South Australian Meningococcal B Expert Working Group

A Meningococcal B Program for South Australia

Public Report

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Government of South Australia

SA Health

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Executive Summary

In 2018, the South Australian Government has decided to implement a meningococcal B vaccination program for South Australia (SA). The South Australian Meningococcal B Expert Working Group has been tasked with advising the Minister for Health and Wellbeing regarding the optimal meningococcal vaccination program for South Australia.

A meningococcal B vaccination program consisting of five separate elements is proposed (see Table 1 below).

Table 1: Summary of elements and costings of proposed meningococcal B program

Program Element	**Cohort**	**Term of Program (years)**	**Cost (by vaccine available for defined cohorts)**		
			Bexsero®	or	**Trumenba®**
Meningococcal B Program: Infant	Six weeks to less than one year of age	Annual (ongoing)	[redacted]		
Meningococcal B Catch Up Program: Childhood	Greater than one year of age to less than four years of age	1.25	[redacted]		
Meningococcal B Catch Up Program: Year 10	Greater than 15 years of age to less than 16 years of age	12	[redacted]	or	[redacted]
Meningococcal B Catch Up Program: Year 11	Greater than 16 years of age to less than 17 years of age	1	[redacted]	or	[redacted]
Meningococcal B Catch Up Program: Year 12 to less than 21 years of age	Greater than 17 years of age to less than 21 years of age	1	[redacted]	or	[redacted]

The program elements and cohorts have been chosen to ensure coverage for ages with a disease incidence of greater than the average annual incidence of 2.8 cases per 100,000 population for the ages at highest risk 0-25 years. Although this is not the case for 15 year old adolescents (most of whom will be in Year 10), providing the vaccine in Year 10 rather than Year 11 allows sufficient time for vaccine response prior to entering the period of higher risk.

The vaccine used for children less than ten years of age would be Bexsero. The vaccine used in the adolescent/adult program would be either Bexsero or Trumenba. Both vaccines would be used according to registration status as per the Therapeutic Goods Administration and in accordance with recommendations from the Australian Technical Advisory Group on Immunisation. Overall cost may reduce significantly if a proposed reduction in the number of doses required to safely and effectively immunise infants is approved by the Therapeutic Goods Administration in Australia and cost may reduce further through negotiation with vaccine suppliers for purchase of large quantities of vaccine.

The program is proposed to be delivered through the usual service providers: general practice, local government, Aboriginal Health Services, Child and Family Health Services (CaFHS), Country Health SA Local Health Network (CHSALHN) and Women's and Children's Health Network (WCHN) and the school based immunisation program for the Year 10 and Year 11 catch-up programs (local

government and catch-up of missed doses through general practice). Appropriate surveillance and evaluation would be required.

The total estimated cost for this program from 03 September 2018 to 31 December 2031 ranges from [redacted] to [redacted], depending on which combination of vaccines is used. The proposed start date may be subject to change as a result of internal and external factors that include probity and procurement processes, obtaining funding, infrastructure development and manufacturing lead-in times.

On the basis of South Australian disease incidence data since 2000, it is estimated that this program would prevent approximately 12 cases of serogroup B invasive meningococcal disease annually and one death every two years from serogroup B invasive meningococcal disease. There is a significant additional benefit in prevention of permanent disability and other long term effects in those cases that survive serogroup B invasive meningococcal disease.

Introduction

In 2018, the South Australian Government has decided to implement a meningococcal B vaccination program for South Australia (SA). The South Australian Meningococcal B Expert Working Group was established to provide the Minister for Health and Wellbeing with recommendations regarding the optimal meningococcal B vaccination program for SA. The Working Group consists of:

- Professor Paddy Phillips, Chief Medical Officer and Chief Public Health Officer (chair)
- Dr Louise Flood, Interim Director, Communicable Disease Control Branch (CDCB)
- Professor Helen Marshall, Senior Medical Practitioner and Director, Vaccinology and Immunology Research Trials Unit, Women's & Children's Hospital (WCH) and University of Adelaide
- Dr Rodney Pearce, general practitioner with particular expertise in immunisation and Head of GP liaison for the Australian Immunisation Coalition
- Dr Celia Cooper, Head, Infectious Diseases Department, WCH
- Dr David Johnson, Public Health Physician, Aboriginal Health Council (SA)
- Mr Noel Lally, Nursing Director, Immunisation Section (IS), CDCB (Ex officio).

The aim of a state funded meningococcal B vaccination program would be to target the most at risk populations and:

- reduce deaths from invasive meningococcal B disease; and
- reduce morbidity from invasive meningococcal B disease.

Background

Meningococcal disease is a serious infection caused by the bacterium *Neisseria meningitidis* (often called the meningococcus). There are 13 known serogroups of meningococcus, with five serogroups causing most cases of disease in Australia: A, B, C, W and Y. The meningococcus is carried, usually harmlessly, in the nose and throat of around 10-20% of the population (carriers), with higher carriage in some specific groups (adolescents and young adults) (Christensen et al. 2010). The meningococcus is spread when an infected person (patient or carrier) talks, coughs or sneezes small droplets containing infectious agents into the air. The droplets in the air may be breathed in by those nearby. The meningococcus is also spread by close contact with nose or throat secretions. However, only a very small number of people in close contact with carriers develop meningococcal disease.

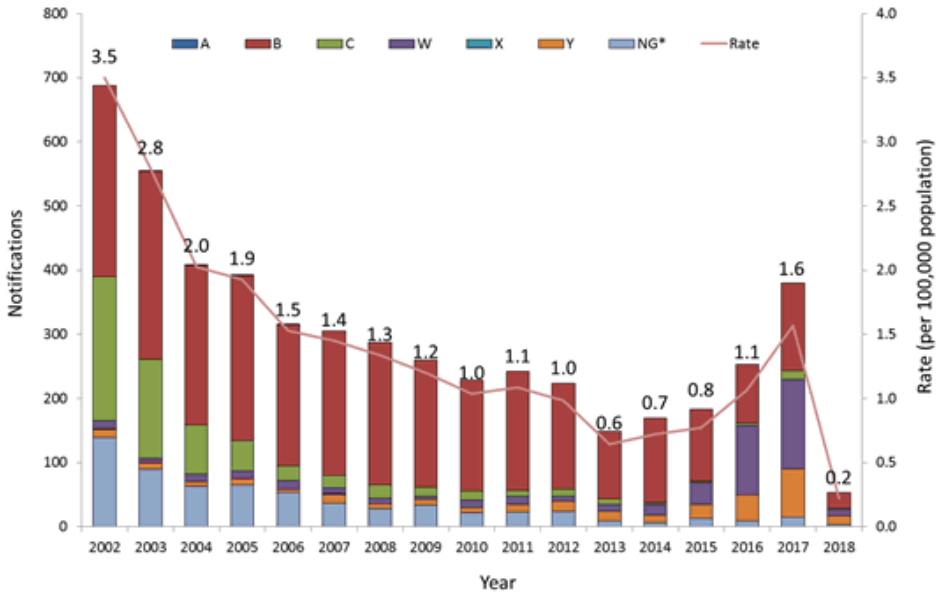
The meningococcus causes non-invasive disease such as conjunctivitis and invasive disease such as meningitis and septicaemia. In Australia, 5 to 10% of people with invasive meningococcal disease (IMD) die, despite rapid treatment. In survivors, there is significant morbidity associated with IMD with up to 40% of cases (Wang et al. 2014) developing necrosis of the skin and gangrene of the limbs requiring extensive skin grafting and amputation, and others having permanent neurological deficits. Whilst these burdens are difficult to quantify in terms of both the individual and attendant health services, it is widely acknowledged to be a significant issue and is one of the most commonly identified fears and concerns of carers and meningococcal B IMD survivors.

