Australian Government

Department of Health

**Australian Technical Advisory Group on Immunisation**

# Public consultation on changes to the recommended use of meningococcal and *Haemophilus influenzae* type B vaccines

The Australian Technical Advisory Group on Immunisation (ATAGI) is consulting with stakeholders on proposed changes to the meningococcal vaccination recommendations for inclusion in *The Australian Immunisation Handbook*, with an intention to submit the recommendations to the National Health and Medical Research Council (NHMRC) for its approval under section 14A of the *National Health and Medical Research Council Act 1992.*

This draft includes new recommendations and the rationale for the proposed changes.

You are invited to make a submission on the draft recommendations by 6 May 2018.

In particular, ATAGI is seeking comments on the following:

- Are there additional potential benefits, harms or unintended consequences which could arise from the proposed changes to the use of meningococcal vaccines, not already outlined, and how likely are they to occur?
- Are there additional clinical or implementation considerations which need to be outlined?

Should you require additional information please contact ATAGI Secretariat on atagi.secretariat@health.gov.au.

## Summary

The Australian Technical Advisory Group on Immunisation (ATAGI), which advises the Australian Government on clinical recommendations for vaccinations, is proposing changes to the recommendations for use of meningococcal vaccines.

The proposed changes reflect the current best clinical practice to prevent invasive meningococcal disease and will be published in *The Australian Immunisation Handbook* online (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10-updates).

Meningococcal disease is a serious infection caused by meningococcal bacteria. In Australia, five subgroups (or serogroups) of meningococcal bacteria are found. ATAGI has been monitoring the epidemiology of meningococcal disease in Australia and observed that:

| | |
|---|---|
| subgroup A | is currently extremely rare, but has historically been significant |
| subgroup B | has continued to be an important cause of disease for the last 10 years or more |
| subgroup C | was more common around 15 years ago, but was controlled through the introduction of a free meningococcal C vaccination on the National Immunisation Program since 2003 |
| subgroup W | is a new strain which has become more common in Australia |
| subgroup Y | was previously rare, but is now also becoming more common |

Several state and territory governments have introduced vaccination programs for adolescents, including through schools, particularly for protection against the emergence of meningococcal W and Y.

Given changes to the epidemiology of meningococcal disease and recognising the new programs available through states, ATAGI has reviewed the meningococcal chapter of *The Australian Immunisation Handbook*.

## Rationale

The Therapeutic Goods Administration has recently registered:

- Trumenba for protection against meningococcal B;
- Menveo for use among infants for protection against meningococcal A, C, W and Y.

There is no single meningococcal vaccine in Australia which can protect against all 5 subgroups. Vaccines are available for protection against:

- meningococcal B – the meningococcal B vaccines: Trumenba and Bexsero
- meningococcal A, C, W and Y all at the same time – the meningococcal ACWY vaccines: Menactra, Menveo, Nimenrix
- meningococcal C only – NeisVacC (subgroup C alone) and Menitorix (combination that also protects against *Haemophilus influenzae* type b).

The review of the meningococcal chapter has prompted a review of the *Haemophilus influenzae* type B chapter recommendations, as meningococcal C vaccination on the National Immunisation Program is currently given as a combination vaccine with *Haemophilus influenzae* type B.

The vaccines are able to be used in different age groups and in different dosing schedules. A full list of vaccines and their details is provided in Attachment 1.

**Recommendations**

**A ATAGI proposes all current recommendations in *The Australian Immunisation Handbook* are revoked with the exception of those relating to meningococcal B and meningococcal ACWY vaccination for people at occupational risk or travellers (refer to Attachment 2).**

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with meningococcal B and meningococcal ACWY vaccines.
2. All children aged 2–23 months (<2 years) are recommended to receive meningococcal ACWY vaccines (according to an age-based dose schedule as shown in Table 1).
    - Children who commence the meningococcal ACWY vaccination schedule before 12 months of age should also receive a dose of meningococcal ACWY vaccine at 12 months of age (refer to Table 1).
3. For people aged ≥2 years, if more than one MenACWY vaccine brand is available, either Nimenrix or Menveo is preferred to Menactra.
4. Adolescents aged 15–19 years are recommended to receive a single dose of meningococcal ACWY vaccine.
5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.
6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive meningococcal ACWY vaccine (Table 1).
8. All Aboriginal and/or Torres Strait Islander infants and children aged 2 months to 4 years (<5 years) are recommended to receive meningococcal B vaccine (Table 2).
9. Infants aged 6–11 months with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1 below) are recommended to receive 3 doses of meningococcal ACWY vaccine (Table 1).

## Table 1: Dose schedule recommendations for immunisation using MenACWY vaccines, by age and vaccine brand, and showing the number of doses required and minimum intervals

| Age at commencement of vaccine course | MenACWY vaccine brand | Without any medical conditions associated with increased risk of meningococcal disease on List 1 | With any specified medical conditions associated with increased risk of meningococcal disease on List 1 |
|---|---|---|---|
| 2*–5 months | Menveo | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age) | 4 doses<br>(8 weeks between doses; 4th dose at 12 months of age or 8 weeks after 3rd dose, whichever is later) |
| 6–11 months | Menveo | 2 doses<br>(2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later) | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age or 8 weeks after 3rd dose, whichever is later) |
| 12–23 months | Menveo | 2 doses<br>(8 weeks between doses) | 2 doses#<br>(8 weeks between doses) |
| | Nimenrix | 1 dose | |
| ≥2 years† | Menveo | 1 dose | 2 doses<br>(8 weeks between doses) |
| | Nimenrix | | |
| | Menactra | | |
| Booster doses for all ages | Any brand | Not required | For those with ongoing increased risk for IMD who completed the primary series at:<br>a) ≤6 years of age: 3 years after completion of primary immunisation schedule, then every 5 years thereafter<br>b) ≥7 years of age: every 5 years after completion of the primary immunisation schedule |

* First dose can be administered at as early as 6 weeks of age.

\# For those with specified medical conditions aged 12–23 months, 2 doses of either Menveo or Nimenrix are required.

† There is no registered upper age limit for use of Menveo®. Although both Menactra® and Nimenrix® are registered for use up to 55 years of age only, either of these brands can be given to people over 55 years of age, as per *The Australian Immunisation Handbook.*

## Table 2: Dose schedule recommendations for immunisation using MenB vaccines, and showing number of doses required and minimum intervals

| Age at commencement of vaccine course | MenB vaccine brand | Without any medical conditions associated with increased risk of meningococcal disease on List 1 | With any specified medical conditions associated with increased meningococcal disease on List 1 |
|---|---|---|---|
| 6 weeks–5 months | Bexsero | 4 doses<br>(8 weeks between doses; 4th dose at 12 months) | 4 doses<br>(8 weeks between doses; 4th dose at 12 months or 8 weeks after 3rd dose, whichever is later) |
| 6–11 months | Bexsero | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later) | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later) |
| 12 months–9 years | Bexsero | 2 doses<br>(8 weeks between doses) | 2 doses<br>(8 weeks between doses) |
| ≥10 years* | Bexsero | 2 doses<br>(8 weeks between doses) | 2 doses<br>(8 weeks between doses) |
| | Trumenba | 2 doses<br>(6 months between doses) | 3 doses<br>(At least 4 weeks between 1st and 2nd doses; 3rd dose at least 4 months after 2nd dose and at least 6 months after 1st dose) |

* Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the primary vaccination course.

**List 1: Specified medical conditions associated with increased risk of meningococcal disease**

- defects in or deficiency of complement components, including factor H, factor D or properdin deficiency
- current or future treatment with eculizumab (a monoclonal antibody directed against complement component C5)
- functional or anatomical asplenia
- HIV infection, regardless of stage of disease or CD4+ count
- haematopoietic stem cell transplant

**Note: This list is unchanged from the conditions specified in the current online chapter of *The Australian Immunisation Handbook***

**C ATAGI proposes that the recommendation for the 4th dose of vaccine for protection against *Haemophilus influenzae* type B currently given at 12 months is revoked.**

**D ATAGI proposes the following changes to the use of *Haemophilus influenzae* type B vaccines in Australia:**

- All children should receive a 4th dose of vaccine for protection against *Haemophilus influenzae* type B at 18 months of age.

## Research evidence

***Recommendations A and B 1-4***

**A ATAGI proposes all current recommendations in *The Australian Immunisation Handbook* are revoked with the exception of those relating to meningococcal B and meningococcal ACWY vaccination for people at occupational risk or travellers (refer to Attachment 2).**

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with meningococcal B and meningococcal ACWY vaccines.
2. All children aged 2–23 months (<2 years) are recommended to receive meningococcal ACWY vaccines (Table 1).
3. For people aged ≥2 years, if more than one MenACWY vaccine brand is available, either Nimenrix or Menveo is preferred to Menactra.
4. Adolescents aged 15–19 years are recommended to receive a single dose of meningococcal ACWY vaccine.

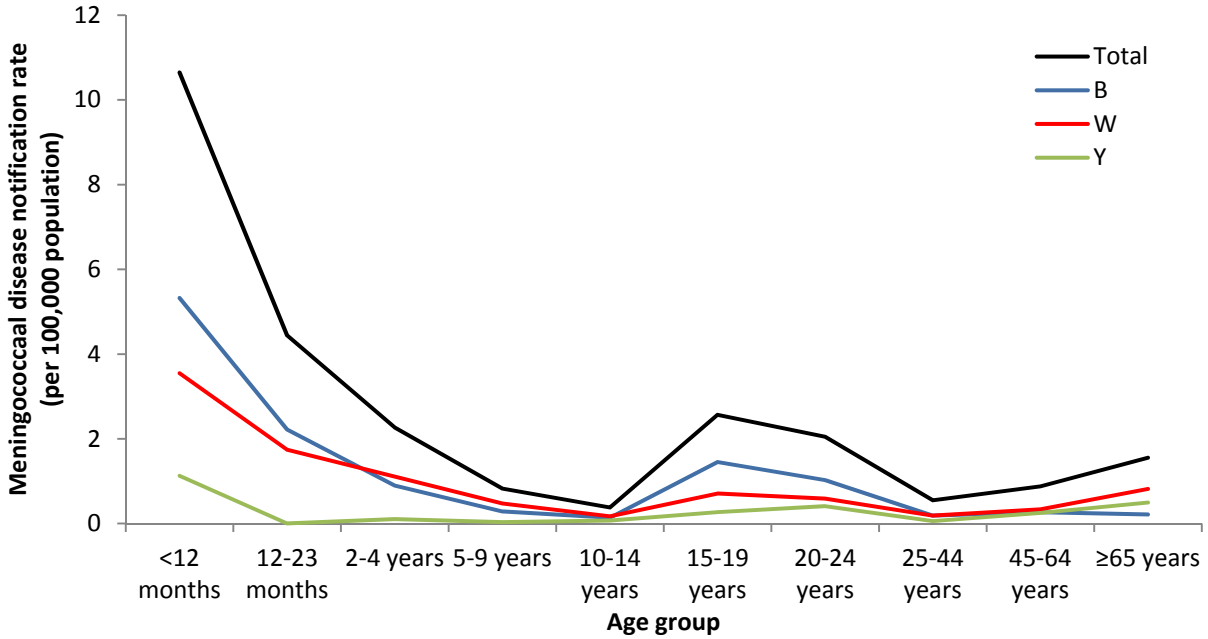
The meningococcal subgroups that cause meningococcal disease have been changing in the last few years. Since 2013, the occurrence of meningococcal W disease has been increasing rapidly. Many meningococcal W cases are caused by a strain (sequence type ST 11) associated with severe disease and a higher risk of death.[1]

A smaller yet steady rise in the occurrence of meningococcal Y disease has also been seen since 2016. Meningococcal B has historically caused the majority of meningococcal disease in Australia and it continues to cause around half of all reported cases of meningococcal disease.

Data from recent years show that young children aged <2 years have the highest rates of new cases reported. Among these young children, meningococcal disease occurs most often in infants between 3 and 5 months of age. Vaccination with meningococcal ACWY vaccine can prevent disease in this vulnerable age group. A high number of meningococcal disease cases also occur among adolescents aged 15–19 years (Figure 1).

People can carry the meningococcal bacteria in their throat and/or nose (i.e. ‘carriage’), with studies showing that adolescents and young adults have the highest carriage rates of meningococcal bacteria.[2] Vaccinating populations with high carriage rates is critical to achieve protection of the community more broadly (community or herd immunity).

**Figure 1: Age-specific rates of meningococcal disease by subgroup and age group, Australia, 2016–2017***




*Data is for cases with a diagnosis date from 1 January 2016 onwards, as of 14 December 2017. Rates for 2017 have not been annualised. Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

### *Safety of meningococcal ACWY vaccines*

Meningococcal ACWY vaccine safety has been shown in multiple clinical trials and large population studies (conducted in countries after the vaccines have become available) in people of different ages, from infants to adults.[3-18] The vast majority of reactions after vaccination are mild and resolve on their own. Meningococcal ACWY vaccines are safe for use in patients with human immunodeficiency virus (HIV) infection.[19,20]

Meningococcal ACWY vaccines can be safely administered at the same time as other routine vaccines provided to young children through the National Immunisation Program. Clinical trials in young children have included giving meningococcal ACWY vaccines with:

- diphtheria-tetanus-acellular pertussis (DTPa) combination vaccines (which included hepatitis B vaccine, inactivated polio vaccine [IPV] and/or *Haemophilus influenzae* type B vaccine),
- 7-valent pneumococcal conjugate vaccine (7vPCV) and 13-valent PCV (13vPCV),
- rotavirus vaccine,
- hepatitis A vaccine,
- measles-mumps-rubella (MMR) vaccine,
- measles-mumps-rubella-varicella (MMRV) vaccine and varicella vaccine.[5,11-14,21-23]

In adolescents, clinical trials have included giving meningococcal ACWY vaccines with:

- 4-valent and 9-valent human papillomavirus (HPV) vaccine,
- diphtheria-tetanus-acellular pertussis (dTpa) vaccine,
- combined hepatitis A and B vaccine and seasonal influenza vaccine.[24-28]

In most studies, the frequency of reactions following vaccination were similar regardless of whether the vaccines were given together or separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

***Immune responses to meningococcal ACWY vaccines***

The number and spacing of meningococcal vaccine doses vary by brand and the age the vaccination commences.

*i) Children aged <2 years at commencement of vaccination*

ATAGI proposes the following vaccination schedules in children aged <2 years (refer to Table 1 in Recommendations section above):

- 2–5 months: 3 doses of Menveo (ideally given at 2, 4 and 12 months of age)
- 6–11 months: 2 doses of Menveo (ideally given at 6 and 12 months of age)
- 12–23 months: a single dose of Nimenrix or 2 doses of Menveo (given at least 8 weeks apart)

As the highest rates of meningococcal disease occur very early in life, it is highly desirable to start vaccination as early as possible so that infants can develop an immune response early. Clinical trials have shown that Menveo is safe to use in children from 2 months of age.[10-13] When given in a 3-dose schedule at 2, 4 and 12 months of age, more than 99% of children in the clinical trial developed protection against meningococcal W and Y after the completion of the course.[13]

For children who commence vaccination at age 6 to <12 months, a 2-dose schedule with Menveo produces a good immune response. In one large study with over 1,600 participants, more than 96% of children given 2 doses of Menveo at age 7–9 months and 12 months developed protection against meningococcal C, W and Y.[14] Another smaller study showed that 100% of children who received Menveo at 6 and 12 months of age produced an immune response against meningococcal C, W and Y after the second dose.[16] In both studies, the response to meningococcal A was slightly lower (87-88%).

Although the vaccine is currently registered in a 2-dose schedule from 7 months onwards, data from these clinical trials showed that the immune response in children starting vaccination at 6 months of age was similar. The 6-months schedule point is well-established and accepted in Australia, with consistently high vaccine coverage.[29]

Two vaccines are available for children aged 12–23 months of age – Nimenrix and Menveo. Because of differences in the ingredients in the vaccines, there are differences in the level of immune response produced. However, both vaccines have been shown to produce good immune responses in children 1 month after vaccination when given in the appropriate schedule. There is no preference for one vaccine over the other.

Data from clinical studies have shown that 1 dose of Nimenrix produces a strong immune response in toddlers of this age, with over 97% of children developing an immune response against all four subgroups of meningococcal (A,C,W,Y).[5,6,22,23] With Menveo, 97% of children developed a protective immune response to all four subgroups of meningococcal after 2 doses.[10]

*ii) Children aged ≥2 years, adolescents and adults at commencement of vaccination*

ATAGI proposes the following vaccination schedule in children aged ≥2 years, adolescents and adults:

- a single dose of Nimenrix, Menveo or Menactra

There are three registered meningococcal ACWY vaccines available for people aged 2 years or older: Nimenrix, Menveo and Menactra. Each of these produces an immune response against the four meningococcal subgroups included in the vaccine when given as a single dose.[7,9,24,25,30-32]

In studies with adolescents, 67–100% of vaccine recipients developed an immune response to the vaccine.[3,9,24,25,30,31,33] Population data collected in the United States showed that the vaccine (Menactra) was 80-85% effective in preventing clinical infection in a population during the first year after vaccination.[34,35]

Because of differences in the ingredients in the vaccines, there are differences in the level of immune response produced by the three vaccines. It is not known whether these differences have an impact on a person's protection against meningococcal disease. The differences in immune response between Nimenrix and Menveo are very minor, so either vaccine may be given.

However, the level of antibody responses produced after a dose of Nimenrix or Menveo is modestly higher than that after a dose of Menactra, especially for meningococcal subgroups W and Y.[7,30,32] There is also some evidence showing that immunity decreases more quickly with Menactra than with Nimenrix or Menveo.[7,32,36]

Therefore, ATAGI proposes that either Nimenrix or Menveo be given over Menactra whenever possible. If Nimenrix or Menveo are unavailable, Menactra can be given as it will still provide adequate protection against meningococcal disease caused by subgroups A, C, W and Y, and is highly preferred to no vaccination.

***Recommendation B5***

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.

Adolescents and young adults have the highest rates of meningococcal carriage (i.e. presence of meningococcal bacteria in the upper respiratory tract without any signs or symptoms of infection) and are thought to play an important role in how the bacteria are transmitted in a community.[2] Living in close or prolonged contact with a person who is carrying meningococcal bacteria can increase the chances of the bacteria being passed between people.[37-39]

A clinical study of vaccination with Menveo in 18- to 24-year-old university students showed that there were reductions in meningococcal carriage among those who were vaccinated,[40] potentially reducing the chances of disease transmission.

As Australian data show that the risk of meningococcal disease caused by serogroup B is also high among adolescents and young adults aged 20–24 years (compared with other age groups) (refer to Figure 1 above), ATAGI is also proposing that the existing recommendation for meningococcal B vaccination (currently for ages 15–19 years as per *The Australian Immunisation Handbook*) be extended to also include those aged 20–24 years.

***Recommendation B6***

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.

