TT vaccine is \$ [REDACTED].

Source: Table 4.3-1 and Table 4.3-2, p139 in the submission and Table 4.4-1, p141 in the submission.

Hib = Haemophilus influenzae type b

6.53 The estimated financial implications for the NIP are uncertain. There are three scenarios of budget impact that the PBAC may wish to consider:

- The monovalent Hib vaccine is not supplied in Australia when the MenACWY-TT is approved and Hib-MenC is used as a Hib booster (p19 of the ATAGI pre-submission advice 2017). In this case, there will be additional costs of using Hib-MenC to the NIP.
- The monovalent Hib vaccine is supplied in Australia at the price of the Hib component of the Hib-MenC vaccine. In this case, listing the MenACWY-TT vaccine will be cost-neutral to the NIP.
- The monovalent Hib vaccine is supplied in Australia but its price is unknown: In this case, the financial implication of listing the MenACWY-TT vaccine for the NIP is unknown.

Quality Use of Medicines

6.54 The submission noted that educational activities should be undertaken to inform the change of the NIP schedule. Given the potential for confusion between the proposed MenACWY-TT and the current Hib-MenC vaccine, extensive health professional and parent education programs should be undertaken. The submission did not propose a post-marketing surveillance study. Given the lack of pre-market data on vaccine efficacy and the limited pre-market vaccine data on safety, a longitudinal post marketing study is warranted. The need for post-marketing surveillance was also noted by ATAGI, who considered enhanced safety surveillance of 12-month old children receiving MenACWY-TT to be essential (p2 and p22 of the ATAGI pre-submission advice 2017). Post marketing studies on impact of the proposed vaccine on nasopharyngeal carriage could also be considered.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

- 7.1 The PBAC recommended that meningococcal polysaccharide serogroups A, C, W135 and Y conjugate vaccine (MenACWY-TT) vaccine be a designated vaccine for the purposes of the *National Health Act 1953* for the prevention of invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* serogroups A, C, W135, and Y (MenA, MenC, MenW135 and MenY, respectively) in infants.
- 7.2 In line with the ATAGI advice, the PBAC recommended that the administration of the MenACWY-TT vaccine occur at around 12 months of age and further that administration of the Hib containing vaccine be moved to around 18 months of age.
- 7.3 The PBAC considered the MenACWY-TT vaccine would be acceptably cost-effective if subsidised on a cost-minimisation basis with the MenC component of the Hib-MenC vaccine (Menitorix).
- 7.4 The PBAC accepted the ATAGI advice that the clinical claim of non-inferiority to the MenC component of the Hib-MenC vaccine based on rSBA-MenC protection at one

month and the added benefit of serogroup A, W135 and Y antibody protection, was reasonable.

- 7.5 The PBAC accepted the ATAGI advice that overall, MenACWY-TT had a similar safety profile to the comparator.
- 7.6 The PBAC advised that the equi-effective doses are MenACWY-TT 1 x 5 µg dose and the MenC component of the Hib-MenC vaccine 1 x 5 µg dose.
- 7.7 The PBAC further noted the ATAGI's advice –
- That the 12 month of age Hib vaccine would be displaced to 18 months of age;
 - That there is a need for educational activities to inform the public and health professionals of the change to the NIP schedule; and
 - That post market studies and surveillance should be undertaken.
- 7.8 The PBAC advised the Minister that the financial implications of implementing this recommendation will be dependent on the availability of a monovalent Hib vaccine at a price commensurate with that of the Hib component of the Hib-MenC vaccine, together with any additional costs associated with adding an extra vaccination at 18 months, and the associated educational, post marketing and surveillance studies. The PBAC noted the advice from the Office of Health Protection that work on securing a supply of monovalent Hib vaccine is well progressed.
- 7.9 The PBAC noted that this submission is not eligible for independent review as independent review is only relevant to PBS listing.

Outcome:

Recommended

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

Pfizer Australia welcomes the PBAC recommendation to list Nimenrix on the NIP for infants. Nimenrix is a meningococcal polysaccharide conjugate vaccine (MenACWY-TT) for the prevention of invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* serogroups A, C, W135, and Y. Infants will receive protection against meningococcal serogroups W135, Y and A in addition to serogroup C from a single vaccine dose.