IMD prevention strategies are: appropriate infection control, provision of clearance antibiotics to cases and close contacts, and, for some serogroups, vaccination.

IMD is a notifiable condition.

Epidemiology

Figure 1: Notification and rates of IMD, Australia, 2002 to 2018, by year and type



Notes:

- *#Data from the NNDSS with a diagnosis date up until of 31 March 2018. Data were extracted on 23 April 2018.*
- **NG includes where meningococcal isolates could not be identified ('not groupable'), other isolates not grouped and where serogroup was not known.*

Australian Government Department of Health 2018[a]

Nationally, notification rates of IMD have been decreasing, primarily due to a decline in serogroup C disease following the national meningococcal C vaccination program and also partly due to a decline in serogroup B disease nationally (see Figure 1 above).

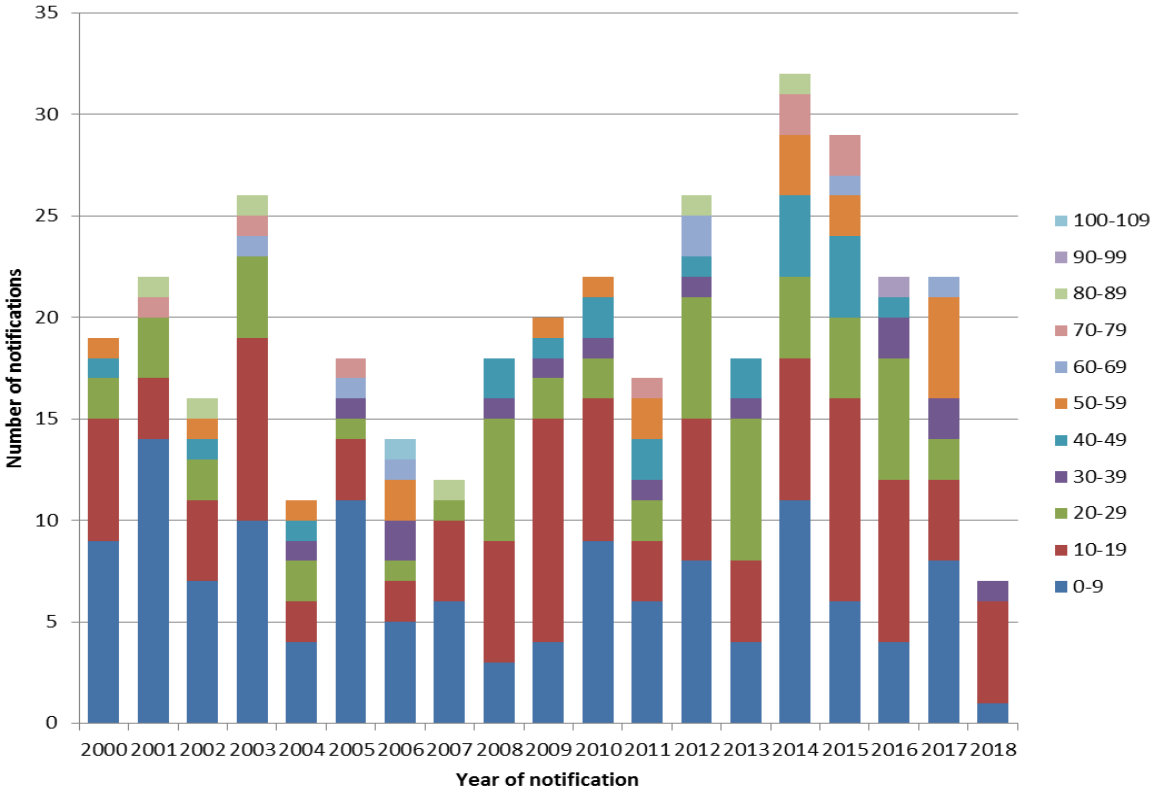
The Australian Technical Advisory Group on Immunisation (ATAGI) has observed:

- 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 in 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.

ATAGI 2018

In Australia, from 2006 to 2011, the highest incidence of serogroup B disease was in children aged <5 years (5.7 cases per 100 000), particularly infants aged <1 year (14.0 cases per 100,000) and toddlers aged 12–23 months (6.3 cases per 100,000). There was also a lower, secondary peak in late adolescence and early adulthood (2.8 cases per 100,000 aged 15–19 years) and this pattern for IMD serogroup B continues to be reflected in current data for SA (see Figure 2 and Figure 3).

Figure 2: Notification of serogroup B IMD notifications in SA, 2000 to 24 April 2018 by year and age group at notification (years)



Over the last 18 years meningococcal B disease in SA has **not** declined (contrary to national experience) and has predominantly affected children, adolescents and young adults, with additional cases distributed with no discernible pattern across all other ages (Figure 2 above). Looking at these data in more detail (Table 8 to Table 12 in Appendices) it is evident that over this period (01 January 2000 to 24 April 2018):