Smoking tobacco is known to increase the risk of carrying the meningococcal bacteria in the upper respiratory tract and of passing the bacteria to close contacts. Active smokers are at greater risk of meningococcal disease as they have high meningococcal carriage rates, which are approximately 1.5–2 times higher than those found in non-smokers.[41]

In a study of 14,000 teenagers aged 15–19 years, twice as many active smokers were carrying meningococcal bacteria compared with non-smokers, even after accounting for other risk factors known to impact carriage.[42] The risk of meningococcal carriage increases with heavier smoking[43] and studies have also shown adolescents in close contact to smokers are more likely to develop meningococcal disease.[42,44-46]

***Recommendations B7-8***

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

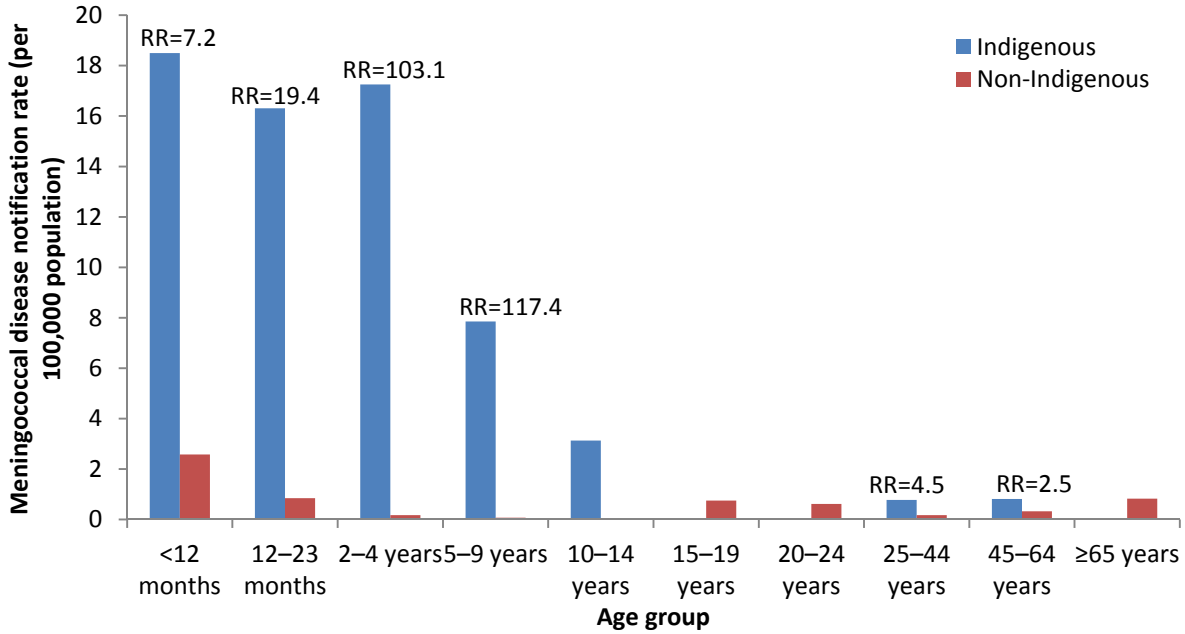
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive meningococcal ACWY vaccine (Table 1).
8. All Aboriginal and/or Torres Strait Islander infants and children aged 2 months to 4 years (<5 years) are recommended to receive meningococcal B vaccine (Table 2).

Aboriginal and Torres Strait Islander Australians have much higher incidence rates of meningococcal disease compared to non-Indigenous Australians. This is particularly observed among children aged <15 years for the two most common meningococcal subgroups B and W.

During 2012–2017, the incidence rate of meningococcal disease caused by subgroup W was higher in Aboriginal and Torres Strait Islander children aged <5 years (3.10 versus 0.34 per 100,000; rate ratio=9.1).

More recently in 2016–2017, this disparity was even more striking, with meningococcal disease rates among Aboriginal and Torres Strait Islanders being greater than 100 times those observed among non-Indigenous Australians in certain age groups (refer to Figure 2). This has been partly due to the outbreak of serogroup W disease in Central Australia which particularly affected young Aboriginal and Torres Strait Islander people in remote communities.

**Figure 2: Notification rates for meningococcal disease caused by serogroup W and rate ratio for Indigenous and non-Indigenous people, by age group, 2016–2017***

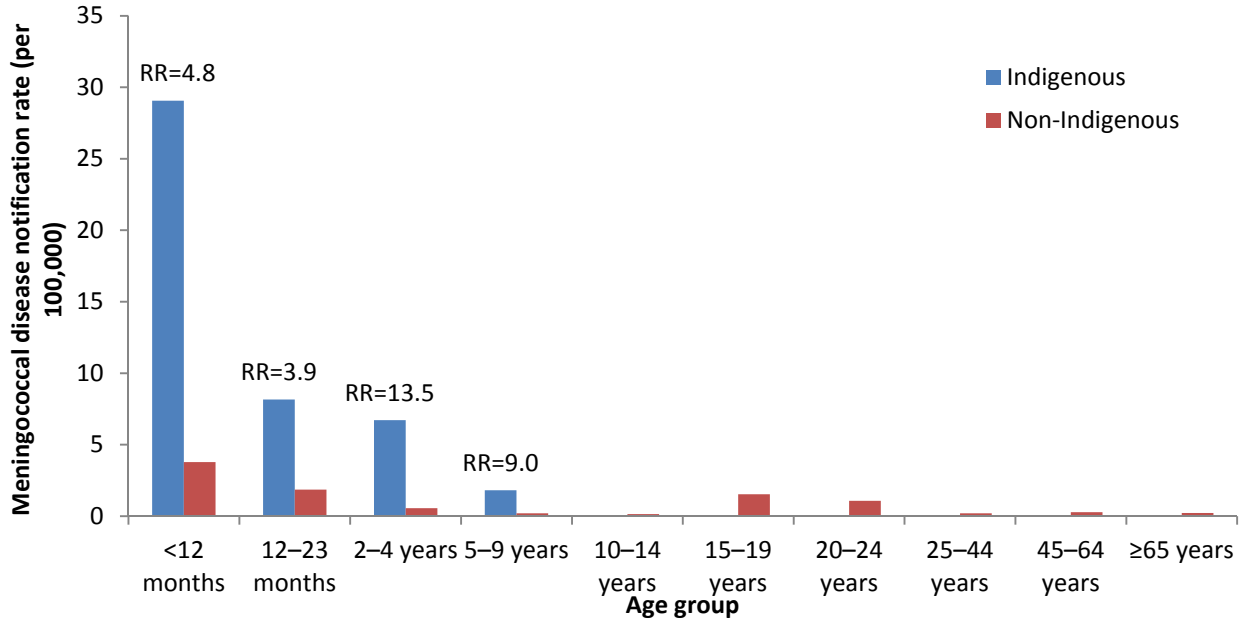



RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised.
Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

In 2016-17, there was a substantial disparity in the reported cases of meningococcal disease caused by subgroup B between Aboriginal and Torres Strait Islander people compared with non-Indigenous Australians, particularly among children aged <5 years old (refer to Figure 3).

This trend appears to be longstanding. Between 2006 and 2015, rates of meningococcal disease caused by subgroup B disease were reported as being 3.4 times and 3.8 times higher among Aboriginal and Torres Strait Islander infants aged <12 months and children aged 1–4 years, respectively, compared with non-Indigenous infants and children of the same age.[47]

**Figure 3: Notification rates for meningococcal disease caused by serogroup B and rate ratio for Indigenous and non-Indigenous people, by age group, 2016–2017***




RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised. Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

***Recommendation B9***

**B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.**

9. Infants aged 6–11 months with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1) are recommended to receive 3 doses of meningococcal ACWY vaccine (Table 1).

Clinical trials of Menveo in infants aged 6–11 months have only examined immune responses after 1 or 2 doses of the vaccine. No studies have examined immune response after 3 doses and no studies have been conducted in infants or young children with the specified medical conditions in List 1.

However, clinical studies of Menveo in young healthy infants starting vaccination at age 2 months show that immune responses were better after a 3rd dose (given 6 months of age) compared with immune responses after a 2nd dose (given at 4 months of age).[13]

While the differences in immunity are minor and likely to be unimportant in a healthy infant, ATAGI considers the higher risk of disease in an infant with a specified medical condition justifies the extra dose of vaccine. Studies with another meningococcal ACWY vaccine, Menactra, in older children and adolescents with HIV infection have shown that 2 doses, rather than 1, are required for an adequate immune response.[19,48]

Studies with meningococcal C vaccines have also shown that people with immunocompromising medical conditions have a lower immune response to vaccination and require additional doses.[49-53]

Extrapolating from these research findings, ATAGI considers a 3-dose course of Menveo (refer to Table 1 for dosing schedule) to be appropriate for infants commencing vaccination at age 6–11 months with a specified medical condition. The extra dose given to infants, compared with infants

without specified medical conditions, is similar to the schedule for older age groups, for whom an additional dose is currently recommended.

***Recommendations C and D***

**C ATAGI proposes that the recommendation for the 4th dose of vaccine for protection against *Haemophilus influenzae* type B currently given at 12 months is revoked.**

**D ATAGI proposes the following changes to the use of *Haemophilus influenzae* type B vaccines in Australia:**

- All children should receive a 4th dose of vaccine for protection against *Haemophilus influenzae* type B at 18 months of age.

A 4th dose of *Haemophilus influenzae* type B vaccine in the second year of life (in addition to the 3 doses given at 2, 4 and 6 months of age) is required to ensure long-term protection against *Haemophilus influenzae* type B disease and prevent cases of this disease later in childhood. A review of *Haemophilus influenzae* type B cases from 1996 to 2013 found that more than half were either unimmunised or partially vaccinated.[54]

Currently, a 4th dose is given at 12 months of age as a combined vaccine, Menitorix, which includes both *Haemophilus influenzae* type B and meningococcal C.

In January 2018, the Pharmaceutical Benefits Advisory Committee recommended the listing of Nimenrix on the NIP for infants 12 months of age.

The introduction of a meningococcal ACWY vaccine at 12 months of age means the meningococcal C component of Menitorix will no longer be required and the 4$^{th}$ dose of *Haemophilus influenzae* type B can be given in a monovalent formulation (i.e. containing only *Haemophilus influenzae* type B).

In addition, the Chief Executive Officer of the National Health and Medical Research Council agreed to amend a pneumococcal recommendation in the Australian Immunisation Handbook, proposed by ATAGI in late 2017, to move the 3$^{rd}$ dose of the infant pneumococcal vaccine from 6 months to 12 months.

The Pharmaceutical Benefits Advisory Committee is considering a submission to amend the infant pneumococcal schedule to align with the recommendations in the Australian Immunisation Handbook.

ATAGI has reviewed the epidemiology of all of the diseases with a vaccine scheduled at 12 months and proposes that the 4$^{th}$ dose of *Haemophilus influenzae* type B be moved to the 18-month schedule point.

Analysis of data on *Haemophilus influenzae* type B disease in Australia found that between 1993 and 2016, only 17 cases of invasive *Haemophilus influenzae* type B disease occurred in partially vaccinated children aged 6–23 months, with the majority (n=15/17) not having completed the initial 3-dose infant course (usually given at 2, 4 and 6 months of age).

In the United States, shifting the *Haemophilus influenzae* type B booster dose by 18 months in response to a vaccine supply shortage did not cause an increase in the incidence of invasive *Haemophilus influenzae* type B disease.[55]

On the basis of this information, ATAGI believes that moving the schedule point for the *Haemophilus influenzae* type B booster dose from age 12 months to 18 months is unlikely to result in more cases of *Haemophilus influenzae* type B in Australia.

## Additional information to be included in *The Australian Immunisation Handbook*

***Information on Trumenba, the newly registered alternative meningococcal B vaccine***

Trumenba is a newly available alternative vaccine that provides protection against meningococcal disease caused by meningococcal subgroup B and is registered and suitable for use in people aged ≥10 years. Trumenba was licensed for use in Australia in September 2017 and has been supplied since early 2018. Clinical trials have shown that Trumenba is a safe and effective vaccine for use in adolescents and young adults. It can be used in a 2-dose or a 3-dose schedule depending on the patient's risk of meningococcal disease.[56,57]

People aged 11–18 years show good immune responses after receiving 2 doses of Trumenba 6 months apart and also after receiving 3 doses of Trumenba using a 0, 1–2-month and 6-month vaccination schedule.[56] A protective immune response was produced in 82–83% of participants after 3 doses given at 0, 1 and 6 months or 0, 2 and 6 months, and in 73.5% of participants after 2 doses given at 0 and 6 months. Several clinical trials in people aged 10–25 years have also shown that both 3-dose and 2-dose schedules are safe and can be administered with other vaccines.[56-60]

The recommended dosing schedule (3 doses or 2 doses) depends on the patient's level of risk of meningococcal disease. ATAGI proposes that adolescents without specific medical conditions, who have a lower risk of meningococcal disease, receive 2 doses of Trumenba. However, adolescents with a specified medical condition (refer to List 1) have a higher risk of meningococcal disease, so it is preferable that the 3-dose schedule of Trumenba is used.

There is no preference for the use of Trumemba or Bexsero for the prevention of meningococcal B disease. However, the vaccines should not be used interchangeably, that is, a person who has a first dose of one brand of meningococcal B vaccine should complete the course with the same brand.

***Information on potential use of alternative meningococcal ACWY vaccines for infants if Menveo is not available***

Currently, Menveo is the only meningococcal ACWY vaccine that is registered for use for infants (age <12 months) in Australia. In the possible event of a vaccine shortage of Menveo, Nimenrix can be used as an alternative for infants from age 6 weeks, and Menactra can be used as the other alternative from age 9 months. These age-based recommendations are consistent with age-groups approved for use by regulatory authorities in Europe (Nimenrix) and the United States (Menactra), based on clinical trial data which demonstrated adequate antibody responses and safety. This recommendation is a "Variation with Product Information" in Australia. In the event of shortages, further information on the dose schedule of alternative vaccines would be provided online at www.health.gov.au/immunisation.

## Benefits/Harms

There are five key benefits from these proposed changes to the use of meningococcal vaccines:

1. Vaccination with meningococcal ACWY vaccine will provide protection to those age and population groups with the highest reported cases of meningococcal disease, particularly against disease caused by subgroups W and Y that have emerged and contributed significantly to total meningococcal disease cases in the past 2 years.
2. High uptake of meningococcal ACWY vaccine among adolescents has the potential to stop transmission of meningococcal bacteria in the community and provide community (herd) protection to the remainder of the population even if they are not vaccinated.

3. Vaccination of additional age groups among Aboriginal or Torres Strait Islander Australians with meningococcal ACWY and meningococcal B vaccines can address the large gap in the meningococcal disease burden compared with non-Indigenous Australians.
4. Additional vaccination recommendations to protect adolescents and young adults living in close quarters and those who are smokers can provide protection against the meningococcal subgroups that cause the majority of meningococcal disease in these high-risk individuals, and also stop transmission.
5. An additional dose of meningococcal ACWY vaccine given to infants aged 6–11 months with specified medical conditions diagnosed in infancy, who are most vulnerable to meningococcal disease, will provide them with additional protection against meningococcal disease, especially disease caused by subgroups W and Y.

There are potential concerns that may arise from the proposed changes to the use of meningococcal vaccines:

1. *Potential concern of 'schedule crowding'*

   Whilst ATAGI aims to minimise multiple visits for vaccinations scheduled at the same point ('schedule crowding'), ATAGI has a strong preference for avoiding adding new National Immunisation Program vaccination schedule points. Vaccination with meningococcal ACWY vaccine from infancy and shifting the 4th dose of *Haemophilus influenzae* type B vaccine will increase the number of vaccines administered at the 18-month schedule point. Non-Indigenous children without specified medical conditions will receive a maximum of 3 injections at both the 12- and 18-month schedule points. However, with the proposed changes, Aboriginal and Torres Strait Islander children living in four jurisdictions (Western Australia, South Australia, Northern Territory and North Queensland) will receive at least 4 injections at both the 12- and 18-month schedule points (because of the additional hepatitis A vaccine doses). In addition, children with various medical conditions (including but not limited to those in List 1) may require additional doses of other vaccines. This may impact acceptability for these population groups and may require additional visit(s) to receive all the recommended vaccines, which can affect compliance with the recommended schedule.

2. *Potential increased frequency and/or severity of adverse events due to a greater number of vaccinations being co-administered*

   Clinical trials have documented the general safety of meningococcal ACWY vaccines when given together with multiple routinely administered vaccines in both children aged <2 years and adolescents. In most studies, rates of adverse events when meningococcal ACWY and other vaccines were given together were similar to those when vaccines were given separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

3. *Potential for increased number of Hib cases occurring prior to the booster dose scheduled at 18 months of age.*

   Based on available Australian data and on the experience from a comparable situation in the United States, the postponement of the Hib dose from 12 months to 18 months is unlikely to lead to an increased number of Hib disease cases among children aged 12–18 months. In Australia, there has been a low number of Hib vaccine failures in the past two decades and a high population Hib vaccination coverage and community immunity. While an increase in Hib disease cases occurring among children aged 12–18 months who have received 3 primary doses of Hib-containing vaccine in infancy is not expected, there will be ongoing surveillance to detect any changes in the number of Hib cases in relation with age and vaccine-doses received.

**Preference and values**

The proposed changes to the use of meningococcal vaccines are in line with the best available clinical advice and with the ages for which the vaccines are currently registered. It is anticipated that use of the available meningococcal vaccines will result in additional protection for people most at risk and the wider community (including those who are not vaccinated) against meningococcal disease. This is considered consistent with societal expectations of the best use of vaccines in Australia, including vaccination use in the National Immunisation Program. Also, there has been substantial media interest in meningococcal vaccines following cases of meningococcal disease in young children and adolescents, and feedback from clinicians indicates a growing demand among parents for use of these vaccines especially for their young children. In 2017–2018, most states and territories initiated adolescent vaccination programs with meningococcal ACWY vaccine which were well-received, showing the importance of these vaccines in preventing this rare but serious condition.

**Resources and other considerations**

Product Information for Nimenrix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02123-1

Product Information for Menveo is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-02475-3

Product Information for Menactra is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-01448-1

Product Information for Bexsero is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02131-1

Product Information for Trumenba is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-PI-02674-1

Product Information for Hiberix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05633-3

**Practical information**

Communication to providers will need to be made clear in *The Australian Immunisation Handbook* and other guidance to minimise confusion and ensure smooth implementation of these proposed changes in recommendations. In particular, the availability of three meningococcal ACWY vaccines and two meningococcal B vaccines, all registered in different schedules for different age groups, may cause confusion among immunisation providers. The shift in the schedule point for the 4$^{th}$ dose of *Haemophilus influenzae* type B from 12 to 18 months of age may cause further confusion in the initial stages of implementation of the revised vaccination schedule. Clear clinical advice, including fact sheets with answers to frequently asked questions, will need to be available for immunisation providers.