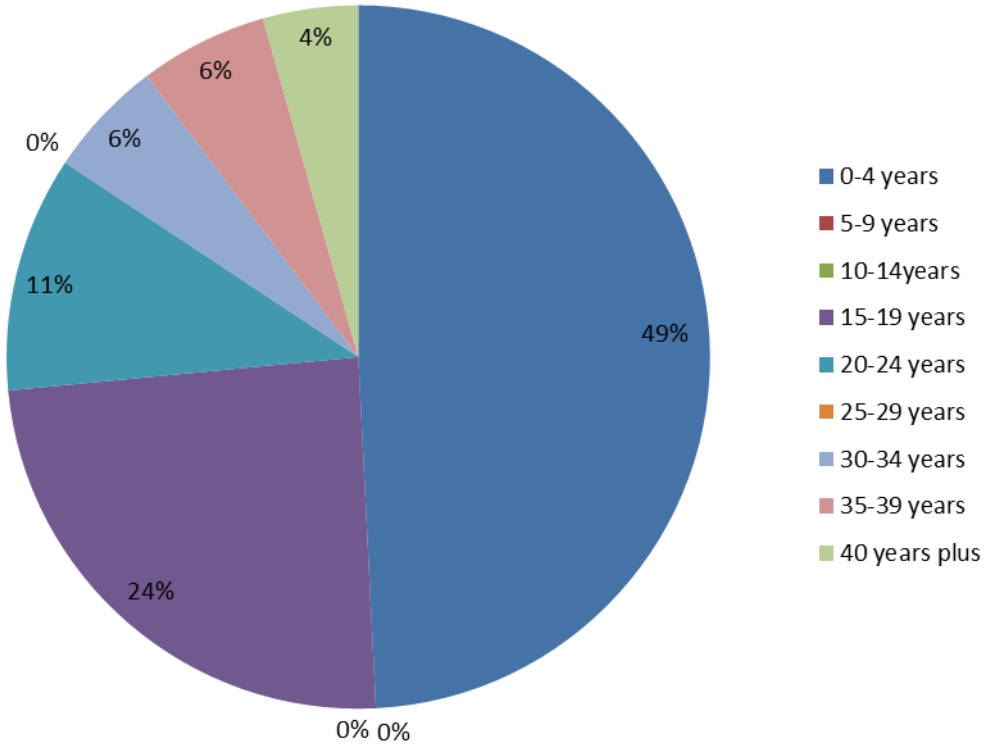
- 371 cases have been notified across all ages:
    - These 371 cases have resulted in 14 deaths
    - 235 of the 371 cases occurred in those up to 20 years of age

- Of the 235 cases in those up to 20 years of age:
    - 110 occurred in those less than four years of age (30% of all cases)
    - 89 occurred in those 15 up to and including 20 years of age (24% of all cases)
    - 19 of these cases occurred in people identifying as Aboriginal (5% of all cases)
    - There were ten deaths resulting from these cases:
        - Two deaths in infants less than one year of age
        - Four deaths in infants greater than one year and less than two years of age
            - One of these deaths was in a child who identified as Aboriginal
        - Two deaths in adolescents 18 years of age
        - Two deaths in adolescents 19 years of age

- Of the 110 cases that occurred in those less than four years of age:
    - 55 occurred in those up to and including 12 months of age (15% of all cases)
        - 8 of these cases occurred in people identifying as Aboriginal (2% of all cases)

- 27 occurred in those from 12 months of age up to and including 24 months of age (7% of all cases)
  - 4 of these cases occurred in people identifying as Aboriginal (1% of all cases)
- 28 occurred in those greater than 24 months up to and including four years of age (8% of all cases)
  - 4 of these cases occurred in people identifying as Aboriginal (2% of all cases).

Figure 3: Serogroup B IMD notification incidence rates by age group as a proportion, in South Australia, 2017



South Australian data on the incidence rates of meningococcal B for the most recent complete year of data (2017) is also consistent with the longer term disease incidence in the state, with proportionally, the disease occurring more frequently in those aged zero to four years of age and 15 to 19 years of age. Average notification rates are shown in Table 2 below and age specific incidence rates are also included in Table 12 in the Appendices. Rates have been calculated using Australian Bureau of Statistics data on estimated resident population for SA.

Table 2: Average annual notification rate of IMD serogroup B for those aged 0-25 years, in South Australia, 2000 to 2017

Age at notification	Total number of notifications	Average annual notification rate
0	51	14.9
1	26	7.6
2	20	5.8
3	12	3.5
4	9	2.6
5	4	1.1
6	2	0.6
7	3	0.9
8	1	0.3
9	1	0.3
10	3	0.8
11	5	1.4
12	2	0.6
13	2	0.6
14	3	0.8
15	5	1.4
16	12	3.2
17	13	3.5
18	31	8.2
19	24	6.2
20	12	3.1
21	9	2.3
22	6	1.5
23	6	1.5
24	4	1.0
25	2	0.5
Overall (0-25 years)	**268**	**2.8**

The average annual incidence for all ages 0-25 years old is 2.8 cases per 100,000 population. Utilising an average annual notification rate above this as an indicator for cohorts experiencing a greater burden of invasive meningococcal B disease provides a threshold for definition of cohorts experiencing a comparatively higher burden of disease in SA. This means that those from birth to less than four years of age and those from 16 to less than 21 years of age have higher than average annual incidence rates. It should be noted that for 16 year olds there is a need for these children to be vaccinated in the year prior to entering the period of higher risk. The average annual incidence rates for IMD serogroup B by Aboriginal[1] status is shown in Table 3 below.

[1] Note: in this document the term Aboriginal is inclusive of Aboriginal and Torres Strait Islander peoples.

Table 3: Number and average annual rate of notifications of Invasive Meningococcal Disease serogroup B in persons aged 0-24 years by Indigenous status — South Australia, 1 January 2000-24 April 2018[23]

Age/age group	Indigenous population			Non-Indigenous population		
	Total number of notifications	Average annual notification rate per 100,000 population	2011 Census population estimate	Total number of notifications[1]	Average annual notification rate per 100,000 population[2]	2011 Census population estimate
0	7	41.8	882	45	12.9	18,430
1	3	17.3	915	23	6.5	18,579
2	2	11.8	894	18	5.0	18,790
3	4	22.6	930	8	2.3	18,652
4	0	0.0	837	9	2.6	18,517
5-9	1	1.2	4,318	10	0.6	90,658
10-14	1	1.2	4,313	15	0.8	93,944
15-19	1	1.3	3,959	99	5.1	101,849
20-24	0	0.0	2,826	37	1.7	111,433

[2] Denominator data source: ABS. Estimated resident Aboriginal and Torres Strait Islander and Non-Indigenous population, States and Territories, Single year of age, 30 June 2011. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3238.0.55.001June%202011?OpenDocument. Last accessed: 12 June 2018

[3] As population estimates for previous census years (2001, 2006) and the most recent census year (2016) were not publicly available, 2011 census data was used as the population denominator for all calendar years included in the analysis.[3]

Known undercounts of Aboriginal and Torres Strait Islander persons in the census and uncertainty regarding fluctuations in true population size in the years 2000-2010 and 2012-2018 mean that rates need to be interpreted with caution. Considerable rate fluctuation between time periods may also occur due to the influence of small numbers on rate estimates.

IMD vaccination programs in Australia

As previously noted, there has been a funded meningococcal C vaccination program in place in all states and territories since January 2003 under the National Immunisation Program (NIP). Serogroup C disease has become very rare (1.2% of cases with identified serogroup in 2016) since the introduction of the conjugate meningococcal C vaccine (NCIRS 2018).

Several state and territory governments have more recently introduced vaccination programs for protection against the emergence of meningococcal W and Y (NCIRS 2017) and the federal government has now committed to the introduction of a meningococcal ACWY vaccine (Nimenrix®) onto the NIP schedule at one year of age as of 01 July 2018.

In response to outbreaks of meningococcal W, SA has introduced three time limited programs: Ceduna and region (in 2017), the Anangu Pitjantjatjara Yankunytjatjara (APY) Lands (in 2017 and 2018) and a targeted vaccination program in the Eyre, Upper North, Far North and Flinders regions in Aboriginal populations (current).

At this stage, no state or territory has introduced a meningococcal B vaccination program.

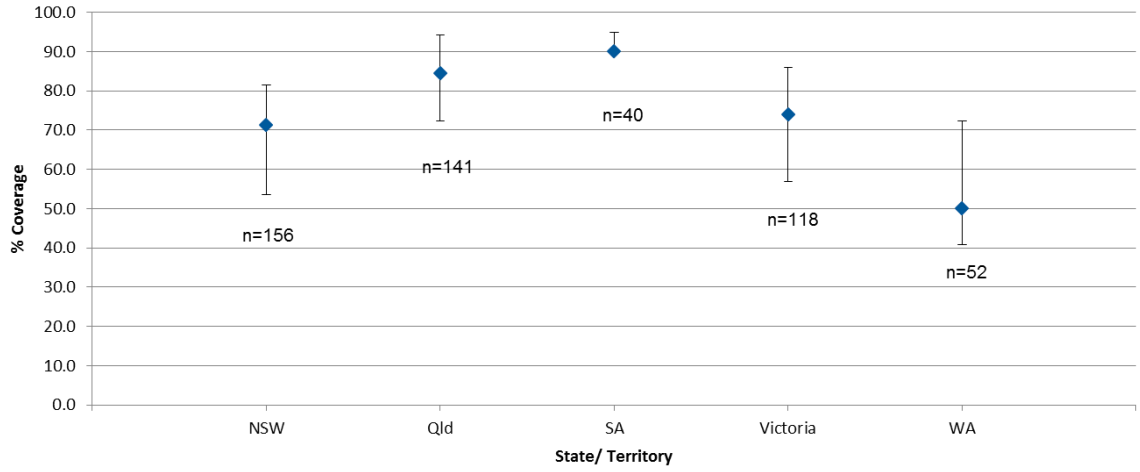
Vaccination against IMD serogroup B

For protection against meningococcal B disease, vaccines that are available in Australia include:

- Bexsero (4CMenB) GlaxoSmithKline (GSK) which is registered for use from two months of age and older. According to ATAGI recommendations in the Australian Immunisation Handbook it can be used from 6 weeks of age (Australian Government Department of Health 2018[b])
- Trumenba (MenB-FHbp) Pfizer which is registered for use in those from 10 years of age.

SA has the highest proportion of invasive meningococcal B disease due to the New Zealand strain (genotype PorA 1.7,2.4) compared to any other state. It is predicted through the meningococcal antigen typing system (MATS) (Plikaytis et al. 2012) that in SA, Bexsero should be 90% effective against invasive strains (Tozer et al. 2012). In addition, as well as providing protection against meningococcal B disease, there is also some evidence of cross protection against other IMD serogroups (Tozer et al. 2012) and against *Neisseria gonorrhoeae* (which causes gonorrhoea) (Petoussis-Harris et al 2017).

Figure 4: Meningococcal Antigen Testing System (MATS) Coverage by at Least One Antigen by Australia State/Territory



Trumenba contains subfamily A and subfamily B factor H binding protein (fHBP) and should provide protection against a high proportion of circulating strains causing IMD. Vaccine effectiveness in a population program has not been established as Trumenba has not been included in any national immunisation programs to date.

Most of the vaccines provided as part of the NIP and state funded programs generate 'herd immunity' through the process of high levels of immunisation in the community, thereby interrupting spread of disease amongst unvaccinated people. There is currently limited evidence that Bexsero and no evidence that Trumenba provide herd immunity[4]. In the United Kingdom (UK), a randomised, multi-centre controlled study (Read et al. 2014) was conducted to examine carriage in 18-24 year old university students. Bexsero vaccination resulted in significantly lower carriage of any meningococcal serogroup (18.2% (95% Confidence Interval (CI) 3.4-30.8) carriage reduction), and 26.6% (95% CI 10.5, 39.9) reduction in serogroups BCWY. A significant carriage reduction for disease-associated sequence types of capsular B meningococci compared to controls was not observed (12.6% (95%CI -15.9-34.1). As these results are inconclusive and results are not yet available from the B Part of It: Meningococcal B Herd Immunity Study it must be assumed that any state wide meningococcal B program would be providing protection for the individual vaccinated rather than any additional indirect (herd immunity) effects.

In terms of long term immunogenicity, most data in population programs, such as in Cuba and New Zealand, show that there has not been any return of meningococcal B disease, suggesting long term immunity in a population program (Read et al. 2014).

While both Bexsero and Trumenba are licensed by the Therapeutic Goods Administration as effective for immunisation against meningococcal B, neither has been accepted onto the subsidised National Immunisation Program by the Pharmaceutical Benefits Advisory Committee (PBAC) and so must be supplied privately to consumers under prescription. While Trumenba is yet to be submitted for a decision to the PBAC, Bexsero has been submitted for decision several times.

In July 2015 the PBAC rejected the last resubmission for inclusion of Bexsero on the National Immunisation Program Schedule for the prevention of meningococcal B disease in infants and adolescents; "*The basis of the rejection was that the re-submission did not address multiple uncertainties in relation to the clinical effectiveness of the vaccine against the disease when delivered in a vaccination program, that the optimistic assumptions about the extent and duration of effect and herd immunity raised by the PBAC in previous consideration of this vaccine were not addressed, and the unacceptably high and uncertain ICER [incremental cost effectiveness ratio], presented in the re-submission"* (PBAC 2015). A resubmission addressing these issues is expected, probably in 2019.

Bexsero

The number of doses of Bexsero vaccine required depends on the age of the individual at commencement of the vaccine course. Recommendations from the Immunisation Handbook 10th edition (Australian Government Department of Health 2018[c]) are:

- infants from six weeks to five months require three primary doses plus a booster at 12 months
- infants aged six to 11 months require two primary doses plus a booster at 12 months
- persons aged 12 months and over require two primary doses.

The need for a booster dose later in life is currently unknown.

[4] The SA Meningococcal B Herd Immunity Study will provide evidence as to whether or not Bexsero generates herd immunity.

In the UK and in Ireland a three dose schedule has been implemented for all infants up to 12 months of age (two months, four months and 12 months of age) with an estimated vaccine effectiveness (VE) of 83% against all meningococcal B disease and a VE of 94% against matched circulating strains (UK) (Parikh et al. 2016).

GSK has applied for a new licensing through the Therapeutic Goods Administration (TGA) in Australia for an alternative three dose schedule in addition to the current license of a four dose schedule in infants six weeks to 12 months, with a determination expected in October 2018.