**Glossary**

| | |
|---|---|
| Adverse event | An unwanted reaction usually following administration of a vaccine, which may or may not be caused by the vaccine. Adverse events may be at the site of injection or may be a general illness or a general allergic |

| | |
|---|---|
| | reaction. |
| Antibodies | A special protein produced by immune cells in response to antigens (foreign substances, bacteria, viruses or other microorganisms). Antibodies bind with antigens on microorganisms as one of the initial steps of the body's immune response against infection. |
| Carriage, or meningococcal carriage | The continual presence of bacteria (meningococci) in the upper respiratory tract, particularly the throat and/or nose, without causing disease to the host. |
| Carrier | A person who has carriage of bacteria, which are not currently causing disease or symptoms in that person, but which have the potential to be transmitted to others or to invade and cause disease in the individual. |
| Co-administration of vaccines | When two or more vaccines are administered at the same time (usually at different sites). |
| Conjugate vaccines | These are vaccines in which the vaccine antigen (the polysaccharides from the bacterial wall of meningococcal bacteria) has been joined or conjugated to a carrier protein to improve the immune response and immunological memory to the vaccine. |
| Herd protection | Herd protection, or herd immunity, is the protection of unvaccinated people indirectly, through a high vaccination rate in the rest of the population. The high level of vaccination and immunity in the population limits the number of people susceptible to infection and the ability for the infection to circulate. |
| Incidence or incidence rate | The number of, or rate of, new cases of a particular disease within a given period of time. |
| Immune response | The body's defence against a foreign object or infection, as shown in the case of a vaccine, by a rise in the level of antibodies above a threshold, or by an amount that is considered to provide protection against a particular disease. |
| Immunocompromising medical condition | A medical condition associated with a weakened immune system, either due to the condition or its treatment, which means that it is less able to fight off infection. People with these conditions are more vulnerable to infection and may have more severe disease than a healthy person. |
| Interchangeability of vaccines | This refers to the ability to use a different brand of vaccine against the same disease to complete a course of vaccination when more than one dose of vaccine is required. |
| Invasive disease (meningococcal or Hib) | Disease that results when bacteria (e.g. meningococcal or *Haemophilus influenzae* type B), which are usually harmlessly carried by the body, invade and cause clinical infection. The bacteria may infect the blood, spinal fluid or another part of the body that would normally be sterile (or germ-free). Invasive meningococcal disease most commonly causes meningitis and/or septicaemia (i.e. infection of the blood). |

| | |
|---|---|
| Monovalent vaccine | A vaccine against only one bacterium/virus that causes a disease or one variant subgroup of that bacterium/virus. |
| National Immunisation Program (NIP) | The National Immunisation Program was set up by the Commonwealth and state and territory governments to increase national immunisation coverage of important vaccines in Australia. The NIP provides free vaccines to eligible people to reduce the occurrence of diseases that can be prevented by vaccination. |
| Quadrivalent vaccine | A vaccine that targets four variant subgroups of a virus or bacterium that causes a disease. |
| Routinely administered vaccines | These are vaccines that are already included in the current NIP schedule and are to be given at specified schedule points. |
| Schedule point | These are time points or age milestones (e.g. 12 months of age) throughout a person's lifetime when a vaccine is scheduled to be given. The schedule points for vaccines have been selected to provide the best possible protection against diseases preventable by vaccination. |
| Serogroups | Serogroups are subgroups of certain bacteria distinguished by the presence of a common antigen. In the case of meningococcal bacteria, these antigens are the 'sugars' on their outer coating. The most common meningococcal serogroups that cause serious disease are A, B, C, W and Y. |
| Therapeutic Goods Administration (TGA) registration | Vaccines, like all medicines, are regulated by the TGA. They must be approved and registered for use by the TGA before they are available to the public in Australia. Before they are made available for use they are rigorously tested in human clinical trials to confirm that they are safe and that they stimulate protective immune responses. For a vaccine to be registered, the TGA reviews these data to ensure that the vaccine (or other medicine) works as it should and is safe to use. |

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## Attachment 1: Meningococcal vaccine formulations and brands available for use in Australia and number of doses recommended by ATAGI for healthy individuals by age*

| Vaccine | Formulation | Provides protection against serogroup | Currently registered age for its use | Number of doses recommended by ATAGI, according to age group* |
|---|---|---|---|---|
| **Quadrivalent meningococcal conjugate vaccines (4vMenCV)** | | | | |
| **Menveo** | Quadrivalent $CRM_{197}$ conjugate | A, C, W, Y | From 2 months†‡ | 2 to 5 months:<br>• 2 primary doses and a booster<br>6 to 11 months:<br>• 1 primary dose and a booster<br>12 to 23 months:<br>• 2 primary doses<br>From ≥2 years:<br>• 1 primary dose |
| **Nimenrix** | Quadrivalent tetanus toxoid conjugate | A, C, W, Y | 12 months to 55 years‡ | • 1 primary dose |
| **Menactra** | Quadrivalent diphtheria toxoid conjugate | A, C, W, Y | 2 to 55 years‡ | • 1 primary dose |
| **Multicomponent meningococcal B vaccines (MenBV)** | | | | |
| **Bexsero** | Recombinant multicomponent MenB | B | From 6 weeks§ | 6 weeks to 5 months:<br>• 3 primary doses and a booster<br>6 months to 11 months:<br>• 2 primary doses and a booster<br>From 12 months:<br>• 2 primary doses |
| **Trumenba** | Recombinant bivalent fHBP MenB | B | From 10 years§ | • 2 primary doses |
| **Meningococcal C conjugate vaccines (MenCCV)#** | | | | |
| **Menitorix** | Hib–MenC conjugate combination | C | From 6 weeks | Currently 1 dose at age 12 months.<br>ATAGI recommends this dose to be replaced by a dose of meningococcal ACWY vaccine at 12 months and a dose of monovalent Hib vaccine at 18 months |
| NeisVac-C | Monovalent MenC conjugate | C | From 8 weeks | Currently ATAGI recommends 1 dose of meningococcal C vaccine at age 12 months, but monovalent meningococcal C vaccine is not currently used on the National Immunisation Program, as this dose is given in a combination vaccine with the Hib vaccine as Menitorix (refer to above) |

* Dosing schedules are based upon ATAGI recommendations and may differ from the respective Product Information.

† The first dose of Menveo can be administered as early as 6 weeks of age.

‡There is no registered upper age limit for use of Menveo. Although both Menactra and Nimenrix are registered for use up to 55 years of age, either of these brands can be given to persons >55 years of age, as per *The Australian Immunisation Handbook.*

§ Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the vaccination course.

# Currently in the National Immunisation Program a dose of meningococcal C vaccine is given at age 12 months; this is different from the youngest age at which this vaccine can be given as stated in the Product Information.

## Attachment 2: Recommendations for the use of meningococcal ACWY conjugate vaccine and meningococcal B vaccine by age group

| Age group | Healthy people | | Special risk groups* | Travellers† |
|---|---|---|---|---|
| | Aboriginal or Torres Strait Islanders | Non-Indigenous | | |
| 2§–23 months | MenB | MenB | MenB<br>MenACWY | MenACWY |
| 2–4 years | | – | MenB<br>MenACWY | MenACWY |
| 5–14 years | | – | MenB<br>MenACWY | MenACWY |
| 15–19 years | MenB | MenB | MenB#<br>MenACWY | MenACWY |
| ≥20 years | – | – | MenB<br>MenACWY | MenACWY |

* Includes those with a specified medical condition associated with increased risk of meningococcal disease (refer to List 1), laboratory personnel who are at occupational risk of exposure to *Neisseria meningitides*

\# Young adults living in close quarters (such as new military recruits and students living in residential accommodation) are recommended to receive MenB vaccine

† People (age ≥2 months) who are planning overseas travel to regions with an increased risk of exposure to meningococcal serogroups A, C, W, or Y disease.

§ First dose can be administered as early as 6 weeks of age.

# Australian Immunisation Handbook

# Responses to Public Consultation Submissions

# Meningococcal and *Haemophilus Influenzae* Type B Vaccine Recommendations

Public consultation period: from 06 April 2018 to 06 May 2018

# Contents

# 1 Introduction

Public consultation for the revised meningococcal and *Haemophilus influenzae* type B vaccine recommendations in *The Australian Immunisation Handbook* (the Handbook) was conducted over a four-week period from 06 April to 06 May 2018, during which time the draft recommendations were available on the Citizen Space website. The Immunisation Branch invited a range of stakeholders, committees, working groups and interested people to provide submissions. A list of organisations formally invited to comment on the draft guidelines is provided in **Appendix A**.

This report outlines the public consultation comments received for the revised meningococcal and *Haemophilus influenzae* type B vaccine recommendations. Nineteen submissions were received using the submission template provided on Citizen Space. Of these, 11 were on behalf of an organisation and 8 were as individuals (Table 1).

**Table 1: List of respondents who made comment on the revised meningococcal and *Haemophilus influenzae* type B vaccine recommendations**

| Responder No. | Organisation |
|---|---|
| 1 | Individual |
| 2 | NT Health Department – CDC - Immunisation |
| 3 | Individual |
| 4 | Individual |
| 5 | Victorian Department of Health and Human Services – Immunisation Unit |
| 6 | Individual |
| 7 | Individual |
| 8 | Individual |
| 9 | Individual |
| 10 | Western Australia Primary Health Alliance |
| 11 | Meningitis Centre Australia |
| 12 | Northern Territory Health |
| 13 | Royal Australian College of General Practitioners |
| 14 | GlaxoSmithKline |
| 15 | Individual |
| 16 | Queensland Health – Prevention Division |
| 17 | South Australia Health – Communicable Disease Control Branch |
| 18 | Health Protection New South Wales |
| 19 | Sanofi Pasteur |

## Responses to public consultation submissions

The Australian Technical Advisory Group on Immunisation (ATAGI) considered all responses from the public consultation in June 2018 and, where necessary, revised the recommendations in accordance with the submissions. Comments from the public consultation submissions and the ATAGI responses are summarised in the following section.

This report was submitted to the National Health and Medical Research Council (NHMRC) in June 2018 and was approved in July 2018.

# 2 Responses to public consultation submissions

## 2.1 Revised meningococcal and *Haemophilus influenzae* type B Recommendations

| No. | Organisation | Comment | Proposed Action | Rationale |
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| **1a** | Individual | Ensure Commonwealth, State Health and Primary Health Networks are consulted during development of resource/educational materials. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **1b** | Individual | "Adolescents and young adults (aged 20–24 years)" wording is unclear. Could wording be age inclusive e.g. "aged 15–24 years"? | **Reviewed. No changes in recommendations made. Clarification to wording made.** | Revised recommendations in the Handbook will be clarified with to respect relevant age groups. |
| **1c** | Individual | Majority of parents are accepting of multiple vaccines if they understand the rationale. Providers will guide parents if required. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **1d** | Individual | Very clear communication for providers and community will be essential. Possibility of a webinar or a slide deck explaining the change and rationale behind it. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **1e** | Individual | Very clear detail about funded vaccine versus "recommended" vaccine e.g. for those with certain medical risk factors, smokers and those living in close quarters. | **Reviewed. No change in recommendations made. Clarification to wording made.** | Comment noted with thanks. This will be clarified. |
| **1f** | Individual | Clear detail on eligible cohort and commencement date. Providers will need to deal with parents of children who are just outside the | **Reviewed. No change in recommendations** | This comment relates to implementation and will be managed by Department of Health as |

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| | | age eligibility criteria (often by 1 day). Any catch-up? | **made. Clarification to wording made.** | per standard processes. |
| **1g** | Individual | Regarding the agreement to move the 3rd dose of the infant pneumococcal vaccine from 6 months to 12 months, this will need to be very clearly articulated:<br>1. Aboriginal and MAR children - currently receive 12 month booster dose. Will they still need 3+1 schedule or does every child revert to 2+1 schedule?<br>2. If a child has received current 2, 4, 6 schedule (not Aboriginal or MAR) and is caught in schedule change before 12 months of age, will they receive another dose at 12 months?<br>3. As Prevenar 13 is recommended to be administered into a separate limb, a "recommended injection sites" chart would be useful | **Reviewed. No change in recommendations made. Clarification to wording made.** | This comment relates to pneumococcal vaccination. The issue has already been considered by ATAGI and discussed in the pneumococcal public consultation document. Information will be included in other sections of the Handbook. This comment also relates to implementation and will be managed by Department of Health as per standard processes. |
| **2a** | NT Health Department – CDC - Immunisation | The reviewed section is clear and understandable. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **3a** | Individual | Risk is not having indigenous children IUTD after cramming another vaccine at 18m milestone and the parents losing confidence in the whole program at all milestones. | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation. |
| **3b** | Individual | Yes, the addition of Hib to the 18m age group would result in Indigenous children receiving 5 vaccines at that milestone - Hib + 2nd Hep A, Prev13, Infanrix, and MMRV. I suggest this is not practical and will lead to vaccines being overdue and putting the cohort at risk of these diseases. I suggest combining vaccines, such as Hib with Infanrix and investigation whether Trihibit or Tetramune | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>Trihibit and Tetramune are not currently |

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| | | would be suitable at this milestone. | | registered or available in Australia. |
| **3c** | Individual | The schedule is complex I know this because I field many calls per day about catch-up and how to calculate the intervals and the timings of vaccines from both doctors and nurses in GP practices, hospitals, community health settings, Aboriginal Medical Services and council clinics, and of course I respond to errors that arise due to this complexity.<br><br>I understand the needs and support vaccination but fear we are creating something which the lay-man does not understand and therefore pushing support away from the program.<br><br>And from reading the doc there is consideration of adding a MenB (Bexsero) vaccine as well, a vaccine that has been to PBAC and been found unacceptable previously. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **4a** | Individual | I have a plea to streamline the Handbook (including the online version). It is almost unreadable in its current form. It can be reduced to a fraction of its size if it was presented in a concise and logical fashion.<br>Repetition, repetition, repetition is the way I would characterize the current Handbook.<br>The same information is repeated multiple times (in the same chapter).<br>This is not only time-consuming and confusing for the reader, it can lead to errors. | **Reviewed. No change in recommendations made. Clarification to wording made.** | Comment noted with thanks.<br><br>Clarification to wording has been made in these recommendations. The digital version of the Handbook is also currently being revised to improve clarity. |
| **5a** | Immunisation | Page 14, Information on Trumenba - immune response data is | **Reviewed. No change** | Data for Bexsero has not changed and is in |

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| | Unit, Department of Health and Human Services Victoria | provided but similar information is not provided for Bexsero to compare with. | **in recommendations made.** | included in the current Handbook. |
| **5b** | Immunisation Unit, Department of Health and Human Services Victoria | Menactra is the least preferred of the ACWY brands. For people who have previously received Menactra, will vaccine providers be recommended to administer a booster dose? | **Reviewed. No change in recommendations made.** | Information on booster dose requirements are listed in the public consultation document and the Handbook. As stated, only people with on-going increased risk of IMD are recommended to receive a booster dose. Menactra provides adequate protection against meningococcal disease and is acceptable, although not the preferred vaccine brand. No additional vaccine doses are required following age-appropriate vaccination with Menactra. Clarification to wording has been made in these recommendations. |
| **5c** | Immunisation Unit, Department of Health and Human Services Victoria | A preterm infant requiring a booster of hepatitis B at 12 months, then DTP and Hib at 18 months could potentially have those 3 injections given as Infanrix hexa at either 12 months or 18 months to reduce needles and schedule crowding. | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>Of note, Infanrix Hexa is only funded for use under the NIP for the primary immunisation series at 2, 4, 6 months of age. |
| **5d** | Immunisation Unit, | At 18 months of age, DTP and Hib may mean a provider gives | **Reviewed. No change in recommendations** | The issue of schedule crowding has been considered by ATAGI and will be monitored |

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| | Department of Health and Human Services Victoria | Infanrix hexa to reduce needles. | **made.** | post-implementation.<br><br>Of note, Infanrix Hexa is only funded for use under the NIP for the primary immunisation series at 2, 4, 6 months of age. |
| **5e** | Immunisation Unit, Department of Health and Human Services Victoria | A monovalent Hib will be a benefit to be used for a vaccine catch up purpose. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **5f** | Immunisation Unit, Department of Health and Human Services Victoria | The current AIH states preterm infants need their 4th Hib at 12 months of age. So moving the dose to 18 months is not considered to be an issue for this cohort? | **Reviewed. No change in recommendations made.** | Preterm infants are currently recommended to receive Hib vaccine according the same schedule as all other infants (i.e. 2, 4, 6, 12 months). Moving the dose of Hib from 12 months to 18 months is not expected to have an impact in either term or preterm infants. |
| **5g** | Immunisation Unit, Department of Health and Human Services Victoria | Page 13, The AIH Hib catch-up information and table will need to align with the Hib schedule change at 18 months. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. This will be addressed in overall update to the Handbook |

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| **5h** | Immunisation Unit, Department of Health and Human Services Victoria | Page 24, Attachment 2 table, ACWY vaccine is missing from the healthy people columns. Plus tobacco smokers are not listed in the footnote. | **Reviewed. No change in recommendations made.** | Attachment 2 describes current recommendation prior to the proposed new recommendations. Changes to document have been made to clarify this and other points. |
| **5i** | Immunisation Unit, Department of Health and Human Services Victoria | Interchangeability between brands for course doses started with Nimenrix, Menveo and Menactra is not discussed. | **Reviewed. No change in recommendations made.** | This is a practice point and will be detailed in the Handbook. |
| **6a** | Individual | Important for all people in the community to have access to the vaccines and so cost needs to be supported by government with funded vaccines. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **6b** | Individual | There will be some community concern about the number of vaccines that the children are now advised to receive and primary care providers need to be supported in allaying these concerns. | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **6c** | Individual | It is really important that those from the CALD communities have access to these vaccines and to information about these vaccines. | **Reviewed. No change in recommendations** | Comment noted with thanks. |

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| | | | **made.** | |
| **6d** | Individual | I don't see any acknowledgement that many of the young children especially of refugee background return to places overseas where the risks are even higher as they visit friends and relatives. If they don't seek travel advice (and often they don't) and if they don't have supported vaccines wrt cost (i.e. even with travel advice many people decide that they can't afford to vaccinate five young children with their meningitis vaccines so in these situations there are Australian children who are at high risk of severe infection and it is the Australian community who will need to fund the health consequences of such illnesses. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **6e** | Individual | There needs to be better education to enhance the health literacy within multiple CALD communities to ensure that they seek appropriate advice and there needs to be adequate access to the appropriate funded vaccines to ensure that these vaccines that ATAGI recommend are available and funded. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **6f** | Individual | Yes - as per Q6 - need enhanced information for communities and for primary health care providers - to GPs and PHNs. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **6g** | Individual | Implementation requires a general community campaign to reduce any concerns within the community about the number of vaccines. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **6h** | Individual | I think it is easy to underestimate the risk as many of those from CALD communities are heading overseas as young children to visit friends and relatives and are at higher risk than our general community and yet the info available to them is less than that | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |

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| | | available to those of lower risk. Recent data on homelessness has identified that even in Australia, many people of refugee background are living in crowded circumstances and are therefore at high risk (see work on homelessness from Victoria) and also note that the incidences of these illnesses in these children will not necessarily be flagged as the children of refugee-background in any of the databases as they are often Australian-born! So the data being collected in this area is not helpful if we are to effect change in the high risk communities. We need to start collecting more than country of birth - we need year of arrival and ethnicity and language spoken at home and whether or not an interpreter in needed. This will help capture better data. | | |
| **7a** | Individual (General practitioner) | I agree with the proposed changes. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **7b** | Individual (General practitioner) | Financial considerations. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **7c** | Individual (General practitioner) | There is much potential benefit to including the meningococcal ACWY and meningococcal B vaccinations to the schedule, particularly to cover young children. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **7d** | Individual (General practitioner) | Currently these vaccines are only available for purchase on private script, and that is prohibitively expensive for most families, so vaccination rates are low. Community exposure particularly for strains W and Y are on the increase and young children are at risk of severe consequences of infection. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. A nationally-funded dose of Nimenrix is being introduced at 12 months of age under the NIP to address the increase in Men W and Y incidence. |

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| **8a** | Individual | The risk of fever following Bexsero (and ?Trumenba) in children aged <2 years needs highlighting in this document. ATAGI currently recommends paracetemol prophylaxis in conjunction with serogroup B meningococcal vaccination (Handbook section 2.2.4, last paragraph) and this should also be referenced in this section. Additional ATAGI advice around concomitant serogroup B meningococcal vaccines and influenza vaccine administration in young infants may be beneficial to providers. | **Reviewed. No change in recommendations made.** | Information on Bexsero is provided in the current Handbook, including use of prophylactic paracetamol with Bexsero and this recommendation remains unchanged.<br><br>Concomitant vaccination with Bexsero and other vaccines is associated with higher fever risk and this is mentioned in the current Handbook.<br><br>Trumenba is not licensed for use in children <10 years of age and there have not been significant fever safety concerns in the registered age group. |
| **8b** | Individual | No – but there will be significant "cherry picking" of vaccines at the 18 months of age immunisation schedule point and I am concerned that it will be MMRV that will be impacted. | **Reviewed. No change in recommendations made.** | Comment noted with thanks.<br><br>The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>As per current surveillance practices, impact on coverage for all vaccines will be evaluated. |
| **8c** | Individual | The Australian Immunisation Handbook is not only an excellent, NH&MRC endorsed guideline but a reference tool used by health professionals both nationally and internationally. As such, the | **Reviewed. No change in recommendations made. Clarification to** | Comment noted with thanks. 'Subgroup' will be replaced with 'serogroup'. The Handbook already uses 'serogroup'. Clarification to |

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| | | terminology used throughout the Handbook should be technically correct. The internationally recognised nomenclature for classifying the capsular polysaccharide of Neisseria meningitidis is serogroup not subgroup. There is inconsistency throughout the document with serogroup occasionally used then the incorrect term subgroup used. These are not interchangeable terms.<br><br>At no time during the section on meningococcal disease and the available vaccines, is the actual causative organism, Neisseria meningitidis even mentioned. Haemophilus influenzae type B is written (in full) 26 times throughout the document.<br><br>Consistent use of abbreviations will make the document more coherent.<br>Whilst the preference would be to use serogroup ACWY vaccine or serogroup B vaccine, please use meningococcal ACWY once then MenACWY from then on in the document; likewise use meningococcal B once then MenB from then on.<br>The term IMD is used for the first time in Table 1 and should be defined.<br>Thanks for the opportunity to comment on this. | **wording made.** | wording will be made and abbreviations will also be consistently applied. |
| **9a** | Individual | There is a discrepancy between the dosing intervals for MenBV vaccine in the handbooks, and the information provided by Bexsero pharmaceutical representatives. It makes it difficult to ensure that an adequate interval is achieved, especially when conflicting information is received from different sources. | **Reviewed. No change in recommendations made.** | The recommendations outlined in the Handbook are the most up to date ATAGI recommendations and dosing intervals will remain unchanged. Variations to the PI are clearly noted in the Handbook. |