Recommendations in this document are based on current TGA recommendations. If the TGA indicate that a three dose schedule in infants six weeks to five months is effective in the Australian setting then it would be advisable for SA to move to a three dose schedule for this age group. Such a schedule change would represent significant savings of approximately [redacted] in terms of the overall cost of the recommended program from 03 September 2018 through to 31 December 2031. These potential savings have been detailed in Table 15 in the Appendices.

Trumenba

In individuals not at increased risk of IMD, the Product Information (PI) for Trumenba recommends two doses administered six months apart. Individuals at increased risk of IMD are recommended to receive two doses at least one month apart, followed by a third dose at least four months after the second dose. An analysis based on fHBP variant prevalence in a large set of 1,814 isolates associated with invasive disease, showed that >91% of all meningococcal serogroup B isolates expressed sufficient levels of fHBP to be susceptible to bactericidal killing by vaccine-induced antibodies (McNeil et al. 2018).

Schedule crowding and potential impact on the broader NIP

The current standard NIP schedule (Australian Government Department of Health 2018[d]) changes frequently in line with evolving disease incidence and as vaccine availability/presentation changes. The NIP schedule is next due to change on 01 July 2018. The NIP program childhood schedule in particular is increasingly complex, with the standard schedule recommending multiple vaccines at set ages (schedule points) and additional vaccines also required at some of these schedule points for Aboriginal children and other 'at risk' groups.

The addition of a meningococcal B program in SA needs careful consideration in terms of:

- vaccination schedule crowding
- public receptivity to these additional vaccines
- potential impact on uptake of the broader NIP schedule
- the impact on the coordination of the NIP with numerous additional vaccination programs across eight states/territories

The number of vaccines potentially recommended at each schedule point in SA (with the introduction of the state based meningococcal B vaccination program recommended in this document) is summarised in Table 14 in the Appendices. Of note is the potential for children to receive four to seven separate injections at 12 months of age, dependent on risk factors and Aboriginal status.

The introduction of Bexsero onto the childhood schedule did not adversely impact uptake in the UK, although the maximum number of vaccine injections at the 12 month schedule point in the UK (four separate injections) is considerably less than the maximum number of injections proposed for the SA 12 month schedule point.

Vaccine Safety

The safety of Bexsero has been assessed following 3 million doses in infants in the UK with no safety concerns or safety signals identified. Safety in around 20,000 adolescents to date in SA in the Meningococcal B Herd Immunity Study has not identified any safety concerns or safety signals.

Trumenba has been used in university cohorts following an outbreak of meningococcal B disease (Fiorito et al, 2018). A survey on adverse events following immunisation (AEFI) was provided to students with 44% completing the survey of 3,700 vaccinated. The most commonly reported AEFI was injection site pain. Reported rates of injection site pain, fatigue, myalgia, fever, and chills were similar to those reported in clinical trials. Reported rates of headache were lower than in clinical trials. This study was the first to examine adverse events of Trumenba in a real-world setting where more than 90% of a college-age population was vaccinated.

Vaccine supply

SA Health requires a formal procurement process to be undertaken with purchase of any asset above the value of $33,000. This involves an approach to market and a transparent selection and decision making process. Procurement and vaccine supply agreements will have to be arranged separately by SA Health as the meningococcal B vaccine is not included under the NIP head deeds for vaccine supply. Procurement can take up to three months from the date of commencement of such a process.

Initial enquiries to manufacturers regarding the ability to supply stock indicate:

[redacted]

Vaccine choice considerations:

[redacted]

Target cohorts

The 'Immunisation Handbook 10th edition' (the 'handbook') contains recommendations relating to vaccination for all diseases, including IMD. Given changes to the epidemiology of meningococcal disease and recognising the new programs available through states, ATAGI has reviewed the meningococcal chapter of the handbook (Australian Government Department of Health 2018[c]) and on Friday 06 April 2018 released a document for public consultation proposing changes to

recommendations for vaccination against meningococcal disease (ATAGI 2018), with changes to recommendations for vaccination against meningococcal B disease summarised in Table 4: National recommendations and proposed vaccination recommendations regarding IMD serogroup B

The draft recommendations have yet to be agreed and formalised, but include an expansion of the recommendations in the current edition of the handbook with the most notable changes being:

- an expansion of the childhood schedule to include all Aboriginal children greater than two months to less than five years of age
- an expansion of the adolescent/adult schedule to include those aged 20 to 24 years who smoke or live in close quarters.

Table 4: National recommendations and proposed vaccination recommendations regarding IMD serogroup B

Recommendations	**Immunisation Handbook 10th Edition (Current)**	**Proposed Recommendations (ATAGI Public Consultation)**
Meningococcal B vaccine is recommended for infants and young children, particularly those aged <2 years, due to their higher risk of serogroup B meningococcal disease. The number of doses required depends on the age at which the vaccine course is commenced.	Current recommendation	Retain
Meningococcal B vaccine is recommended in a 2-dose schedule for all adolescents aged 15–19 years due to their higher risk of serogroup B meningococcal disease compared with other ages.	Current recommendation	Retain
A number of medical conditions or treatments increase a person's risk of IMD and additional doses of meningococcal B vaccine are recommended for persons with identified risk factors.	Current recommendation	Retain
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 two doses of meningococcal B vaccine.	N/A	New recommendation
Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive two doses of meningococcal B vaccine.	N/A	New recommendation
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.	N/A	New recommendation

The recommendations relating to adolescents and young adults are problematic from a subsidised program perspective as it would be difficult to budget for potential uptake and for providers to accurately establish eligibility.

Funding considerations

All costings in this document exclude GST.

Vaccine cost

Based on communications with the predicted vaccine suppliers, the vaccine cost is [redacted] for Bexsero or [redacted] for Trumenba. [redacted]

[redacted]

For the purpose of the catch up programs proposed below, if any individual in the eligible cohort commences their course prior to the end date of the catch up program they will be eligible and funded to complete the course.

Service delivery

[redacted]

Logistics

[redacted]

[redacted]

Communication strategy and resources

There will be a requirement, especially in the initial stages of the rollout of such a program, to communicate both to the public and immunisation providers regarding the program. This will require a funded communication strategy along with the development of online and hard copy educational resources. [redacted] (see 'Communication Strategy' section below).

Safety surveillance

As with all public immunisation programs, and particularly with new programs, monitoring for safety is an important component of the program especially if the vaccine has not previously been used on a large scale in Australia. This is especially important given the increased likelihood of febrile events associated with Bexsero in children less than two years of age and the fact that a meningococcal B vaccination program for SA would be setting a precedent in terms of widespread vaccination against this disease; there is a critical requirement for a valid and robust post vaccination safety/surveillance program. The program would be designed to detect safety signals associated with administration of the vaccine/s and there would be a cost associated with the measures required to ensure public safety – see Table 16 in the Appendices.

Program implementation

Implementation of a state wide meningococcal B program as recommended below, which is without precedent in either the Australian or global setting, will require significant coordination to ensure successful implementation of all elements of the program. This includes development and coordination of the following systems:

- Business processes (procurement, budget and contract management)
- Operational/logistics (storage and distribution)
- Patient informatics (data collection, storage and reporting to the Australian Immunisation Register)
- Resource development – public and providers (clinical and consumer information)
- Vaccine safety surveillance (active enhanced surveillance requiring case management)
- Evaluation (data collection, synthesis).

Costs are estimated at [redacted] in the first five years of the proposed program.

Vaccination Programs: Options Considered and Rejected

Ongoing program for children greater than six weeks to less than one year of age with one year catch up program up to two years of age only with no other age groups included

Vaccination of this specific cohort is a current recommendation in the Immunisation Handbook 10th Edition. The largest burden of meningococcal B disease occurring in any single birth year is for infants in the zero to one year of age cohort (52 cases in SA since 2000), with a further comparatively large number of cases occurring in the greater than one year to less than two years of age cohort (26 cases in SA since 2000). On the basis of these data, an ongoing program targeting this cohort would be expected to prevent:

- approximately four cases of IMD serogroup B per year

- approximately one death from IMD serogroup B every three years.

Cost: Approximately [redacted] in first year and [redacted] thereafter.

Whilst the evidence supports vaccinating all infants in this cohort and immunising this cohort is recommended as part of a larger program (see 'Recommended Meningococcal B Program for SA' section below), targeting a program just to this cohort is not recommended as:

- it only targets half of the cohort with the greatest burden of disease in SA (it does not provide any protection to children from two years up to four years of age (32 cases in SA since 2000))
- it does not provide any protection to the cohort with the next most significant burden of disease (adolescents 15 to 19 years of age).

Ongoing program for greater than six weeks to less than one year of age with one year catch-up for greater than one year of age to less than four years of age and no adolescent program

Consideration was given to extending the above program by offering an ongoing program for those six weeks to one year of age and running a catch up program for children from greater than one year of age up to less than four years of age (based on the relevant age specific annual incidences being >3 cases per 100,000 per year – see above). On the basis of SA data since 2000, this approach would prevent:

- approximately six cases of IMD serogroup B per year
- approximately one death from IMD serogroup B every three years.

Cost: Approximately [redacted] in first year and [redacted] thereafter.

However, this option which excludes an adolescent program is not recommended because it does not provide any immediate protection to the cohort with the next most significant burden of disease (adolescents 15 to 19 years of age).

Ongoing program for greater than six weeks to less than one year of age and Year 10 catch-up program, without catch up program for young children and adolescents in high risk cohorts

Consideration was given to providing an ongoing program targeting those from greater than six weeks of age to less than one year of age alongside a 14 year catch up program for adolescents at age 15 (year 10). On the basis of SA data since 2000, this approach would prevent:

- approximately three cases of meningococcal B disease per year
- approximately one death from meningococcal B disease every three years.

Cost: Approximately [redacted] to [redacted] over life of 14 year catch up program and [redacted] thereafter.

This option (without catch up programs in high risk cohorts) is not recommended for the following reasons:

- it does not provide any immediate protection to children from one to less than four years of age and adolescents and young adults up to the age of 21 years, in whom the next most significant number of cases and deaths also occur
- it would take three years for children from one to less than four years of age to be vaccinated
- it would take six years for adolescents and young adults up to the age of 21 years to be vaccinated.

Ongoing program for Aboriginal children greater than six weeks to less than one year of age and one year catch up program for Aboriginal children greater than one year to less than five years of age alone with no other groups included

In line with the draft ATAGI recommendations for vaccination against meningococcal B as noted above, a program targeting just Aboriginal children from 6 week to less than five years of age was considered. On the basis of SA data since 2000, this approach would prevent:

- approximately one case of meningococcal B disease per year
- approximately one death from meningococcal B disease every 18 years.

Cost: [redacted] in first year and [redacted] thereafter.

This option is not recommended for the following reasons:

- it does not provide any protection to non-Aboriginal children in whom a greater number of cases are occurring
- it does not protect Aboriginal and non-Aboriginal adolescents from 15 to less than 21 years of age, in whom the next most significant number of cases and deaths occur.

Recommended Meningococcal B Program for SA

Ongoing infant program with time limited catch up for children and adolescents/young adults

Given the burden of disease in SA and the significant clustering of disease in two main cohorts, alongside uncertainty regarding available vaccine's ability to create a herd immunity effect, the recommended program consists of five separate program elements (summarised in Table 5 below).

Cohorts

- Six weeks to less than one year of age (ongoing)
- Greater than one year of age to less than four years of age (15 month catch-up program)
- Year 10 catch up program (11 year catch-up program)
- Year 11 catch up program (one year catch-up program)
- Catch-up program for adolescents and young adults from Year 12 to less than 21 years of age (one year catch-up program).

This approach would prevent:

- approximately 12 cases of meningococcal B disease per year
- approximately one death from meningococcal B disease every two years.

Cost: total cost [redacted] estimated at [redacted] to [redacted] (refer to Table 6 below).

As with all of the above options, it is expected that the number of preventable cases and preventable deaths would increase in subsequent years as protection extends through the population.

Table 5: Recommended meningococcal B vaccination program for SA

Program Element	Infant	Catch Up Program: Childhood	Catch Up Program: Year 10	Catch Up Program: Year 11	Catch Up Program: Year 12 to less than 21 years of age
Cohort	All infants six weeks of age to less than 12 months of age	All children > 1 year to <4 years of age	All adolescents in year 10	All adolescents in year 11	Persons > 17 years to < 21 years of age
Estimated number of people	20,000 annually	65,000 over term of catch up program	20,000	20,000	44,000 over term of catch up program
Vaccine	Bexsero	Bexsero	Bexsero or Trumenba	Bexsero or Trumenba	Bexsero or Trumenba
Rationale: using data in SA since 2000	55 cases resulting in two deaths in this cohort. This represents 15% of all cases and 14% of all deaths.	55 cases, resulting in four deaths in this cohort. This represents 15% of all cases and 29% of all deaths	101 cases, resulting in four deaths in the greater than 15 years of age (Year 10) to less than 21 years of age cohort. This represents 27% of all cases and 29% of all deaths. Individuals in the Year 12 to < 21 years of age part of this group would still be in the at risk age group but would not have been eligible for the year 10 or year 11 programs. The four deaths in this cohort occurred in individuals in the year 12 to < 21 years part of this cohort.		
Schedule	4 doses: 6 weeks (2 months), 4 months, 6 months & booster at 12 months	2 dose schedule: administered a minimum of 8 weeks apart	*2 dose schedule: minimum interval of 8 weeks if using Bexsero or 6 months if using Trumenba		
Timeline	Start 03 September 2018. Ongoing program.	Start 03 September 2018 & end 31/12/2019.	Start 01 January 2019 & end 31/12/2030.	Start 01 January 2019 & end 31/12/2019.	Start 01 January 2019 & end 31/12/2019.
Model	GP, LGA, CaFHS, Community, CHSALHN, WCHN	GP, LGA, CaFHS, Community, CHSALHN, WCHN	School Immunisation Program	School Immunisation Program	GP, LGA, CaFHS, Community, CHSALHN, WCHN

*3 doses indicated for individuals at increased risk of IMD if being vaccinated with Trumenba

Service model

The most appropriate model would be to leverage existing service provision mechanisms for the delivery of NIP and state-funded vaccination programs.