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| **10a** | WA Primary Health Alliance | Potential communication gaps to General Practice. Open communication channels between the jurisdictions and general practice essential. Consider messaging directly to individual immunisation service providers. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **10b** | WA Primary Health Alliance | A robust monitoring process to ensure the revised schedule is adhered to and that immunisation coverage rates remain constant. | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>As per current surveillance practices, impact on coverage for all vaccines will be evaluated. |
| **10c** | WA Primary Health Alliance | Consider HealthPathways as a communication vehicle. Clinical editors notes/alerts and news can be added to the corresponding pathways and homepage. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **11a** | Meningitis Centre Australia | Unknown, am not a clinician | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **11b** | Meningitis Centre Australia | Unlikely | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |
| **11c** | Meningitis Centre Australia | Meningitis Centre Australia wishes to make a submission to the Australian Technical Advisory Group on changes being made to The Australian Immunisation Handbook and proposed changes to meningococcal vaccination recommendations.<br><br>I refer to Point 9 on page 3 of your Public Consultation Document "Infants aged 6-11 months with specified medical conditions | **Reviewed. No change in recommendations made. Clarification to wording made.** | Meningococcal B vaccine is currently recommended for all 2–23 month olds and remains unchanged. This existing information will be included in the Handbook.<br><br>Funding vaccines under the NIP is assessed by |

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| | | associated with an increased risk of meningococcal disease (refer to List 1 below) are recommended to receive 3 doses of meningococcal ACWY vaccine (Table 1)." As a parent of a severely disabled daughter through Pneumococcal meningitis I understand the need to vaccinate and protect our young from debilitating diseases like meningococcal.<br><br>The Centre is asking ATAGI to consider extending this vaccination program to include Meningococcal B for those at an increased risk of meningococcal disease in this age group.<br>I refer to page 6 of your document in para 2 after your dot points where you say "Meningococcal B ….continues to cause around half of all reported cases of meningococcal disease." The Centre feels that if half of these cases are Men B, then those most at risk to meningococcal should be better protected from a disease that is vaccine preventable.<br><br>My daughter Ashleigh contracted meningitis at six months of age in 1989, when no vaccines were available in Australia. I helped start up the Centre to advocate for meningitis vaccines and over the past 26 years we have been successful in discussions with several Federal and State Governments in ensuring that our children are better protected from such horrific diseases like meningococcal or Pneumococcal.<br><br>The Centre has also advocated for meningitis vaccines since and including the HiB vaccine in 1992/3, the pneumococcal vaccine from 2001/2004 with its inclusion onto the NIP in 2005 and most recently | | the Pharmaceutical Benefits Advisory Committee under a separate process to formulation of recommendations for the Handbook. |

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| | | the ACWY vaccine in 2016/17 in our home state of WA. Our states decision was followed by most other states in 2017.<br><br>The Centre is currently lobbying the South Australian Government to put the Men B vaccine on to its State Immunisation Plan where we have seen an increasing number of the disease in that state.<br>We cannot sit idly by and allow a vaccine preventable disease to take hold of the most vulnerable, our young and more importantly those most at risk.<br><br>MCA agrees with the other recommendations to the Immunisation handbook on meningococcal disease suggested in the discussion paper and we hope they are acted upon.<br><br>Thank you for the opportunity to make comment on the draft recommendations. | | |
| **12a** | NT Health | Risk to allow Haemophilus influenzae type B from 12 months if required, it can still be on the schedule at 18 months but may need to be given earlier in some instances. | **Reviewed. No change in recommendations made.** | The recommendation to move the monovalent Haemophilus influenzae type B dose from 12 to 18 months has been made on a programmatic level to avoid schedule crowding. Where individual clinical need exists, the Hib vaccine may still be given between 12 and 18 months. |
| **12b** | NT Health | The catch up implications of meningococcal ACWY vaccine need to be outlined and the recommendations for people over 12 months that are not eligible for the Meningococcal ACWY whether they should continue to receive meningococcal C vaccine needs to be outlined. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. More information on catch up vaccination will be provided in the Handbook. |

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| **12c** | NT Health | The 4th dose of Haemophilus influenzae type B vaccines should be recommended in the second year of life to allow flexibility of a complex immunisation schedule especially for children with medical risk factors. | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation.<br><br>More information on timing of the Hib vaccine booster dose will be provided in the Handbook, to discuss schedule flexibility where individual clinical need exists. |
| **13a** | Royal Australian College of General Practitioners (RACGP) | The RACGP foresees two main issues that could arise from the proposed changes:<br><br>a)Implementation challenges<br>The ongoing updates to the vaccination schedule in the Australian Immunisation Handbook can pose a challenge to health professionals. Migrating to a new system can be problematic, as it usually requires time from GPs and practice nurses to gain sound knowledge and understanding of new vaccination schedules. Additionally, the new recommendations add complexity, particularly about patients with different levels of risk. It is important to ensure adverse events are minimised by appropriate training, decision aids, posters and catch-up schedules as provided as part of any implementation scheme. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **13b** | Royal Australian College of General | b)'Schedule crowding' effect<br>GPs are aware of the 'schedule crowding' effect with the increased number of doses to be provided in older children i.e. 3 doses at 18 months (or 4 doses for indigenous children). Although the RACGP | **Reviewed. No change in recommendations made.** | The issue of schedule crowding has been considered by ATAGI and will be monitored post-implementation. |

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| | Practitioners (RACGP) | anticipates most patients will accept the changes, parents and carers should be assured that multiple simultaneous injections are safe and well tolerated by infants and young children. As the number of vaccinations given to infants at 12 months of age will increase with the proposed changes, it is beneficial to advise parents and carers to consider the number of vaccinations the child receives at any one time. | | Implementation issues will be managed by Department of Health as per standard processes. |
| **13c** | Royal Australian College of General Practitioners (RACGP) | A well-developed change management strategy is crucial for the successful implementation of the new schedule and should include the following:<br><br>• updating clinical and practice management software used in general practice to reflect the changes in vaccination schedule<br><br>• developing print and online marketing and educational material that highlight the changes to GPs and their teams outlining:<br><br>- the rationale for change in vaccination schedule, and the additional meningococcal strains<br>- the difference between recommended and funded vaccine<br>- the difference between the old and new vaccination schedule, for example using tables with colour coding to ensure the new changes are clearly demonstrated | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **13d** | Royal Australian College of General Practitioners | The consultation paper clearly outlines the rationale and evidence on the proposed changes to the meningococcal and Haemophilus influenzae type B vaccination in the Australian Immunisation Handbook. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |

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| | (RACGP) | The RACGP is supportive of the proposed changes given the trends and variations in the epidemiology of meningococcal disease, and if adopted, we will encourage the implementation across Australian general practice.<br><br>GPs play an important role and have the advantage of being a regular point of contact with a child through all stages of their development. General practices have the appropriate infrastructure in place to support the delivery of early childhood development outcomes. Future changes to the immunisation schedule should take into account not just immunology but also the important health gains from using immunisations as a trigger for opportunistic developmental screening and health checking. In addition, future changes to the immunisation schedule should also consider change-management costs to the community.<br><br>Thank you again for the opportunity to comment and we welcome future opportunities for engagement and progression of the issues discussed in this submission. | | |
| **14a** | GSK | • Regarding Recommendation A<br>GSK would like to highlight that the wording of the proposed change in recommendation A is ambiguous and open to interpretation.<br><br>The two potential interpretations being:<br>1. All the meningococcal B AND meningococcal ACWY recommendations have been revoked except for recommendations in people at occupational risk or travellers<br>2. All recommendations revoked except for those relating to: | **Reviewed. No change in recommendations made. Clarification to wording made.** | Comment noted with thanks.<br><br>The final wording of recommendations in the Handbook will be amended to address concerns regarding ambiguity. |

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| | | a) Meningococcal B<br>b) Meningococcal ACWY for people at occupational risk or travellers<br><br>To avoid confusion, GSK suggests that future documents released for public consultation contain a clear summary of the changes, including a list of the specific recommendations to be revoked, and a table that incorporates new recommendations in addition to those that remain in place.<br><br>To that end, GSK highlight the need to ensure the meningococcal vaccination recommendations are clearly laid out in revised chapter to mitigate the risk of confusion amongst healthcare professionals, in turn enhancing clarity and compliance with ATAGI recommendations. | | |
| **14b** | GSK | • Regarding current meningococcal B (MenB) recommendations in the Australian Immunisation Handbook<br>Currently, the Australian Immunisation Handbook recommends MenB vaccination for infants and young children, particularly those aged <2 years.<br><br>In addition to the epidemiology data used by ATAGI in the Public Consultation Document, GSK would like to highlight a recent publication (1) which looked at the historical epidemiology of MenB disease in Australia from 2006 to 2015. The publication concluded that priority at risk age/population groups for MenB vaccination include all children between 2 months and 5 years of age, Indigenous children under 10 years of age and all adolescents aged 15-19 years. (1) Importantly, the publication indicates that the | **Reviewed. Changes made to recommendations and public consultation document.** | Meningococcal epidemiology is constantly changing, particularly for serogroup B. The current recommendations have been based on data incorporating the latest epidemiology including data from 2016–2017. The changes to recommendations address additional population groups who are considered to be at the highest risk and for whom maximal benefit would be achieved through vaccination based on these analyses.<br><br>Current recommendations already target those aged <2 years and adolescents 15–19 years of age. New recommendations will address higher |

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| | | highest incidence of MenB disease is observed in infants 3-6 months of age (15.1 per 100,000 person-years) emphasising the need to recommend MenB vaccination in early infancy. (1)<br><br>Based on the recent publication by Archer B et al (1), GSK believes that to ensure high risk populations are protected, the recommendations for MenB vaccination should be extended to include all children <5 years with an emphasis on early vaccination of the younger infants (3-6 months) who are at greatest risk of MenB disease.<br><br>• Regarding "Recommendation B7-8" (page 10)<br>GSK agrees with ATAGI's proposed recommendations to focus on Aboriginal and/or Torres Strait Island (ATSI) persons, who are particularly at elevated risk of invasive meningococcal disease (IMD) when compared to the non-indigenous population. However, the data referred to in Table 2 of the Public Consultation Document and provided by a recent publication (1) supports that all ATSI persons from 2 months to under 10 years should be recommended to receive MenB vaccination. This goes above the proposed recommendations to focus on the younger cohort of under 5 years of age. The MJA publication analysed 10 years of epidemiological data (2006 – 2015) and made recommendations for vaccination of all ATSI persons aged from 2 years to under 10 years based on this extensive data source. (1) This historical data should be considered in addition to the 2016 and 2017 data, as the isolated data from 2016 and 2017 provides only a narrow indication of the burden of disease and is subject to being skewed by specific outbreaks during the two-year period (which particularly affected the young ATSI | | disease burden in Aboriginal and Torres Strait Islanders aged 2–14 years.<br><br>Of note, ATAGI initially proposed extension of MenB vaccination recommendations to Aboriginal and Torres Strait Islanders aged 2–4 years. Upon further review prompted by this comment, ATAGI agrees that this recommendation should be extended to Aboriginal and Torres Strait Islanders aged 2–14 years. Thus the proposed recommendation for MenB vaccination would apply to all Aboriginal and Torres Strait Islanders aged 2 months to 19 years.<br><br>Ongoing disease surveillance will continue after implementation to identify residual at-risk groups. |

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| | | population). | | |
| **14c** | GSK | • Regarding section "Information on Trumenba, the newly registered alternative meningococcal B vaccine" (page 14)<br>The following statement is included in this section: "There is no preference for the use of Trumemba or Bexsero for the prevention of meningococcal B disease." As Trumenba is only indicated from 10 years and above, to ensure patient safety, GSK suggests it is clearly conveyed that there is no preference for the use of Trumenba or Bexsero in individuals from 10 years and above for the prevention of MenB disease. Only Bexsero is indicated for use from 2 months of age and there are safety implications associated with the inadvertent administration of Trumenba to anyone under the age of 10 years. | **Reviewed. No change in recommendations made.** | The final wording of recommendations in the Handbook will be amended to address concerns regarding ambiguity. |
| **14d** | GSK | • Regarding section: "Information on potential use of alternative meningococcal ACWY vaccines for infants if Menveo is not available" (page 14)<br>To ensure appropriate use of available vaccines, GSK suggests a clear statement is included to emphasise that when in stock, Menveo is the preferred brand for use in infants under 12 months of age. Other brands should only be used in the absence of Menveo. | **Reviewed. No change in recommendations made.** | Future changes in registered age ranges for several meningococcal vaccines are pending or planned. The Handbook will undergo updates, as required, to advise on appropriate registered brands for use in various age groups, including those aged <12 months, and where appropriate when use according to "variations from product information" are acceptable. |
| **14e** | GSK | • Additional comments for consideration:<br>- Burden of disease in older adults (≥65 years)<br>It is widely recognised that young children and adolescents have the highest incidence of IMD. (2) However, it is important to note that in recent years there has been an increase in the incidence of IMD disease in older adults, particularly those over 65 years of age. This | **Reviewed. No change in recommendations made.** | ATAGI has reviewed the available evidence. While notifications of serogroup W and Y rose in older adults from 2015, infants, toddlers and adolescents remain at highest risk. |

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| | | increase in disease has mainly been attributed to meningococcal W and Y (MenW and Y). (2,3) In 2016, according to the NCIRS FAQ (3), the rate of MenW and Y in adults ≥65 years was 1.22 per 100,000, which was on par with the rate observed in adolescents (1.21 per 100,000), a recognised risk group. In 2017, this trend continued in the over 65-year old population. (2) It is evident that MenW and Y disease is an emerging risk in the older adults, therefore a recommendation for older adults to receive MenACWY vaccination is warranted to help protect this emerging risk group.<br><br>It is important to note that both Nimenrix and Menactra have an upper age limit of 55 years on their indications and only Menveo doesn't have an upper age limit. Therefore, GSK suggests that a preference for Menveo in this age group should be highlighted if a recommendation for older adults is included. | | Adolescents are also known to have the highest rates of meningococcal carriage and are important to target to reduce transmission.<br><br>The recommendations have been formulated to maximise protection for those currently at highest risk and to provide maximal direct and indirect benefit to the general population achieved through vaccination.<br><br>Of note, a new recommendation proposed in the public consultation document of relevance is that anyone who wishes to protect themselves against meningococcal disease may have a MenACWY or MenB vaccine. |
| **14f** | GSK | - Notification vs rate<br>Notifications and rates are terms commonly used to assess the burden of disease and have very distinct meanings. GSK believes there is potentially a substantial level of misunderstanding around the appropriate application and interpretation of these terms. When assessing the burden of IMD, although both notifications and rates provide valuable insight, it is important to clarify that rates provide a more meaningful and standardised measure of disease than notifications, especially when comparing burden of disease across different age cohorts. For example, according to the December 2017 IMD Surveillance Report (2), the number of MenW notifications for infants <1 year and adults ≥65 years was 15 and 31, respectively. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |

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| | | The rate however was 5 per 100,000 population for infants <1 year and 0.8 per 100,000 population for adults ≥65 years. Based on notifications, the burden of disease may appear to be higher in adults, conversely, the rates indicate that burden is actually higher in infants. Therefore, it is important to reinforce that notifications provide an absolute number whereas rates provide a more relevant estimate of disease as it considers the population size.<br><br>GSK recommends, that succinct guidance on how to appropriately interpret these terms is given to healthcare professionals to ensure the burden of IMD is thoroughly understood.<br><br>References:<br>1. Archer B et al. Epidemiology of invasive meningococcal B disease in Australia, 1999-2015: priority populations for vaccination. MJA 2017; 207(9): 382-7<br>2. Department of Health. Invasive Meningococcal Disease National Surveillance Report: with a focus on MenW. 31 December 2017. http://www.health.gov.au/internet/main/publishing.nsf/Content/5FEABC4B495BDEC1CA25807D001327FA/$File/31-Dec17-IMD-Surveillance-report.pdf [Accessed April 2018]<br>3. NCIRS Meningococcal Vaccines Frequently Asked Questions. February 2018. http://www.ncirs.edu.au/assets/provider_resources/fact-sheets/meningcoccal-vaccines-FAQ.pdf [Accessed April 2018] | | |
| **14g** | GSK | • Regarding "Recommendation B2" (page 3)<br>ATAGI recommends that children who commence the meningococcal ACWY (MenACWY) vaccination schedule before 12 | **Reviewed. No change in recommendations made.** | Children who had Menveo in infancy will still be eligible to receive Nimenrix at 12 months of age. The Handbook will discuss |

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| | | months of age should also receive a dose of MenACWY vaccine at 12 months of age. Earlier this year, the Health Minister announced that Nimenrix will replace Menitorix on the National Immunisation Program (NIP) at the 12-month-old encounter. As Menveo is the only brand indicated for infants <12 months of age, GSK anticipates that healthcare professionals will need guidance on the use of Nimenrix at the 12 months NIP dose when a course of Menveo has already been initiated. Specifically, there may be concerns regarding interchangeability (i.e. can Nimenrix be used to complete a course of Menveo), the minimum interval between a course of Menveo and Nimenrix and the clinical considerations of providing both vaccines. | | interchangeability of brands. |
| **14h** | GSK | In addition to the above, GSK would like to highlight the following information to ATAGI for consideration:<br><br>• The strain coverage of Bexsero has been widely assessed using the Meningococcal Antigen Typing System (MATS), a technique that measures the level of expression of fHbp, NadA and NHBA antigens, and the immunologic cross-reactivity of each with the corresponding vaccine antigen. MATS results predict killing of strains in the serum bactericidal antibody assay (hSBA), the established correlate of disease protection. (1)<br><br>The current meningococcal chapter states the following in relation to MATS in section 4.10.4 Vaccines:<br><br>Specialised laboratory testing (Meningococcal Antigen Typing System or MATS) has predicted that approximately 76% of all MenB strains that caused disease in Australia from 2007 to 2011 would | **Reviewed. No change in recommendations made.** | Comment noted with thanks. |

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| | | have been susceptible to effective killing by vaccine-induced antibodies.<br><br>GSK would like to draw your attention to the vaccine effectiveness data of Bexsero taken from large-scale vaccination programs around the world. Data from which, provides real-life effectiveness in a diverse patient population and may be important for inclusion in this chapter update as it is more relevant than MATS and is recently published.<br><br>Since its initial licensure, Bexsero has accumulated substantial clinical experience. Overall, over 22 million doses of Bexsero have been distributed in 35 countries worldwide since 2013.<br><br>In Canada, 43,740 people received Bexsero during a vaccination programme in the Saguenay–Lac-Saint-Jean region of Quebec, where local disease incidence was high. (2) In the USA, Bexsero was administered to >15,000 individuals during two college outbreaks prior to licensure, under an Investigational New Drug protocol. (3,4)<br><br>In 2015, the UK became the first country to introduce Bexsero on to its national immunisation program. A reduced two-dose priming schedule was offered to infants at 2 and 4 months of age. Approximately 700,000 infants per year were targeted for vaccination. In December 2016, vaccine effectiveness (VE) data were published, showing that the VE of two doses of Bexsero was 82·9% (95% CI 24·1–95·2) against all MenB cases, equivalent to a VE of 94·2% against the highest predicted MenB strain coverage of 88%. Compared with the pre-vaccine period, there was a 50% incidence | | |

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| | | rate ratio (IRR) reduction in MenB cases in the vaccine-eligible cohort (37 cases vs average 74 cases; IRR 0·50 [95% CI 0·36–0·71]; p=0·0001), irrespective of the infants' vaccination status or predicted MenB strain coverage. Similar reductions were observed even after adjustment for disease trends in vaccine-eligible and vaccine-ineligible children. (5)<br><br>To further support the relevance of Bexsero's effectiveness data, earlier this year the Public Health England updated its "Guidance for the public health management of meningococcal disease in the UK" publication. The publication states: "The implementation of Bexsero into the UK national immunisation schedule5 and its recent use in a region of Quebec2 with high disease incidence, has provided more convincing evidence of its effectiveness in the field compared to Trumenba, which has yet to be implemented in a national immunisation schedule." (6)<br><br>As a result of the available effectiveness data for Bexsero, the publication also included the following guidance: "The vaccination dosing and schedule for Bexsero, as well as the licensed age indication, is more suitable for outbreak control than Trumenba. Bexsero also has proven efficacy in the field. Therefore, until more data become available, Bexsero is the vaccine of choice unless the outbreak strain is predicted not to be prevented by this vaccine (MATS, for example, if isolates are available). MATS results, however, are not timely and should not delay public health decisions."<br><br>• Safety data for Bexsero, so far has been limited to clinical trials and | | |