- Infants vaccination delivery would be administered through general practice, local government, Aboriginal Health Services, Child and Family Health Services (CaFHS), Country Health SA Local Health Network (CHSALHN) and Women's and Children's Health Network (WCHN).
- Year 10 and Year 11 catch-up program would be administered as part of the School Immunisation Program (SIP). This program is primarily delivered in metropolitan and rural SA by local government (council) providers, with a small part of the program supported by GP's and Country Health SA Local Health Network (CHSALHN). The program is successful and especially noted for its ability to deliver higher vaccine uptake than any other model in this age group. Missed doses are proposed to be offered via GP or usual community based providers (not via SIP). Preliminary discussion with Department for Education and Childhood Development indicates in principle support for the program

The 'Catch Up Program: Year 12 to less than 21 years of age' would be administered through general practice, local government, Aboriginal Health Services, Child and Family Health Services (CaFHS), Country Health SA Local Health Network (CHSALHN) and Women's and Children's Health Network (WCHN). This model is preferred primarily because many students in this cohort will already have been vaccinated against meningococcal B through the B Part of It: Meningococcal B Herd Immunity Study, and many students in this cohort will have left school.

Cost

Table 6 below summarises estimated cost per year and includes all recommended program elements as outlined above. It assumes [redacted] and includes the following costs only: vaccine supply, service delivery, implementation, safety surveillance, logistics, communication and evaluation strategies. An alternative breakdown looking at of cost of each program element can be found in Table 17 - Overall Cost per Program Element in the Appendices. As mentioned vaccine cost may be lower depending on procurement negotiations.

Table 6: Overall cost per year of recommended meningococcal B vaccination program for SA

YEAR	TOTAL COST BY YEAR	
	Bexsero for all programs	Bexsero for infant and childhood catch up program, Trumenba for all other programs (> 10 yrs)
	Bexsero 4 dose infant schedule	Bexsero 4 dose infant schedule
*2018	[redacted]	[redacted]
#2019	[redacted]	[redacted]
2020	[redacted]	[redacted]
2021	[redacted]	[redacted]
2022	[redacted]	[redacted]
2023	[redacted]	[redacted]
2024	[redacted]	[redacted]
2025	[redacted]	[redacted]
2026	[redacted]	[redacted]
2027	[redacted]	[redacted]
2028	[redacted]	[redacted]
2029	[redacted]	[redacted]
^2030	[redacted]	[redacted]
2031	[redacted]	[redacted]
	[redacted]	[redacted]

[redacted]

* Infant and Childhood catch-up programs commence [redacted]

Infant, Year 11 and Year 12 to less than 21 years of age catch up programs commence [redacted]

[redacted]

^ Year 10 catch up program ends

Safety surveillance

Enhanced passive surveillance

This model relies on parents or individual vaccine recipients taking the time to report a concern. As with current practice, parents, adolescents and immunisation providers would be encouraged as part of the vaccination encounter to report any unexpected or unusual AEFI to SA Health.

This model has been operational in SA for a number of years and has been demonstrably successful in the past with the identification of a safety signal associated with increased adverse reactions in the childhood influenza vaccine program in 2010. More recently, this model has been successfully applied for the state-wide Meningococcal B Herd Immunity Study, with students, parents, immunisation providers and school staff encouraged to report any AEFIs to SA Health. AEFI requiring further follow up are reviewed locally and reported through to the TGA at the national level with further case review as required.

With the Meningococcal B Herd Immunity Study, a total of 139 AEFIs were reported in 138 adolescents of a total of 18,337 students vaccinated in 2017 giving a report rate of 0.39%. Fifty-three students had medical review of their AEFI and there were six serious AEFIs reported. Of those students who were able to be contacted (87%) all AEFIs have resolved.

Active surveillance

This model differs from the enhanced passive surveillance model in that it actively follows up vaccine recipients to enquire about any reactions post vaccination. Active models are generally accepted to be better at eliciting reports of post vaccination events.

[redacted]

Measurement and evaluation

Given the relative significance and precedence of this program in both the Australian and global context, measurement and evaluation of the program is central to demonstrating not just the program's effectiveness, but, more importantly its safety as a public health program. This is an

integral part of a risk management strategy for this program and will be instrumental in building immunisation provider and public trust in the program.

Vaccine Coverage – reporting to the AIR by providers (GP to AIR), councils to SA database/AIR

Data on vaccine coverage can be collected via two methods:

- Data reported via the School Immunisation Program (SIP) providers on the IS-owned database, IRIS (Immunisation Register and Inventory System)
- Data reported to the Australian Immunisation Register (AIR) by other providers.

Reports from AIR on meningococcal B vaccine coverage, particularly for the infant and childhood cohorts, will require generation of specific data extracts/reports and requires discussion with the federal Department for Human Services (DHS).

Reports from IRIS can be generated internal to SA Health.

Coverage is proposed to be measured as detailed in Table 7 below.

Table 7: Measuring Vaccine Coverage

Program	Data Source	Parameters
Six weeks to one year of age (ongoing)	AIR	Monthly/Quarterly/6 Monthly Reports. By provider type, age, dose number, statistical area, as required
Greater than one year of age to less than four years of age (15 month catch-up program)	AIR	
Year 10 catch up program (11 year catch-up program)	IRIS	
Year 11 catch up program (one year catch-up program)	IRIS	
Adult catch-up program (Year 12 to less than 21 years of age) (one year catch-up program)	AIR	

Vaccine Effectiveness

The following points are suggested for consideration of an evaluation methodology that would aim to assess VE and inform public health policy as to the value of the program:

- Surveillance of *Neisseria meningitidis* through SA Health through clinical, public health and laboratory reporting as IMD is a notifiable disease. Laboratory confirmed cases will be followed up and data collected on demographics, vaccination history, clinical presentation and outcome.
- IMD attack rates will be reported by serogroup and subtype.
- Identify vaccine failures – data on serogroup/genogroup, whole genome sequencing and MATS of individual isolates to determine true vaccine failures.
- VE will be estimated for different age groups (infants, toddler and adolescent cohorts) and for all meningococcal B strains and matched vaccine strains.