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| | | isolated local outbreaks. Results from a prospective surveillance study in the UK has recently been published, following the implementation of a nationwide routine immunization program with Bexsero (at age 8 weeks, 16 weeks and then 1 year). The study assessed suspected adverse reactions to Bexsero in children up to 18 months of age from September 2015 to May 2017, during which 1.29 million children received about a combined 3 million doses of Bexsero. The safety profile of Bexsero was broadly as expected, no significant safety concerns were found after widespread use in UK infants and the vaccine appeared to be well accepted by parents. In addition, the anticipated reactogenicity did not appear to adversely affect compliance with subsequent doses. The authors concluded that experience so far from the UK routine immunisation program shows that Bexsero has a favorable benefit–risk profile. (7)<br><br>References:<br>1. Watson P and Turner D. Clinical experience with the meningococcal B vaccine, Bexsero®: Prospects for reducing the burden of meningococcal serogroup B disease. Vaccine 2016;34: 875–80<br>2. De Wals et al. Impact of an Immunization Campaign to Control an Increased Incidence of Serogroup B Meningococcal Disease in One Region of Quebec, Canada. Clinical Infectious Diseases 2017; 64(9):1263-7<br>3. McNamara et al. First Use of a Serogroup B Meningococcal Vaccine in the US in Response to a University Outbreak. Pediatrics 2015; 135:798–804<br>4. Biswas et al. Notes from the Field: Outbreak of Serogroup B Meningococcal Disease at a University — California, 2016. Morb | | |

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| | | Mortal Wkly Rep 2016;65: 520–1<br>5. Parikh et al. Eff ectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. Lancet 2016; 388: 2775- 2872<br>6. Public Health England. Guidance for the public health management of meningococcal disease in the UK Updated February 2018.<br>7. Bryan P et al. Safety of multicomponent meningococcal group B vaccine (4CMenB) in routine infant immunisation in the UK: a prospective surveillance study. 2018 Lancet Child Adolesc Health http://dx.doi.org/10.1016/S2352-4642(18)30103-2 | | |
| **14i** | GSK | Additionally, GSK would like to highlight the following updates which are required within Section 4.10.4 Vaccines of the current chapter.<br>In relation to the various companies responsible for distribution of the meningococcal vaccines in Australia:<br>- Bexsero is listed as:<br>Bexsero – Novartis Vaccines and Diagnostics Pty Ltd<br>Please replace with Bexsero - GlaxoSmithKline Australia Pty Ltd<br>- Menveo is listed as:<br>Menveo – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd<br>Please replace with Menveo - GlaxoSmithKline Australia Pty Ltd<br>- Nimenrix is listed as:<br>Nimenrix – GlaxoSmithKline Australia Pty Ltd<br>Please replace with Nimenrix - Pfizer Australia Pty Ltd | **Reviewed. No change in recommendations made.** | Updates to vaccine information will be made to the Handbook. |
| **15a** | Individual | The problem is that you are recommending Meningococcal vaccination at all.<br>Given most people will be colonised with meningococci at some | **Reviewed. No change in recommendations** | Comments not applicable or supported by body of evidence. |

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| | | point in their lives, anyway, and up to 35% of adolescents/young adults are asymptomatic carriers, you have to ask yourself - what is the point of vaccinating anybody with this?<br>The same could be said about the influenza vaccination. Sometimes it is only as effective as 15%. Often only 50%. With those odds, I think the government is not only wasting its money, but it's putting too many lives at risk with potential adverse reactions to the vaccination.<br>The fact remains that the percentage of asymptomatic carriers is far too high to warrant the Meningococcal vaccinations being used at all. Many, many studies show these high percentages of asymptomatic carriers. 'Herd immunity' can never be reached with these percentages, anyway (carriers are estimated to be at about 10% in older people, too). | **made.** | |
| **15b** | Individual | People who live in close quarters (eg military etc) are going to be 100% exposed to Meningococcal. So vaccination is useless, especially with the very high asymptomatic carrier rates on top of this. Why have them have extra doses of the vaccination that aren't going to work? It will only serve to pay the Pharmaceutical companies. It's not going to stop those living in close quarters contracting Meningococcal! | **Reviewed. No change in recommendations made.** | Comments not applicable or supported by body of evidence. |
| **15c** | Individual | I think there are too many vaccinations on the NIP.<br>There are so many unnecessary ones.<br>In this well-sanitised day and age, do people need to be having Diphtheria vaccinations? No, they do not.<br>Hep B is really only needed if people (eg self or parent) are intravenous drug users or at serious risk of a needle stick injury.<br>Tetanus spores are everywhere anyway, so everyone's always | **Reviewed. No change in recommendations made.** | Comments not applicable or supported by body of evidence. |

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| | | exposed to them. Tetanus only poses a risk in unclean wounds in anaerobic conditions (eg stick injuries). Surely it's best to have the vaccination available only when you have that particular injury scenario? And even then, it's rarely a problem.<br>Rubella times for vaccination are silly, as women are having children in their 30s now, not at 15 years of age. Most women don't have another MMR after school days, so will be most at risk when the vaccination's effectiveness has waned (eg by their early 30s) which is exactly the time that they are in need of being safe (eg when they might actually BE pregnant!).<br>People's nasal cavities are exposed to meningococcal, influenzae and all sorts of other pathogens. Most people do not come close to dying or being permanently scarred by it - and judging by the rates of asymptomatic carriers, an approximate third of young adults/teenagers are obviously not even being affected by having these pathogens in their nasal cavities! So they're obviously not particularly unsafe. Why vaccinate against it at all?<br>Vaccinations should be left for those diseases that are actually really unsafe if you contract it (maybe a 1 in 10 chance, not a 1 in a 10,000 chance of something going wrong), not for those diseases where the risk of the vaccination far outweighs the benefit (which in all honesty is most of the vaccinations on the NIP, if not all). | | |
| **16a** | Prevention Division, Queensland Health | Strongly recommend that The Australian Immunisation Handbook chapter on meningococcal disease clearly indicate the time-points at which National Immunisation Program (NIP) funded MenACWY and monovalent Hib vaccine be routinely administered. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. The updated Handbook chapter will contain information on what is funded under the NIP. |
| **16b** | Prevention Division, | Strongly recommend that changes to the NIP schedule be clearly communicated to immunisation providers. | **Reviewed. No change in recommendations** | Comment noted with thanks. The updated Handbook chapter will contain information on |

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| | Queensland Health | | **made.** | what is funded under the NIP. |
| **16c** | Prevention Division, Queensland Health | Strongly recommend that jurisdiction be given sufficient lead time to amend their vaccination schedules and develop the necessary resources to support implementation. | **Reviewed. No change in recommendations made.** | This comment relates to implementation and will be managed by Department of Health as per standard processes. |
| **17a** | Communicable Disease Control Branch, SA Health | REGARDING:<br>"Recommendation B 5:<br>Adolescents and young adults (aged 20 – 24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive;<br>a) a single dose of meningococcal ACWY vaccine.<br>b) two doses of meningococcal B vaccine"<br><br>This recommendation is problematic from a program perspective - how do you establish eligibility with any degree of reliability and consequently how do you accurately cost such a program? | **Reviewed. No change in recommendations made.** | Eligibility will need assessment by clinicians on a case by case basis using standard immunisation check list, included in the Handbook.<br><br>These groups are not currently funded under the NIP. |
| **17b** | Communicable Disease Control Branch, SA Health | REGARDING:<br><br>"Recommendation B 6:<br>Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:<br>a) a single dose of meningococcal ACWY vaccine. | **Reviewed. No change in recommendations made.** | Eligibility will need assessment by clinicians on a case by case basis using standard immunisation check list, included in the Handbook.<br><br>These groups are not currently funded under the NIP. |

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| | | b) two doses of meningococcal B vaccine.<br><br>This recommendation is problematic from a program perspective - how do you establish eligibility with any degree of reliability and consequently how do you accurately cost such a program? | | |
| **17c** | Communicable Disease Control Branch, SA Health | REGARDING:<br><br>"Recommendation B 8<br>All Aboriginal and/or Torres Strait Islander infants and children aged 2 months to 4 years (<5 years) are recommended to receive meningococcal B vaccine (Table 2)."<br><br>SA supports this recommendation but notes that, since 2000 in SA, there have not been any identified cases of IMD serogroup B in ATSI aged greater than 4 to less than 7 years since 2000. In this period there have been 19 cases in total in Aboriginal people – 16 in children up to four years of age, one in a seven year old, one in an 11 year old and one in a 19 year old. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. Recommendations have been formulated based on identified high risk Aboriginal and Torres Strait Islander age groups on a national level. |
| **17d** | Communicable Disease Control Branch, SA | 1. SA suggests the inclusion of a catch up table for Hib. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. The current catch up table for Hib in the Handbook will be updated accordingly. |

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| **17e** | Communicable Disease Control Branch, SA Health | 2. Questions to consider re due/overdue rules (both for clinical decision making and relating to AIR);<br><br>• When a dose 4 of Hib has been given prior to 18 months of age will recommendations for the minimum age for this dose to be accepted as a valid dose be included?<br>• When a dose 1 of ACWY vaccine has been given prior to 12 months of age will recommendations for the minimum age for this dose to be accepted as a valid dose be included? | **Reviewed. No change in recommendations made.** | Comment noted with thanks.<br><br>This comment relates to implementation, specifically AIR updates, and will be managed by Department of Health as per standard processes. |
| **17f** | Communicable Disease Control Branch, SA Health | 3. The wording of the document was found to be confusing by a number of staff, relating to the following paragraph;<br><br>"ATAGI proposes all current recommendations in The Australian Immunisation Handbook are revoked with the exception of those relating to meningococcal B and meningococcal ACWY vaccination for people at occupational risk or travellers (refer to Attachment 2)"<br><br>This paragraph was read as meaning that all recommendations are revoked except for those relating to meningococcal B (for people at occupational risk or travellers) and meningococcal ACWY vaccination for people at occupational risk or travellers.<br>The apparent inconsistency between this interpretation and Table 2 was noted and it did not make sense that recommendations relating | **Reviewed. No change in recommendations made. Change made to public consultation document.** | Comment noted with thanks.<br><br>The spelling error will be corrected in the public consultation document.<br><br>The final wording of recommendations in the Handbook will be amended to address concerns regarding ambiguity. |

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| | | to vaccination of infants 2 to 23 months and adolescents 15 to 19 years would be revoked, nonetheless it did create a degree of misunderstanding – eventually clarified through direct discussion with OHP.<br><br>4. Trumenba spelt incorrectly in section on "Additional information to be included in The Australian Immunisation Handbook Information on Trumenba, the newly registered alternative meningococcal B vaccine", in the following sentence;<br><br>There is no preference for the use of Trumemba or Bexsero for the prevention of meningococcal B disease. However, the vaccines should not be used interchangeably, that is, a person who has a first dose of one brand of meningococcal B vaccine should complete the course with the same brand. | | |
| **18a** | Health Protection NSW | Yes.<br>Recommendation A: Attachment 2 is confusing. The title indicates that this is a summary of recommendations by age group, yet Men ACWY is not recommended for infants or adolescents. Is it meant to be titled "unfunded recommendations"? Even so, the adolescent ACWY is not funded. Why wouldn't travellers 2 - 23 months be recommended to have menB? etc. | **Reviewed. No change in recommendations made.** | Comment noted with thanks.<br><br>The final wording of recommendations in the Handbook will be amended to address concerns regarding ambiguity. |
| **18b** | Health Protection NSW | Recommendation B.3: This unequivocal statement of the preference for Nimenrix or Menveo over Menactra is substantiated by immunogenicity data [7, 30, 32] but not by clinical outcomes. The text on p.9 indicates that Nimenrix and Menveo have only modestly | **Reviewed. No change in recommendations made.** | While efficacy/effectiveness studies are preferred to immunogenicity studies, only data on effectiveness is available for Menactra. The available effectiveness data shows significant |

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| | | higher immunogenicity. The cited papers are clear that the clinical significance of the immunogenicity differences is unknown. Importantly, persistence of antibodies out to 5 years for Menveo and Menactra appears similar, so the other statement on p9: "There is also some evidence showing that immunity decreases more quickly with Menactra than with Nimenrix or Menveo" is misleading. It is not substantiated by [7], as this measured antibodies at 1 month post-vaccination only, and only marginally (not significantly) for MenA and Men C in [32], and marginally (not significantly) for Men W and Men Y in [36].<br><br>Given the absence of evidence of inferiority for clinical outcomes, such a recommendation has the potential to cause considerable concern in the hundreds of thousands of Australians who have received Menactra. It is appropriate to describe the different immunogenicity responses accurately in the text, but the available evidence does not substantiate a recommendation for one vaccine over the other. | | waning of protection over an 8-year period post vaccination with Menactra.<br><br>Licensure and registration of meningococcal vaccines in Australia and internationally have been based on serological correlates of protection. While the validity of serologic cut-offs to predict protection has limitations, ATAGI considers it appropriate and valid to examine the immunogenicity data comparing Menactra with the two other conjugate MenACWY vaccines, as they do provide a basis for comparison in the absence of head to head efficacy or effectiveness studies.<br><br>Clinical trials in adolescents immediately after vaccination show significantly higher immunogenicity with Menveo or Nimenrix over Menactra, as referenced in the public consultation document. In its assessment of the evidence, ATAGI has considered both published and unpublished data available in the public domain, as well as data provided in-confidence by the vaccine manufacturers.<br><br>Significant differences were still evident at 3 |

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| | | | | year follow up, as discussed and referenced in the public consultation document. Differences evident at 5 years were non-significant, likely due to smaller numbers affecting the ability to demonstrate ongoing significance.<br><br>These studies indicate that a single dose of Nimenrix or Menveo, compared with a single dose of Menactra, may potentially provide better and/or longer-lasting protection against the meningococcal serogroups of greatest concern in Australia, warranting a preferential recommendation.<br><br>However, Menactra remains one of the MenACWY vaccines recommended for use in Australia. As such, it is acceptable in its current use in state/territory funded programs. A preferential recommendation for the alternatives does not imply otherwise. ATAGI does not recommend any additional vaccination of persons who have received Menactra (unless they have a specific immunocompromising condition that puts them at increased risk of IMD). |

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| | | | | Public concerns in previous recipients of Menactra can be addressed by state departments in consultation with the Department of Health. |
| **18c** | Health Protection NSW | Recommendation B.6: the recommendation for smokers to be vaccinated is not substantiated, and may result in perverse outcomes. The statement that active smokers are at greater risk of meningococcal disease is not substantiated by [41], and appears to be confusing carriage with risk of disease. While it is well-established that exposure to passive smoking/people who smoke increases the risk of meningococcal disease in children, the evidence that smokers are at increased risk of meningococcal disease is weak. [44] provides a non-significant adjusted OR of 2.4. [45] provides evidence that exposure to smokers is a risk factor for IMD in England. [46] has a non-significant risk for current smoking and passive smoking for IMD in Queensland teenagers, which was not confirmed in multivariate analysis. While the evidence seems consistent that smokers have increased carriage of NM, thus exposing their contacts to higher risk of IMD, there does not seem to be any evidence that vaccination will influence NM carriage in smokers. in [41] the increased OR of carriage of NM persists in smokers, despite vaccination. A more useful intervention for smokers and their contacts is to recommend they quit. | **Reviewed. No change in recommendations made.** | Comment noted with thanks. A study of vaccination of university students aged 18–24 years in England with Menveo reduced the carriage of serogroup Y by 39.0% (95% CI 17.3–55.0%) and serogroups C/W/Y by 36.2% (95% CI 15.6–51.7%) compared with controls 2 months after vaccination. Reduction in carriage among smokers by vaccination is expected to result in lower risk of disease to the individual and decreased transmission to others, thereby reducing risk of disease.<br><br>Reference: Trotter CL, Maiden MC. *Expert Review of Vaccines* 2009;8:851-61<br><br>The final wording of recommendations in the Handbook will be amended to clarify the rationale for this recommendation. |
| **18d** | Health Protection NSW | Table 1: It is confusing that we are recommending menACWY at 12 months and adolescence, yet this table has "not required" for a booster dose, which is how most people will view the 15 year old dose. | **Reviewed. No change in recommendations made.** | The need for booster doses in healthy children has not been established. Longer term follow-up studies are in progress. |

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| | | | | The current recommendations are based on the need for a dose among adolescents who are not currently vaccinated. The long-term need for a dose in adolescence among cohorts in the future who would have received vaccine at 12 months of age will be assessed in due course.<br><br>Among present cohorts of adolescents who have received a dose of MenACWY vaccine in the past (e.g. due to travel to an endemic area), the need for an additional dose at age 15 years can be assessed on a case-by-case basis. However, an additional dose of vaccine is not harmful, and can be beneficial as it would likely boost immunity. |
| **18e** | Health Protection NSW | Attachment 1: similarly this table is confusing as for Nimenrix and Menactra, and for Menveo from 2+ years, only one primary dose is recommended. What about a second dose at 15 years? | **Reviewed. No change in recommendations made.** | The need for booster doses in healthy children has not been well established. Longer term follow-up studies are in progress. The current recommendations are based on the need for a dose among adolescents who are not currently vaccinated. The need for a dose in adolescence among cohorts who have received vaccine at 12 months of age in the future will be assessed in due course.<br><br>Among present cohorts of adolescents who have received a dose of MenACWY vaccine in |

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| | | | | the past (e.g. due to travel to an endemic area), the need for an additional dose at age 15 years can be assessed on a case-by-case basis. However, an additional dose of vaccine is not harmful, and can be beneficial as it would likely boost immunity. |
| **19a** | Sanofi Pasteur | Page 8, 2d line from the<br>bottom<br>Current doc states<br>*Nimenrix, Menveo and Menoctra*<br><br>Change to:<br>Menactra, Menveo, Nimenrix.<br><br>**Rationale** – list vaccines in alphabetical order as per other chapters | **Reviewed. No change in recommendations made.** | Comment noted with thanks. These are editorial suggestions and will be considered. |
| **19b** | Sanofi Pasteur | Page 4, Table 1 – current doc states:<br>Column 2 (brand)<br>*Menveo*<br>*Nimenrix*<br>*Menactra*<br><br>Change to: | **Reviewed. No change in recommendations made.** | The order of appearance of the brands in the table relates to age-eligibility. |

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| | | Menactra<br>Menveo<br>Nimenrix<br><br>**Rationale** – list vaccines in alphabetical order as per other chapters | | |
| **19c** | | Page 9<br>Current statements:<br>*The differences in immune response between Nimenrix and Menveo are very minor, so either vaccine may be qiven.*<br><br>*However, the level of antibody responses produced after o dose of Nimenrix or Menveo is modestly higher thon that after a dose of Menactra, especially for meningococcal serogroup W and y.7,30,i2 There is also some evidence showing that immunity decreases more quickly with Menactra than with* | **Reviewed. No change in recommendations made.** | While efficacy/effectiveness studies are preferred to immunogenicity studies, only data on effectiveness is available for Menactra. The available effectiveness data shows significant waning of protection over an 8-year period post vaccination with Menactra.<br><br>Licensure and registration of meningococcal vaccines in Australia and internationally have been based on serological correlates of protection. While the validity of serologic cut-offs to predict protection has limitations, ATAGI considers it appropriate and valid to examine the immunogenicity data comparing Menactra with the two other conjugate MenACWY vaccines, as they do provide a basis for comparison in the absence of head to head efficacy or effectiveness studies.<br><br>Clinical trials in adolescents immediately after |

| No. | Organisation | Comment | Proposed Action | Rationale |
|---|---|---|---|---|
| | | *Nimenrix or Menveo. 7,3236*<br><br>*Therefore, ATAGI proposes that either*<br>*Nimenrix or Menveo be given over*<br>*Menactra whenever possible. If*<br>*Nimenrix or Menveo are unavailable,*<br>*Menactra can be given as it will still provide adequate protection against meningococcal disease caused by serogroups A, C, W and Y, and is highly*<br>*preferred to no vaccination.*<br><br>To be removed<br><br>Page 3 and 6, Item 3<br>current statement:<br>*For people Aged >2 years if more thon*<br>*one MenACWY vaccine brand is*<br>*available, either Nimenrix or Menveo*<br>*is preferred to Menactra.*<br><br>To be removed | | vaccination show significantly higher immunogenicity with Menveo or Nimenrix over Menactra, as referenced in the public consultation document. In its assessment of the evidence, ATAGI has considered both published and unpublished data available in the public domain, as well as data provided in-confidence by the vaccine manufacturers.<br><br>Significant differences were still evident at 3 year follow up, as discussed and referenced in the public consultation document. Differences evident at 5 years were non-significant, likely due to smaller numbers affecting the ability to demonstrate ongoing significance.<br><br>These studies indicate that a single dose of Nimenrix or Menveo, compared with a single dose of Menactra, may potentially provide better and/or longer-lasting protection against the meningococcal serogroups of greatest concern in Australia, warranting a preferential recommendation.<br><br>However, Menactra remains one of the MenACWY vaccines recommended for use in |

| No. | Organisation | Comment | Proposed Action | Rationale |
|---|---|---|---|---|
| | | | | Australia. As such, it is acceptable in its current use in state/territory funded programs and would be considered, subject to review and approval by PBAC, in future national programs. A preferential recommendation for the alternatives does not imply otherwise. ATAGI does not recommend any additional vaccination of persons who have received Menactra (unless they have a specific immunocompromising condition that puts them at increased risk of IMD).<br><br>ATAGI's primary role is to provide advice on immunisation policies and programs and guidance on vaccine use based on the best available evidence to maximise protection in Australia. Although other countries do not have a population-based preferential recommendation for all ages, they may have based their considerations on other issues, including that all three MenACWY vaccines are not registered in all the countries specified by Sanofi (including Menactra, which is not registered for use by the EMA). Of note, both the USA and Canada recommend the use of other available MenACWY vaccines (specifically Menveo) over Menactra in children aged <2 years with certain medical conditions that |

| No. | Organisation | Comment | Proposed Action | Rationale |
|---|---|---|---|---|
| | | | | increase their risk of IMD. In Canada, this preferential recommendation is extended to all healthy travellers aged <2 years.<br><br>Comments related to implementation will be managed by Department of Health as per standard processes. |
| **19d** | Sanofi Pasteur | Page 8, current statement<br><br>*'With Menveo, 97% of children developed o protective immune response to oll four serogroups of meningococcal ofter 2 doses.*<br><br>After the sentence about Menveo the following sentence to be added"<br><br>'2 doses of Menactra provided adequate protective response to all serogroups (A 82%,C 100%,Y and W 96%, respectively).<br><br>See Rationale 4 | **Reviewed. No change in recommendations made.** | Appropriate study data documenting adequate immunogenicity with 2 doses in the newly registered age indication for Menactra (9-23 months) will be incorporated into the Handbook. |

| No. | Organisation | Comment | Proposed Action | Rationale |
|---|---|---|---|---|
| **19e** | Sanofi Pasteur | Page 8, current statement<br>*"Two vaccines are available..."*<br><br>Change to<br>*"Three vaccines are available, ... Menactra (from 9 months of age), Menveo and Nimenrix"*<br><br>To be added:<br>*"9-23 months: 2 doses of Menactra (given 3 months apart)"*<br><br>Rationale: Recent TGA decision to lower age limit for Menactra to 9 months | **Reviewed. No change in recommendations made. Changes made to public consultation document.** | Two doses of Menactra (9-23 months) will be incorporated into the Handbook as acceptable dosing for this age range, based on recent approval by TGA for registration. Changes will be made to the public consultation and Handbook recommendations accordingly. |
| **19f** | Sanofi Pasteur | Attachment 1 – page 23<br>Current<br>*Column 4: Menactra 2-55 years*<br>*Column 5: 1 primary dose*<br><br>Change to<br>*9 months - 55 years*<br>*9-23 months - 2 primary doses* | **Reviewed. No change in recommendations made. Changes made to public consultation document.** | Two doses of Menactra (9-23 months) will be incorporated into the Handbook as acceptable dosing for this age range based on recent approval by TGA for registration. Changes will be made to the public consultation and Handbook recommendations accordingly. |

| No. | Organisation | Comment | Proposed Action | Rationale |
|---|---|---|---|---|
| | | *From ≥2 years - 1 primary dose*<br><br>Rationale: Recent TGA decision to lower age limit for<br>Menactra to 9 months | | |

# 3 Appendix A – Public consultation distribution list

An email was sent on 06 April 2018 to the following organisations/committees to provide advice on the consultation:

- Australian Health Protection Principal Committee;
- Communicable Diseases Network Australia;
- National Immunisation Committee;
- Australian Technical Advisory Group on Immunisation;
- Pharmaceutical Benefits Advisory Committee;
- Advisory Committee on Vaccines;
- General Practice Roundtable;
- Royal Australasian College of Physicians;
- Primary Health Networks;
- Consumers Health Forum of Australia; and
- Australian Association of Practice Managers.

Australian Government
Department of Health

**Australian Technical Advisory Group on Immunisation**

**Public consultation on changes to the recommended use of meningococcal and *Haemophilus influenzae* type B vaccines**

The Australian Technical Advisory Group on Immunisation (ATAGI) is consulting with stakeholders on proposed changes to the meningococcal vaccination recommendations for inclusion in *The Australian Immunisation Handbook*, with an intention to submit the recommendations to the National Health and Medical Research Council (NHMRC) for its approval under section 14A of the *National Health and Medical Research Council Act 1992*.

This draft includes new recommendations and the rationale for the proposed changes.

You are invited to make a submission on the draft recommendations by 6 May 2018.

In particular, ATAGI is seeking comments on the following:

- Are there additional potential benefits, harms or unintended consequences which could arise from the proposed changes to the use of meningococcal vaccines, not already outlined, and how likely are they to occur?
- Are there additional clinical or implementation considerations which need to be outlined?

Should you require additional information please contact ATAGI Secretariat on atagi.secretariat@health.gov.au.

## Summary

The Australian Technical Advisory Group on Immunisation (ATAGI), which advises the Australian Government on clinical recommendations for vaccinations, is proposing changes to the recommendations for use of meningococcal and *Haemophilus influenzae* type B vaccines.

The proposed changes reflect the current best clinical practice to prevent invasive meningococcal disease and will be published in *The Australian Immunisation Handbook* online (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10-updates).

Meningococcal disease is a serious infection caused by meningococcal bacteria. In Australia, five serogroups of meningococcal bacteria are found. ATAGI has been monitoring the epidemiology of meningococcal disease in Australia and observed that:

| | |
|---|---|
| serogroup A | is currently extremely rare, but has historically been significant |
| serogroup B | is endemic and has been an important cause of disease for several decades |
| serogroup C | was more common around 15 years ago, but was controlled through the introduction of a nationally-funded meningococcal C vaccination on the National Immunisation Program since 2003 |
| serogroup W | is a new strain which has become more common in Australia |
| serogroup Y | was previously rare, but is now also becoming more common |

Several state and territory governments have introduced vaccination programs for adolescents, including through schools, particularly for protection against the emergence of meningococcal W and Y.

Given changes to the epidemiology of meningococcal disease and recognising the new programs available through states and territories, ATAGI has reviewed the meningococcal chapter of *The Australian Immunisation Handbook*.

## Rationale

The Therapeutic Goods Administration has recently registered:

- Trumenba for protection against meningococcal B in individual ≥10 years;
- Menveo for use among infants and toddlers 2–23 months of age for protection against meningococcal A, C, W and Y;
- Menactra for use among infants and toddlers 9–23 months of age for protection against meningococcal A, C, W and Y.

There is no single meningococcal vaccine in Australia which can protect against all 5 serogroups. Vaccines are available for protection against:

- meningococcal B – the meningococcal B (MenB) vaccines: Trumenba and Bexsero
- meningococcal A, C, W and Y all at the same time – the meningococcal ACWY (MenACWY) vaccines: Menactra, Menveo, Nimenrix
- meningococcal C only – NeisVac-C (serogroup C alone) and Menitorix (combination that also protects against *Haemophilus influenzae* type b; *Hib*).

The review of the meningococcal chapter has prompted a review of the *Haemophilus influenzae* type B (Hib) chapter recommendations, as meningococcal C vaccination on the National Immunisation Program is currently given as a combination vaccine with *Hib*.

The vaccines are able to be used in different age groups and in different dosing schedules. A full list of vaccines and their details is provided in Attachment 1.

**Recommendations**

**A** **ATAGI proposes that the current recommendation in *The Australian Immunisation Handbook* regarding the use of MenC and *Hib* vaccination in children aged 12 months is revoked. Existing recommendations regarding meningococcal vaccination using MenB and MenACWY vaccines, respectively, are retained, as shown in Attachment 2.**

**New and expanded recommendations for meningococcal vaccines are summarised in Recommendation B and for the *Hib* vaccine in Recommendation C below.**

**B** **ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with MenB and MenACWY vaccines.
2. All children aged 2–23 months (<2 years) are recommended to receive MenACWY vaccines (according to an age-based dose schedule as shown in Table 1).
    - Children who have received MenACWY vaccination before 12 months of age should also receive at least one dose of MenACWY vaccine at 12 months of age (refer to Table 1).
3. Adolescents aged 15–19 years are recommended to receive a single dose of MenACWY vaccine.
4. Three MenACWY vaccines are available (Nimenrix, Menveo and Menactra) and recommended for use for protection against serogroups A, C, W and Y. However, among people ≥2 years, if more than one MenACWY vaccine brand is available, a single dose of Nimenrix or Menveo is preferred to a single dose of Menactra.
5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of MenACWY vaccine.
    b) two doses of MenB vaccine.
6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of MenACWY vaccine.
    b) two doses of MenB vaccine.
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive:
    a. MenACWY vaccine (according to an age-based dose schedule as shown in Table 1).
    b. MenB vaccine (according to an age-based dose schedule as shown in Table 2).
8. Infants with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1 below) who are aged 6–11 months old are recommended to receive 3 doses of MenACWY vaccine (instead of 2 doses) (refer to Table 1).

**C ATAGI proposes that the 4th dose of *Hib* vaccine is now recommended at 18 months of age (rather than age 12 months).**

***Detailed overview of ATAGI recommendations***

List 1 shows the specified medical conditions that are associated with increased risk of meningococcal disease. People with these conditions are recommended to receive additional vaccine doses.

Tables 1 and 2 show the proposed ATAGI recommended dosing schedule for the three available conjugate MenACWY vaccines and the two available MenB vaccines, respectively, and according to the new recommendations described above. The number of doses required depends on the age when vaccination is started, the vaccine brand used and whether the person receiving the vaccine has a specified medical condition associated with increased risk of meningococcal disease.

**List 1: Specified medical conditions associated with increased risk of meningococcal disease**

- defects in or deficiency of complement components, including factor H, factor D or properdin deficiency
- current or future treatment with eculizumab (a monoclonal antibody directed against complement component C5)
- functional or anatomical asplenia
- HIV infection, regardless of stage of disease or CD4+ count
- haematopoietic stem cell transplant

**Note: This list is unchanged from the conditions specified in the current online chapter of *The Australian Immunisation Handbook***

**Table 1: ATAGI recommendations for immunisation using MenACWY vaccines, by age and vaccine brand, showing the number of doses required and minimum intervals**

| Age at commencement of vaccine course | MenACWY vaccine brand* | Without any medical conditions (associated with increased risk of meningococcal disease on List 1) | With specified medical conditions (associated with increased risk of meningococcal disease on List 1) | Eligibility for funding through national or state-based immunisation programs[#] |
|---|---|---|---|---|
| 6 weeks–5 months | Menveo or Nimenrix[†] | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age or 8 weeks after 2nd dose, whichever is later) | 4 doses<br>(8 weeks between doses; 4th dose at 12 months of age or 8 weeks after 3rd dose, whichever is later) | Infant schedule not funded<br><br>Note: 1 dose of Nimenrix funded at age 12 months under the NIP from July 2018 |
| 6–8 months | Menveo or Nimenrix[†] | 2 doses<br>(2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later) | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age or 8 weeks after 3rd dose, whichever is later) | Infant schedule not funded<br><br>Note: 1 dose of Nimenrix funded at age 12 months under the NIP from July 2018 |
| 9–11 months | Menveo or Nimenrix[†] or Menactra[§] | 2 doses<br>(2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later) | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at least 8 weeks after 2nd dose) | Infant schedule not funded<br><br>Note: 1 dose of Nimenrix funded at age 12 months under the NIP from July 2018 |
| 12–23 months | Menveo | 2 doses<br>(8 weeks between doses) | 2 doses[‡]<br>(8 weeks between doses) | 1 dose of Nimenrix funded at age 12 months under the NIP from July 2018<br><br>2nd dose for Nimenrix for individuals with a medical condition in List 1 not funded<br><br>Doses of Menveo or Menactra are NOT funded under any program. |
| | Nimenrix | 1 dose | | |
| | Menactra[†] | 2 doses<br>(8 weeks between doses) | | |
| 2–14 years | Any brand | 1 dose | 2 doses<br>(8 weeks between doses) | Not funded |
| 15–19 years | Any brand | 1 dose | 2 doses<br>(8 weeks between doses) | State-funded MenACWY vaccination programs (using differing brands) in all states except SA and NT |
| 20–24 years | Any brand | 1 dose | 2 doses<br>(8 weeks between doses) | Not funded |
| ≥25 years** | Any brand | 1 dose | 2 doses<br>(8 weeks between doses) | Not funded |
| Booster doses for all ages | Any brand | Not required | For those with ongoing increased risk for IMD who completed age-specific primary vaccination at: | Not funded |

| Age at commencement of vaccine course | MenACWY vaccine brand* | Without any medical conditions (associated with increased risk of meningococcal disease on List 1) | With specified medical conditions (associated with increased risk of meningococcal disease on List 1) | Eligibility for funding through national or state-based immunisation programs[#] |
|---|---|---|---|---|
| | | | a) **≤6 years of age:**<br>Give a booster dose at 3 years after completion of primary immunisation schedule,<br>then every 5 years thereafter<br>b) ≥7 years of age:<br>Give a booster dose every 5 years after completion of the primary immunisation schedule | |

Abbreviations: NT – Northern Territory; QLD – Queensland; SA – South Australia; WA – Western Australia

* Wherever possible, Nimenrix or Menveo should be used in preference to Menactra.

\# Information current as of 17 May 2018.

† Use of Nimenrix in this age group is considered a variation to the Product Information, as it is registered for use from 12 months of age as of May 2018. ATAGI's recommendation to use Nimenrix in this age group is based on data from clinical trials.

§ Do not co-administer Menactra with 13vPCV (Prevenar 13). If Menactra is used, there should be a minimum interval of 4 weeks between the dose of 13vPCV and Menactra. Other MenACWY vaccines (Menveo or Nimenrix) may be co-administered with 13vPCV.

‡ For those with specified medical conditions aged 12–23 months, 2 doses of either Menveo, Menactra or Nimenrix are required.

** There is no registered upper age limit for use of Menveo. Although both Menactra and Nimenrix are registered for use up to 55 years of age only, either of these brands can be given to people over 55 years of age, as per *The Australian Immunisation Handbook.*

**Table 2: ATAGI recommendations for immunisation using MenB vaccines, by age and vaccine brand, showing the number of doses required and minimum intervals**

| Age at commencement of vaccine course | MenB vaccine brand | Without any medical conditions associated with increased risk of meningococcal disease on List 1 | With any specified medical conditions associated with increased meningococcal disease on List 1 |
|---|---|---|---|
| 6 weeks–5 months | Bexsero | 4 doses<br>(8 weeks between doses; 4th dose at 12 months) | 4 doses<br>(8 weeks between doses; 4th dose at 12 months or 8 weeks after 3rd dose, whichever is later) |
| 6–11 months | Bexsero | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later) | 3 doses<br>(8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later) |
| 12 months–9 years | Bexsero | 2 doses<br>(8 weeks between doses) | 2 doses<br>(8 weeks between doses) |
| ≥10 years* | Bexsero | 2 doses<br>(8 weeks between doses) | 2 doses<br>(8 weeks between doses) |
| | Trumenba | 2 doses<br>(6 months between doses) | 3 doses<br>(At least 4 weeks between 1st and 2nd doses; 3rd dose at least 4 months after 2nd dose and at least 6 months after 1st dose) |

* Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the primary vaccination course.

## Research evidence

***Recommendations A and B 1-4***

**A ATAGI proposes that the current recommendation in *The Australian Immunisation Handbook* regarding the use of MenC and *Hib* vaccination in children aged 12 months is revoked. Existing recommendations regarding meningococcal vaccination using MenB and MenACWY vaccines, respectively, are retained as shown in Attachment 2.**

**New and expanded recommendations for meningococcal vaccines are summarised in Recommendation B and for the *Hib* vaccine in Recommendation C below.**

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with MenB and MenACWY vaccines.

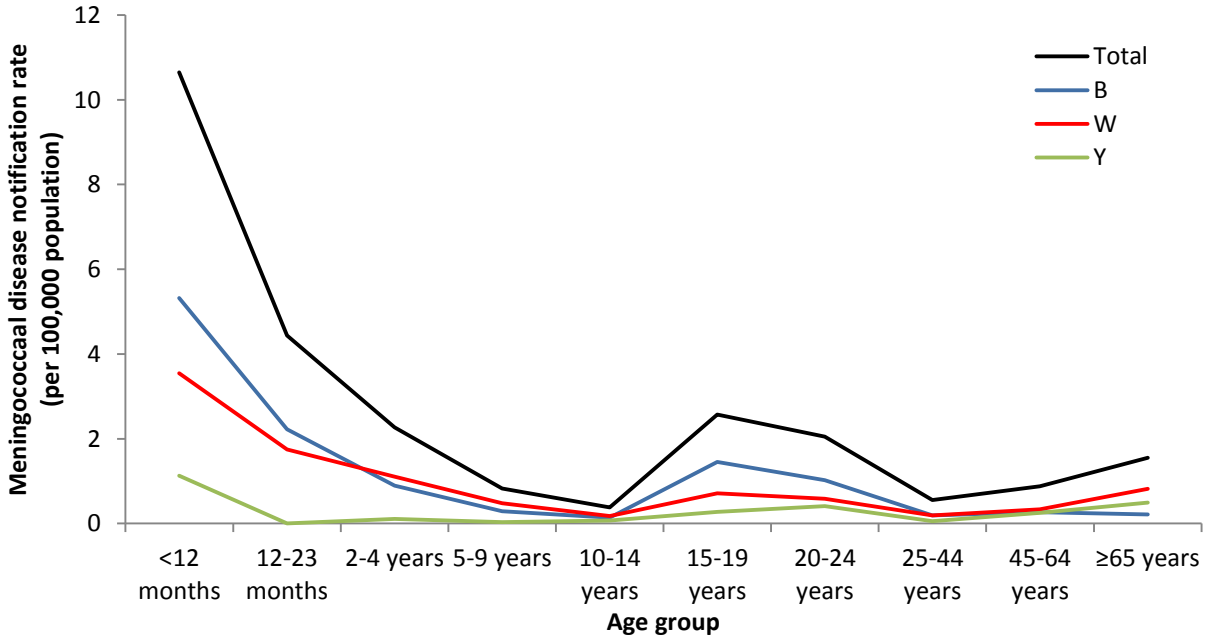
The meningococcal serogroups that cause meningococcal disease have been changing in the last few years. Since 2013, the occurrence of meningococcal W disease has been increasing rapidly. Many meningococcal W cases are caused by a strain (sequence type ST 11) associated with severe disease and a higher risk of death.[1] A smaller yet steady rise in the occurrence of meningococcal Y disease has also been seen since 2016.

Meningococcal B has historically caused the majority of meningococcal disease in Australia and it continues to cause around half of all reported cases of meningococcal disease. In the 17-year period between 1999 and 2015, serogroup B was the most common serogroup causing meningococcal disease.[2]

Data from recent years show that young children aged <2 years have the highest rates of new cases reported, particularly for disease caused by serogroup W. Among these young children, meningococcal disease due to serogroup W occurs most often in infants between 3 and 5 months of age. Serogroup B has historically affected the youngest people in the population, and has been most common in infants and children <2 years.[2] This trend has continued in recent years (Figure 1). Vaccination with MenB and MenACWY vaccines can prevent disease in this higher risk age group. A high number of meningococcal disease cases also occur among adolescents aged 15–19 years (Figure 1).

People can carry the meningococcal bacteria in their throat and/or nose (i.e. ‘carriage’), with studies showing that adolescents and young adults have the highest carriage rates of meningococcal bacteria.[3] Vaccinating populations with high carriage rates is critical to achieve protection of the community more broadly (community or herd immunity).

**Figure 1: Age-specific rates of meningococcal disease by serogroup and age group, Australia, 2016–2017***




*Data is for cases with a diagnosis date from 1 January 2016 onwards, as of 14 December 2017. Rates for 2017 have not been annualised. Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

2. All children aged 2–23 months (<2 years) are recommended to receive MenACWY vaccines (according to an age-based dose schedule as shown in Table 1).
    - Children who have received MenACWY vaccination before 12 months of age should also receive at least one dose of MenACWY vaccine at 12 months of age (refer to Table 1).
3. Adolescents aged 15–19 years are recommended to receive a single dose of MenACWY vaccine.
4. Three MenACWY vaccines are available and recommended for use for protection against serogroups A, C, W and Y (Nimenrix, Menveo and Menactra). However, among people ≥2 years, if more than one MenACWY vaccine brand is available, a single dose of Nimenrix or Menveo is preferred to a single dose of Menactra.

### *Safety of MenACWY vaccines*

MenACWY vaccine safety has been shown in multiple clinical trials and large population studies (conducted in countries after the vaccines have become available) in people of different ages, from infants to adults.[4-19] The vast majority of reactions after vaccination are mild and resolve on their own. MenACWY vaccines are safe for use in patients with human immunodeficiency virus (HIV) infection.[20,21]

MenACWY vaccines can be safely administered at the same time as other routine vaccines provided to young children through the National Immunisation Program. Clinical trials in young children have included giving MenACWY vaccines with:

- diphtheria-tetanus-acellular pertussis (DTPa) combination vaccines (which included hepatitis B vaccine, inactivated polio vaccine [IPV] and/or *Hib* vaccine),
- 7-valent pneumococcal conjugate vaccine (7vPCV) and 13-valent PCV (13vPCV),

- rotavirus vaccine,
- hepatitis A vaccine,
- measles-mumps-rubella (MMR) vaccine,
- measles-mumps-rubella-varicella (MMRV) vaccine.[6,12-15,22-25]

In adolescents, clinical trials have included giving MenACWY vaccines with:

- 4-valent and 9-valent human papillomavirus (HPV) vaccine,
- diphtheria-tetanus-acellular pertussis (dTpa) vaccine,
- combined hepatitis A and B vaccine and seasonal influenza vaccine.[26-31]

In most studies, the frequencies of reactions following vaccination were similar regardless of whether the vaccines were given together or separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

***Immune responses to MenACWY vaccines and their dose schedules***

Invasive meningococcal disease is rare; studies assessing the effectiveness of vaccination in preventing IMD are difficult to conduct due to the requirement to vaccinate very large numbers of people and follow them for long periods of time to demonstrate a benefit. As an alternative, studies with meningococcal vaccines measure and report the immune response to the vaccines. This information is used to indicate how effective the vaccine is likely to be and support registration of the vaccines. An immune response is considered to have occurred if antibodies are detected above a standard threshold that is likely to be protective against the disease. The proportion of vaccinated people who develop antibodies above this threshold is taken into account when making vaccine recommendations.

The number and spacing of meningococcal vaccine doses vary by brand and the age the vaccination commences. There is currently no recommendation for additional or booster doses among healthy individuals in any age group (other than those who are travelling to a country where there is a high risk of getting meningococcal disease, or who have an occupational risk) once the age-appropriate primary course of either Nimenrix, Menveo or Menactra is completed.

*i) Children aged <2 years at commencement of vaccination*

ATAGI proposes the following vaccination schedules in children aged <2 years (refer to Table 1 in Recommendations section above). The number of doses required is different depending on how old the child is when they receive their first dose, as shown in Table 1.

As the highest rates of meningococcal disease occur very early in life, it is highly desirable to start vaccination as early as possible so that infants can develop an immune response early. Clinical trials have shown that Menveo and Nimenrix are safe to use in children from 2 months of age.[11-14,32] When given in a 3-dose schedule at 2, 4 and 12 months of age, more than 99% of children in clinical trials of Menveo or Nimenrix developed protection against meningococcal W and Y after the completion of the course.[14,32]

For children who commence vaccination at age 6 to <12 months, a 2-dose schedule with Menveo produces a good immune response. In one large study with over 1,600 participants, more than 96% of children given 2 doses of Menveo at age 7–9 months and 12 months developed protection against meningococcal C, W and Y.[15] Another smaller study showed that 100% of children who received Menveo at 6 and 12 months of age produced an immune response against meningococcal C, W and Y after the second dose.[17] In both studies, the response to meningococcal A was slightly lower (87-88%).

Although Menveo is currently registered in a 2-dose schedule from 7 months onwards, data from these clinical trials showed that the immune response in children starting vaccination at 6 months of age was similar. The 6-months schedule point is well-established and accepted in Australia, with consistently high vaccine coverage.[33]

Regarding Nimenrix, a study showed that among those given Nimenrix at 6 and 15–18 months of age, 94% developed an immune response against all four meningococcal serogroups after the first dose at 6 months, with all but 1 out of 139 vaccinated subjects having a protective response to all four serogroups after the booster dose in the second year of life.[34] In another study, a 2-dose schedule of Nimenrix given at age 9 and 12 months produced immune responses against all four serogroups in 98% of vaccinated infants after the first dose and in all children after the second dose.[35]

A 2-dose schedule with Menactra produces a good immune response in infants and children 9 months of age and older after the second dose. In a small study of infants aged 9 months who were given 1 dose of Menactra, the proportion of infants who had an immune response was low, especially against serogroups W and Y (20–27% of children). However, after a second dose was given at either 12 or 15 months of age, more than 92% of children had an immune response against serogroups C, W and Y and 89% against serogroup A.[36] A larger study showed similar results, although the proportion of children who had an immune response against serogroup W was slightly lower (between 81–88%).[25]

All three MenACWY vaccines (Nimenrix, Menveo and Menactra) are registered for use in children aged 12–23 months of age. Because of differences in some of the vaccine components, there are differences in the level of immune response produced. However, the vaccines have been shown to produce immune responses in the vast majority of children 1 month after vaccination when given in the appropriate schedule. Data from clinical studies have shown that 1 dose of Nimenrix produces an immune response against all four meningococcal serogroups (A, C, W and Y) in over 97% of children in this age group.[6,7,23,24] With Menveo, 97% of children developed a protective immune response to all four meningococcal serogroups after 2 doses.[11] Two doses of Menactra given at 12 and 18 months of age resulted in more than 96% of children developing a protective immune response against all four meningococcal serogroups.[37]

*ii) Children aged ≥2 years, adolescents and adults at commencement of vaccination*

ATAGI proposes that children aged ≥2 years, adolescents and adults receive a single dose of MenACWY vaccine for protection against meningococcal disease caused by serogroups A, C, W and Y. Of note, in this population of people aged ≥2 years, the highest rates of meningococcal disease occur in adolescents aged 15–19 years. Therefore, vaccination for adolescents aged 15–19 years is particularly recommended.

There are three registered MenACWY vaccines available for people aged ≥2 years: Nimenrix, Menveo and Menactra. Each of these produces an immune response against the four meningococcal serogroups included in the vaccine when given as a single dose.[8,10,26,27,38-40]

In studies with adolescents, 67–100% of recipients of a MenACWY vaccine developed an immune response.[4,10,26,27,38,39,41] Population data collected in the United States showed that Menactra was 79% effective in preventing clinical infection in a population during the first year after vaccination.[42]

*iii) Choice of MenACWY vaccine brand*

Because of differences in the components of the vaccines, there are differences in the level of immune response produced by the three vaccines. It is not certain that these differences will have an

impact on a person's protection against meningococcal disease; however, as population-level data on the effectiveness of all three vaccines are lacking, data on immune responses of subjects in clinical trials have been taken into account in the following proposed recommendations.

Choice of MenACWY vaccine brand among people ≥2 years old

ATAGI proposes that either Nimenrix or Menveo be given in preference to Menactra among people aged ≥2 years. If Nimenrix or Menveo are unavailable, Menactra can be given at an appropriate age as it will still provide adequate protection against meningococcal disease caused by serogroups A, C, W and Y, and is highly preferred to no vaccination.

The differences in immune responses between Nimenrix and Menveo are very minor, based on studies in young children (see below) and adolescents.[43] Either vaccine may be given as a single dose in those aged ≥2 years.

Data from some clinical trials in adolescents and adults indicate that the immune responses produced after a single dose of Nimenrix or Menveo are better than after a dose of Menactra. This is especially true for the immune response against meningococcal serogroups W and Y which are the most common of the four vaccine serogroups in Australia. Both the proportion of subjects who had an immune response above the standard threshold and the level of antibodies produced against serogroups W and Y were better following vaccination with Nimenrix or Menveo than with Menactra.[8,19,38,40] Another study comparing Menactra with Menveo in children aged 2–10 years found results similar to the adolescent studies, i.e. that immune responses against serogroups W and Y were higher with Menveo than with Menactra.[44]

Data from vaccinated adolescents in the United States has shown that the effectiveness of Menactra declines over time (from 79% in the first year after vaccination to 69% between 1 and 3 years after vaccination, and to 61% between 3 and 8 years after vaccination). During this follow-up time, cases of meningococcal disease occurred in people who had received the vaccine.[42] Although there is no population use data on effectiveness of Nimenrix or Menveo, some evidence from clinical trials shows that antibody levels were lower several years after vaccination with Menactra than with Nimenrix or Menveo.[8,40,45]

Choice of MenACWY vaccine brand among infants and toddlers <2 years old

ATAGI proposes that any one of the three available MenACWY vaccines can be given to infants and toddlers aged <2 years, in their respective age-appropriate schedules,.

A study[i] of 1 dose of either Nimenrix or Menveo in toddlers aged 12–15 months found that a similar proportion of children developed a protective immune response immediately after vaccination.[16] However, 6 months after vaccination, the proportion of children with protective antibody levels was lower with Menveo than with Nimenrix. Of note, this study used a single dose schedule of Menveo, whereas a 2-dose schedule in this age group is recommended and is expected to have similar protection to 1 dose of Nimenrix. Therefore, the recommended schedules for toddlers aged 12–23 months for Nimenrix (single dose) and Menveo (2 doses) are considered to be equivalent.

There are no clinical trials directly comparing Menactra with either Nimenrix or Menveo in infants and toddlers aged <2 years. Clinical trials of Menactra indicated that immune responses after 1 dose were inadequate for protection, but that 2 doses resulted in protective immune responses in more than 92% of vaccinated children.[36,37] Results of comparative clinical trials in adolescents cannot be generalised to infants and toddlers <2 years as those studies compared a single dose of Menactra with a single dose of either Nimenrix or Menveo, whereas a 2 dose schedule of Menactra is recommended in infants and toddlers <2 years.

[i] Includes review of published data and unpublished data provided in-confidence by the vaccine manufacturer

As there is no evidence that any of the MenACWY vaccines provides better protection than the others when given in the age-appropriate schedules, any MenACWY vaccine can be used for infants and toddlers <2 years, according to their respective age-appropriate schedules.

However, there are possible concerns regarding concurrent administration of Menactra with some other vaccines routinely given to infants and toddlers. Specifically, a study has shown that co-administration with a pneumococcal conjugate vaccine can lead to lower immune responses to certain pneumococcal serotypes,[25] which could potentially reduce the protective benefit against pneumococcal disease expected from the vaccine. Therefore, as a precautionary measure, Menactra should not be co-administered with 13-valent pneumococcal vaccine (13vPCV). Recently, the NIP schedule was amended to give the final dose of 13vPCV at the age 12-month schedule point and is expected to be implemented in the latter half of 2018.

Additionally, some studies in young children (aged 4–6 years) and adolescents have shown that receiving Menactra one month after diphtheria-tetanus-acellular pertussis combination vaccines can lead to lower immune responses against the meningococcal serotypes.[46,47] Clinical guidance will be provided for infants and toddlers <2 years who may require catch-up of meningococcal vaccination close to the 18-month NIP schedule point (when DTPa is administered).

***Recommendation B5***

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of MenACWY vaccine.
    b) two doses of MenB vaccine.

Adolescents and young adults have the highest rates of meningococcal carriage (i.e. presence of meningococcal bacteria in the upper respiratory tract without any signs or symptoms of infection) and are thought to play an important role in how the bacteria are transmitted in a community.[3] Living in close or prolonged contact with a person who is carrying meningococcal bacteria can increase a person's chances of acquiring the bacteria.[48-50]

A clinical study of vaccination with Menveo in 18-24 year-old university students showed that there were reductions in meningococcal carriage among those who were vaccinated.[51] This reduction of the chances of transmission of the meningococcal bacteria is thought to reduce the risk of meningococcal disease occurring.

As Australian data show that the risk of meningococcal disease caused by serogroup B is also high among adolescents and young adults aged 20–24 years (compared with other age groups) (refer to Figure 1 above), ATAGI is proposing that the existing recommendation for MenB vaccination (currently for ages 15–19 years as per *The Australian Immunisation Handbook*) be extended to also include those aged 20–24 years.

***Recommendation B6***

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of MenACWY vaccine.
    b) two doses of MenB vaccine.

Smoking tobacco is known to increase the risk of carrying the meningococcal bacteria in the upper respiratory tract and of passing the bacteria to close contacts. Active smokers are at greater risk of meningococcal disease as they have high meningococcal carriage rates, which are approximately 1.5–2 times higher than those found in non-smokers.[52]

In a study of 14,000 teenagers aged 15–19 years, twice as many active smokers were carrying meningococcal bacteria compared with non-smokers, even after accounting for other risk factors known to impact carriage.[53] A study of meningococcal disease cases in Queensland found that regular smoking or passive exposure to tobacco smoke were risk factors for developing IMD at any age.[54] The risk of meningococcal carriage increases with heavier smoking[55] and studies have also shown adolescents in close contact to smokers are more likely to develop meningococcal disease.[53,54,56,57]

Vaccinating smokers can, therefore, reduce both the risk of meningococcal disease as well as carriage of the meningococcal bacteria in a person. By preventing carriage, transmission of the bacteria to others in the population can be reduced. As adolescents and young adults aged 15–24 years have the highest rates of meningococcal carriage,[3] the greatest possible individual-level and population-wide benefits are likely to be attained by vaccinating smokers aged 15–24 years. As 15–19 year olds are already recommended to receive MenACWY vaccine (as per recommendation B3), ATAGI proposes extending the recommendation for MenACWY vaccine to also include smokers aged 20–24 years.

***Recommendation B7***

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

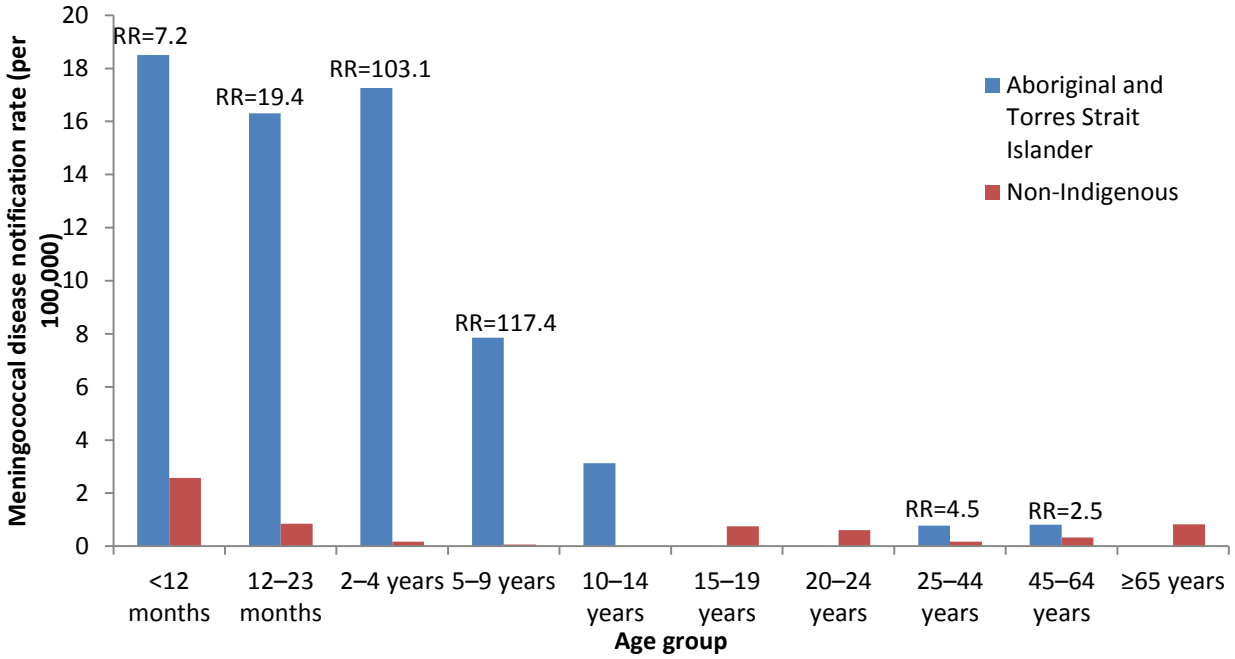
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive:
    a. MenACWY vaccine (according to an age-based dose schedule as shown in Table 1).
    b. MenB vaccine (according to an age-based dose schedule as shown in Table 2).

Aboriginal and Torres Strait Islander Australians have much higher incidence rates of meningococcal disease compared to non-Indigenous Australians. This is particularly observed among children aged <15 years for the two most common meningococcal serogroups B and W.

During 2012–2017, the incidence rate of meningococcal disease caused by serogroup W was higher in Aboriginal and Torres Strait Islander children aged <5 years (3.10 versus 0.34 per 100,000; rate ratio=9.1).

More recently in 2016–2017, this disparity was even more striking, with meningococcal disease rates among Aboriginal and Torres Strait Islanders being greater than 100 times those observed among non-Indigenous Australians in certain age groups (refer to Figure 2). This has been partly due to the outbreak of serogroup W disease in Central Australia which particularly affected young Aboriginal and Torres Strait Islander people in remote communities.

**Figure 2: Notification rates for meningococcal disease caused by serogroup W and rate ratio for Aboriginal and Torres Strait Islanders compared with non-Indigenous people, by age group, 2016–2017***

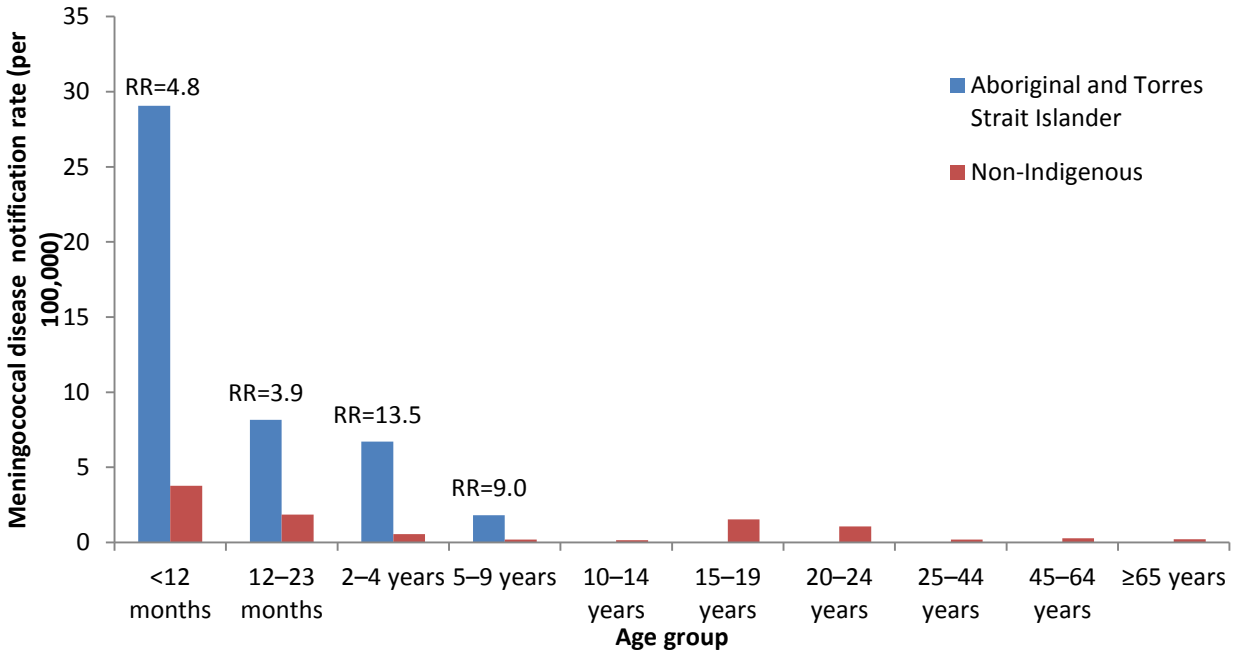



RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised.
Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

In 2016–17, there was a substantial disparity in the reported cases of meningococcal disease caused by serogroup B between Aboriginal and Torres Strait Islander people compared with non-Indigenous Australians, particularly among children aged <10 years old (refer to Figure 3).

This trend is longstanding. Between 2006 and 2015, rates of meningococcal disease caused by serogroup B disease were reported as being 3.4 times and 3.8 times higher among Aboriginal and Torres Strait Islander infants aged <12 months and children aged 1–4 years, respectively, compared with non-Indigenous infants and children of the same age.[2] Rates of serogroup B disease among older children up to and including age 14 years are also elevated in Aboriginal and Torres Strait Islander children compared with non-Indigenous children, occurring 6.3 times and 2.5 times among Aboriginal and Torres Strait Islander children aged 5–9 years and 10–14 years, respectively, compared with non-Indigenous children of the same age.[2]

**Figure 3: Notification rates for meningococcal disease caused by serogroup B and rate ratio for Aboriginal and Torres Strait Islanders compared with non-Indigenous people, by age group, 2016–2017***




RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised. Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

***Recommendation B8***

**B ATAGI proposes the following NEW expanded recommendations for the use of meningococcal vaccines in Australia.**

8. Infants with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1 below) who are aged 6–11 months old are recommended to receive 3 doses of MenACWY vaccine (instead of 2 doses) (refer to Table 1).

Clinical trials of Menveo and Menactra in infants aged 6–11 months and 9–11 months, respectively, have only examined immune responses after 1 or 2 doses of the vaccine. No studies have examined immune response after 3 doses and no studies have been conducted in infants or young children with the specified medical conditions in List 1.

However, clinical studies of Menveo in young healthy infants starting vaccination at age 2 months show that immune responses were better after a third dose (given 6 months of age) compared with immune responses after a second dose (given at 4 months of age).[14] There are no studies of 3-dose primary schedules with Menactra; however there is some concern that immune responses to Menactra may be slightly lower than the other MenACWY vaccines (see Recommendation B4 above). Therefore, an additional dose of Menactra is recommended for infants with these specified medical conditions if Menactra is to be used (from age 9 months). This is consistent with the same principle used for the dosing schedule of the other MenACWY vaccines.

While the differences in immunity are minor and likely to be unimportant in a healthy infant, ATAGI considers the higher risk of disease in an infant with a specified medical condition justifies

the extra dose of vaccine. Studies with Menactra in older children and adolescents with HIV infection have shown that 2 doses, rather than 1, are required for an adequate immune response.[20,58]

Studies with meningococcal C vaccines have also shown that people with immunocompromising medical conditions have a lower immune response to vaccination and require additional doses.[59-63]

Extrapolating from these research findings, ATAGI considers a 3-dose course of Menveo or Menactra (refer to Table 1 for dosing schedule) to be appropriate for infants commencing vaccination at age 6–11 months or 9–11 months, respectively, with a specified medical condition. The extra dose given to infants, compared with infants without specified medical conditions, is similar to the schedule for older age groups, for whom an additional dose is currently recommended.

***Recommendation C***

**C ATAGI proposes that the 4th dose of *Hib* vaccine is now recommended at 18 months of age (rather than age 12 months)**

A 4th dose of *Hib* vaccine in the second year of life (in addition to the 3 doses given at 2, 4 and 6 months of age) is required to ensure long-term protection against *Hib* disease. A review of *Hib* cases from 1996 to 2013 found that more than half were either unimmunised or partially vaccinated.[64]

Currently, a 4$^{th}$ *Hib* vaccine dose is given at 12 months of age using the combination vaccine brand, Menitorix, which includes both *Hib* and meningococcal C.

In January 2018, the Pharmaceutical Benefits Advisory Committee recommended the listing of Nimenrix on the NIP for infants 12 months of age.

The introduction of a MenACWY vaccine at 12 months of age means the meningococcal C component of Menitorix will no longer be required and the 4$^{th}$ dose of *Hib* can be given in a monovalent formulation (i.e. containing only *Hib*).

In addition, the Chief Executive Officer of the National Health and Medical Research Council agreed to amend a pneumococcal recommendation in the Australian Immunisation Handbook, proposed by ATAGI in late 2017, to move the 3$^{rd}$ dose of the infant pneumococcal vaccine from 6 months to 12 months.

ATAGI has reviewed the epidemiology of all of the diseases with a vaccine scheduled at 12 months and proposes that the 4$^{th}$ dose of *Hib* be moved to the 18-month schedule point to reduce the number of vaccines given at 12 months of age.

Analysis of data on *Hib* disease in Australia found that between 1993 and 2016, only 17 cases of invasive *Hib* disease occurred in partially vaccinated children aged 6–23 months, with the majority (n=15/17) not having completed the initial 3-dose infant course (usually given at 2, 4 and 6 months of age).

In the United States, deferring the *Hib* booster dose by 18 months in response to a vaccine supply shortage did not cause an increase in the incidence of invasive *Hib* disease.[65]

On the basis of this information, ATAGI believes that moving the schedule point for the *Hib* booster dose from age 12 months to 18 months is unlikely to result in more cases of *Hib* in Australia.

## Additional information to be included in *The Australian Immunisation Handbook*

***Information on Trumenba, a newly registered MenB vaccine***

Trumenba is a newly available alternative vaccine that provides protection against meningococcal disease caused by meningococcal serogroup B and is registered and suitable for use in people aged ≥10 years. Trumenba was licensed for use in Australia in September 2017 and has been supplied since early 2018. Clinical trials have shown that Trumenba is a safe and effective vaccine for use in adolescents and young adults.

Trumenba can be used in a 2-dose or a 3-dose schedule depending on the patient's risk of meningococcal disease[ii].[66,67] Among people aged 11–18 years, immune responses above the predefined protective threshold were produced in 82–83% of participants after 3 doses of Trumenba given at 0, 1 and 6 months or 0, 2 and 6 months, and in 73.5% of participants after 2 doses given at 0 and 6 months.[66] Several clinical trials in people aged 10–25 years have also shown that both 3-dose and 2-dose schedules are safe and can be administered with other vaccines.[66-70]

The recommended dosing schedule (3 doses or 2 doses) depends on the patient's level of risk of meningococcal disease. ATAGI proposes that adolescents without specific medical conditions, who have a lower risk of meningococcal disease, receive 2 doses of Trumenba. However, it is preferable that adolescents with a specified medical condition (refer to List 1), who have a higher risk of meningococcal disease, get the greatest protection as early as possible. The 3-dose schedule provides more rapid protection within the first 2 months of commencing vaccination, and the 3rd dose at 6 months ensures long term effectiveness. This is particularly important for these at-risk individuals, in whom responses to the 2-dose schedule may be suboptimal. Therefore, the 3-dose schedule of Trumenba is recommended for people with medical conditions listed in List 1.

There is no preference for the use of Trumenba or Bexsero for the prevention of meningococcal B disease. However, the vaccines should not be used interchangeably, that is, a person who has a first dose of one brand of meningococcal B vaccine should complete the course with the same brand.

### Benefits/Harms

There are five key benefits from these proposed changes to the use of meningococcal vaccines:

1. Vaccination with MenACWY vaccine will provide protection to those age and population groups with the highest reported incidence rates of meningococcal disease; this is particularly true for disease caused by serogroups W and Y, the two serogroups that have emerged and contributed significantly to the total number of meningococcal disease cases in the past 2 years.
2. High uptake of MenACWY vaccine among adolescents has the potential to stop transmission of meningococcal bacteria in the community and provide community (herd) protection to other members of the population even if they are not vaccinated.
3. Vaccination of additional age groups (specifically 2–14 year olds) among Aboriginal or Torres Strait Islander Australians with MenACWY and MenB vaccines can address the large gap in the meningococcal disease burden compared with non-Indigenous Australians.
4. Additional vaccination recommendations to protect adolescents and young adults living in close quarters and those who are smokers can provide protection against the meningococcal serogroups that cause the majority of meningococcal disease in these high-risk individuals, and also reduce transmission.
5. An additional dose of MenACWY vaccine given to infants aged 6–11 months with specified medical conditions diagnosed in infancy, who are most vulnerable to meningococcal disease, will provide them with additional protection against meningococcal disease

[ii] [ii] Includes review of published data and unpublished data provided in-confidence by the vaccine manufacturer

compared with the dosing recommendations for healthy infants, especially disease caused by serogroups W and Y.

There are potential concerns that may arise from the proposed changes to the use of meningococcal vaccines:

1. *Potential concern of 'schedule crowding'*

   ATAGI has a strong preference for avoiding adding new National Immunisation Program vaccination schedule points and multiple visits for vaccinations scheduled at the same point. Vaccination with MenACWY vaccine from infancy and shifting the 4th dose of *Hib* vaccine will increase the number of vaccines administered at the 18-month schedule point. Non-Indigenous children without specified medical conditions will receive a maximum of 3 injections at both the 12- and 18-month schedule points. However, with the proposed changes, Aboriginal and Torres Strait Islander children living in four jurisdictions (Western Australia, South Australia, Northern Territory and North Queensland) will receive at least 4 injections at both the 12- and 18-month schedule points (because of the additional hepatitis A vaccine doses). In addition, children with various medical conditions (including but not limited to those in List 1) may require additional doses of other vaccines. This may impact acceptability for these population groups and may require additional visit(s) to receive all the recommended vaccines, which can affect compliance with the recommended schedule.

2. *Potential increased frequency and/or severity of adverse events due to a greater number of vaccinations being co-administered*

   Clinical trials have documented the general safety of MenACWY vaccines when given together with multiple routinely administered vaccines in both children aged <2 years and adolescents. In most studies, rates of adverse events when MenACWY and other vaccines were given together were similar to those when vaccines were given separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

3. *Potential for increased number of Hib cases occurring prior to the booster dose scheduled at 18 months of age.*

   Based on available Australian data and on the experience from a comparable situation in the United States, the postponement of the Hib dose from 12 months to 18 months is unlikely to lead to an increased number of Hib disease cases among children aged 12–18 months. In Australia, there has been a low number of Hib vaccine failures in the past two decades and a high population Hib vaccination coverage and community immunity. While an increase in Hib disease cases occurring among children aged 12–18 months who have received 3 primary doses of Hib-containing vaccine in infancy is not expected, there will be ongoing surveillance to detect any changes in the number of Hib cases in relation with age and vaccine-doses received.

**Preference and values**

The proposed changes to the use of meningococcal vaccines are in line with the best available clinical advice and with the ages for which the vaccines are currently registered. It is anticipated that use of the available meningococcal vaccines will result in additional protection for people most at risk and the wider community (including those who are not vaccinated) against meningococcal disease. This is considered consistent with societal expectations of the best use of vaccines in Australia, including vaccination use in the National Immunisation Program. Also, there has been substantial media interest in meningococcal vaccines following cases of meningococcal disease in young children and adolescents, and feedback from clinicians indicates a growing demand among parents for use of these vaccines especially for their young children. In 2017–2018, most states and territories initiated adolescent vaccination programs with MenACWY vaccine which were well-received, showing the importance of these vaccines in preventing this rare but serious condition.

**Resources and other considerations**

Product Information for Nimenrix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02123-1

Product Information for Menveo is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-02475-3

Product Information for Menactra is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-01448-1

Product Information for Bexsero is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02131-1

Product Information for Trumenba is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-PI-02674-1

Product Information for Hiberix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05633-3

**Practical information**

Communication to providers will need to be made clear in *The Australian Immunisation Handbook* and other guidance to minimise confusion and ensure smooth implementation of these proposed changes in recommendations. In particular, the availability of three MenACWY vaccines and two MenB vaccines, all registered in different schedules for different age groups, may cause confusion among immunisation providers. The shift in the schedule point for the 4$^{th}$ dose of *Hib* from 12 to 18 months of age may cause further confusion in the initial stages of implementation of the revised vaccination schedule. Clear clinical advice, including fact sheets with answers to frequently asked questions, will need to be available for immunisation providers.

**Glossary**

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| Adverse event | An unwanted reaction usually following administration of a vaccine, which may or may not be caused by the vaccine. Adverse events may be at the site of injection or may be a general illness or a general allergic reaction. |
| Antibodies | A special protein produced by immune cells in response to antigens (foreign substances, bacteria, viruses or other microorganisms). Antibodies bind with antigens on microorganisms as one of the initial steps of the body's immune response against infection. |
| Carriage, or meningococcal carriage | The continual presence of bacteria (meningococci) in the upper respiratory tract, particularly the throat and/or nose, without causing disease to the host. |
| Carrier | A person who has carriage of bacteria, which are not currently causing disease or symptoms in that person, but which have the potential to be transmitted to others or to invade and cause disease in the individual. |
| Co-administration of | When two or more vaccines are administered at the same time (usually |

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| vaccines | at different sites). |
| Conjugate vaccines | These are vaccines in which the vaccine antigen (the polysaccharides from the bacterial wall of meningococcal bacteria) has been joined or conjugated to a carrier protein to improve the immune response and immunological memory to the vaccine. |
| Herd protection | Herd protection, or herd immunity, is the protection of unvaccinated people indirectly, through a high vaccination rate in the rest of the population. The high level of vaccination and immunity in the population limits the number of people susceptible to infection and the ability for the infection to circulate. |
| Incidence or incidence rate | The number of, or rate of, new cases of a particular disease within a given period of time. |
| Immune response | The body's defence against a foreign object or infection, as shown in the case of a vaccine, by a rise in the level of antibodies above a threshold, or by an amount that is considered to provide protection against a particular disease. |
| Immunocompromising medical condition | A medical condition associated with a weakened immune system, either due to the condition or its treatment, which means that it is less able to fight off infection. People with these conditions are more vulnerable to infection and may have more severe disease than a healthy person. |
| Interchangeability of vaccines | This refers to the ability to use a different brand of vaccine against the same disease to complete a course of vaccination when more than one dose of vaccine is required. |
| Invasive disease (meningococcal or *Hib*) | Disease that results when bacteria (e.g. meningococcal or *Hib*), which are usually harmlessly carried by the body, invade and cause clinical infection. The bacteria may infect the blood, spinal fluid or another part of the body that would normally be sterile (or germ-free). Invasive meningococcal disease most commonly causes meningitis and/or septicaemia (i.e. infection of the blood). |
| Monovalent vaccine | A vaccine against only one bacterium/virus that causes a disease or one variant serogroup of that bacterium/virus. |
| National Immunisation Program (NIP) | The National Immunisation Program was set up by the Commonwealth and state and territory governments to increase national immunisation coverage of important vaccines in Australia. The NIP provides free vaccines to eligible people to reduce the occurrence of diseases that can be prevented by vaccination. |
| Quadrivalent vaccine | A vaccine that targets four variant serogroups of a virus or bacterium that causes a disease. |
| Routinely administered vaccines | These are vaccines that are already included in the current NIP schedule and are to be given at specified schedule points. |
| Schedule point | These are time points or age milestones (e.g. 12 months of age) throughout a person's lifetime when a vaccine is scheduled to be given. |

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| | The schedule points for vaccines have been selected to provide the best possible protection against diseases preventable by vaccination. |
| Serogroups | Serogroups are classifications of certain bacteria distinguished by the presence of a common antigen. In the case of meningococcal bacteria, these antigens are the 'sugars' on their outer coating. The most common meningococcal serogroups that cause serious disease are A, B, C, W and Y. |
| Therapeutic Goods Administration (TGA) registration | Vaccines, like all medicines, are regulated by the TGA. They must be approved and registered for use by the TGA before they are available to the public in Australia. Before they are made available for use they are rigorously tested in human clinical trials to confirm that they are safe and that they stimulate protective immune responses. For a vaccine to be registered, the TGA reviews these data to ensure that the vaccine (or other medicine) works as it should and is safe to use. |

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## Attachment 1: Meningococcal vaccine formulations and brands available for use in Australia and number of doses recommended by ATAGI for healthy individuals by age*

| Vaccine | Formulation | Provides protection against serogroup | Currently registered age for its use | Number of doses recommended by ATAGI, according to age group* |
|---|---|---|---|---|
| **Quadrivalent meningococcal conjugate vaccines (4vMenCV)** | | | | |
| **Menveo** | Quadrivalent $CRM_{197}$ conjugate | A, C, W, Y | From 2 months†‡ | 2 to 5 months:<br>• 2 primary doses and a booster<br>6 to 11 months:<br>• 1 primary dose and a booster<br>12 to 23 months:<br>• 2 primary doses<br>From ≥2 years:<br>• 1 primary dose |
| **Nimenrix** | Quadrivalent tetanus toxoid conjugate | A, C, W, Y | From 2 months# to 55 years‡ | 2 to 5 months:<br>• 2 primary doses and a booster<br>6 to 11 months:<br>• 1 primary dose and a booster<br>From ≥12 months<br>• 1 primary dose |
| **Menactra** | Quadrivalent diphtheria toxoid conjugate | A, C, W, Y | 9 months to 55 years‡ | 9 to 23 months:<br>• 2 primary doses<br>From ≥2 years:<br>• 1 primary dose |
| **Multicomponent meningococcal B vaccines (MenBV)** | | | | |
| **Bexsero** | Recombinant multicomponent MenB | B | From 6 weeks§ | 6 weeks to 5 months:<br>• 3 primary doses and a booster<br>6 months to 11 months:<br>• 2 primary doses and a booster<br>From 12 months:<br>• 2 primary doses |
| **Trumenba** | Recombinant bivalent fHBP MenB | B | From 10 years§ | • 2 primary doses |
| **Meningococcal C conjugate vaccines (MenCCV)**** | | | | |
| **Menitorix** | Hib–MenC conjugate combination | C | From 6 weeks | Currently 1 dose at age 12 months.<br>ATAGI recommends this dose to be replaced by a dose of meningococcal ACWY vaccine at 12 months and a dose of monovalent Hib vaccine at 18 months |
| **NeisVac-C** | Monovalent MenC conjugate | C | From 8 weeks | Currently ATAGI recommends 1 dose of meningococcal C vaccine at age 12 months, but monovalent meningococcal C vaccine is not currently used on the National Immunisation Program, as this dose is given in a combination vaccine with the Hib vaccine as Menitorix (refer to above) |

* Dosing schedules are based upon ATAGI recommendations and may differ from the respective Product Information.

† The first dose of Menveo can be administered as early as 6 weeks of age.

# The use of Nimenrix in infants aged 6 weeks to 11 months is a variation from the Product Information, and is based on data from clinical trials supporting its use in this age group.

‡There is no registered upper age limit for use of Menveo. Although both Menactra and Nimenrix are registered for use up to 55 years of age, either of these brands can be given to persons >55 years of age, as per *The Australian Immunisation Handbook.*

§ Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the vaccination course.

** Currently in the National Immunisation Program a dose of meningococcal C vaccine is given at age 12 months; this is different from the youngest age at which this vaccine can be given as stated in the Product Information.

**Attachment 2: Existing recommendations for the use of meningococcal ACWY conjugate vaccines and meningococcal B vaccines by age group in the current *Australian Immunisation* Handbook that are to be retained**

| Age group | Healthy people | | Special risk groups* | Travellers# |
|---|---|---|---|---|
| | Aboriginal or Torres Strait Islanders | Non-Indigenous | | |
| 2†–23 months | MenB | MenB | MenB<br>MenACWY | MenACWY |
| 2–4 years | – | – | MenB<br>MenACWY | MenACWY |
| 5–14 years | – | – | MenB<br>MenACWY | MenACWY |
| 15–19 years | MenB | MenB | MenB§<br>MenACWY | MenACWY |
| ≥20 years | – | – | MenB<br>MenACWY | MenACWY |

* Includes those with a specified medical condition associated with increased risk of meningococcal disease (refer to List 1), laboratory personnel who are at occupational risk of exposure to *Neisseria meningitides*# People (age ≥2 months) who are planning overseas travel to regions with an increased risk of exposure to meningococcal serogroups A, C, W, or Y disease.

† First dose can be administered as early as 6 weeks of age.

§ Young adults living in close quarters (such as new military recruits and students living in residential accommodation) are recommended to receive MenB vaccine