Also, to assess for possible waning immunity in children who are vaccinated under the proposed ongoing infant program, the following will be undertaken:

1. Monitoring of any cases in previously vaccinated children that suggest waning immunity.

2. Whole genome sequencing on invasive strains would provide information on whether any break through disease was due to vaccine type or non-vaccine type strains.

The overall cost of the proposed monitoring for these aspects of the program is estimated at an average of [redacted] of the program (see Table 16).

Communication Strategy

The communication strategy for the proposed program would inform parents and carers of eligible children, as well as providers and the general public, about the new meningococcal B program and how to access the vaccines. Communications would be timed in two phases alongside the program rollout, commencing at program launch and continuing through to the end of 2019 in line with the conclusion of the majority of the catch-up programs.

The SA Health website can house full details about the program, with a new web page for the program and a short URL at www.sahealth.sa.gov.au/menb. GPs would be communicated with via the SA Health GP Portal, with feature articles linking through to the new meningococcal B web page.

Existing communications channels to parents and carers can be utilised, including updates to the 'Blue Book' and immunisation consent folders. Case studies featuring parents who have successfully gained access to the vaccine for their child can be created and uploaded to the web page and to the SA Health Facebook page.

A targeted advertising campaign should be used to encourage parents and carers to access the meningococcal B vaccinations that may be made available through the new vaccination program. Paid advertising would be recommended by the Government's Master Media Agency (MMA) but may include boosted social media posts to maximise reach for the content that may be developed and targeted press advertising. The MMA would also be asked to make recommendations on reaching Aboriginal parents and carers, and parents from culturally and linguistically diverse (CALD) backgrounds, such as community radio.

Budget estimate for communication strategy up until [redacted] is estimated at [redacted] with the need for any further communication strategy beyond that date to be reassessed then.

Change Management

As the proposed program is implemented and as evidence relating to meningococcal B vaccination evolves, there will be a requirement for the proposed program to evolve and respond to identified external factors and/or emerging evidence indicating a need for change. Some examples of potential drivers for change include:

1. Inclusion of meningococcal B vaccine in the National Immunisation Program

A national program could include an infant program, adolescent program or both and therefore would indicate an adjustment to the SA meningococcal B vaccine program depending on age groups funded for meningococcal B vaccine.

2. Safety concerns / safety signal

Evidence of a safety signal following introduction of a meningococcal B vaccine program in SA may require a halting of the program until an investigation of the safety signal is undertaken. A recent publication has shown a good safety profile for Bexsero following administration to over 3 million infants in the UK. Safety surveillance of greater than 20,000 doses of Bexsero to adolescents 15-18 years of age in SA has shown a good safety profile of the vaccine in this age group. It is highly

unlikely that a safety signal will be identified. There is less safety data published on Trumenba so it will be important to identify any early safety signals if this vaccine is used in the adolescent program.

3. Lack of vaccine effectiveness

Active surveillance of meningococcal disease will be important during the role out of the MenB vaccine program. Any IMD associated isolates in the vaccinated cohorts will be sent for MATS testing in the UK (Prof. Ray Borrow). VE estimates will be provided following the first year of the program and estimated annually. Both the screening method and case control methodology will be used to assess VE.

If a meningococcal B program is implemented in SA, it is proposed that these factors will be managed, alongside existing change management and risk management controls, in a Risk Management Plan.

Conflict of Interest statements

- Professor Paddy Phillips
    - as part of his role in SA Health is a member of the Reference Group for the B Part of It: Meningococcal B Herd Immunity Study
    - has no other conflicts of interest to declare in relation to membership of the committee.
- Dr Louise Flood
    - as part of her role in SA Health is involved in assessment of adverse events following immunisation for South Australia, including those from the B Part of It: Meningococcal B Herd Immunity Study
    - has children who may eligible for vaccination as a result of this program
    - has no other conflicts of interest to declare in relation to membership of the committee.
- Professor Helen Marshall
    - is an investigator on clinical vaccine trials sponsored by pharmaceutical companies, but receives no personal payments from these companies
    - her institution receives funding for Investigator led studies from Industry (GSK, Pfizer) and she is the Principal Investigator on the B part Of It: Meningococcal B vaccine Herd Immunity study
    - has no other conflicts of interest to declare in relation to membership of the committee.
- Dr Rodney Pearce
    - Has been paid by Sanofi to go to Japan in 2018 (4 days) to talk about meningococcal ACWY but has had no contracts or payments with GSK or Pfizer
    - As a general practitioner receives payments for vaccinating children and adults.
    - Is a Member of the Immunisation Coalition that receives funding for its scientific meetings from vaccine manufacturers.
    - has no other conflicts of interest to declare in relation to membership of the committee.
- Dr Celia Cooper
    - has no conflicts of interest to declare in relation to membership of the committee.
- Dr David Johnson
    - as part of his role in the Aboriginal Health Council is a member of the Reference Group for the B Part of It: Meningococcal B Herd Immunity Study
    - has no other conflicts of interest to declare in relation to membership of the committee.
- Mr Noel Lally
    - As part of his role in SA Health is involved in coordinating the provision of operational support for the B Part of It: Meningococcal B Herd Immunity Study; specifically; maintaining vaccine safety monitoring and reporting for the study and assisting with operational delivery of the program.
    - has no other conflicts of interest to declare in relation to membership of the committee.

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Appendices

Table 8: IMD serogroup B notifications aged 0-29 years in South Australia 2000-24 April 2018: year by age in years at notification

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
2000	4	2	3									1					1	2	1	1	1									1
2001	3	2	4	1	1		1	1		1	1		1							1					2					1
2002	3	1		2				1								1	2			1								1		1
2003	3	3	1	1	2						1	3		1		2	1	1					1		1	1				1
2004	3		1												1				1								1	1		
2005	4	1	1		2	1	1		1								1		2						1					
2006	3		1		1												1		1										1	
2007	3	1		1		1											2	1	1					1						
2008	2	1																	3	3	1		1	1		1		1		1
2009	2	2												1	1	1	1	2	3	2	1							1		
2010	3	2	2	2							1	1	1					1	2	1	1	1								
2011	3	1		1		1													2	1	1									1
2012	3	2	2		1													1	4	2		1	2				1	2		
2013	2	1						1										1	1	2	3	2	1					1		
2014	4	2	2	1	1	1											1	1	2	3	2	1		1						
2015	3	1	1	1														2	5	3	1	1	1	1						
2016		2	1	1											1		1	1	3	2		3		1					1	1
2017	3	2	1	1	1											1	1			2	1			1						
2018	1											1				2	1	1												
	52	26	20	12	9	4	2	3	1	1	3	6	2	2	3	7	13	14	31	24	12	9	6	6	4	2	2	7	2	7

Table 9: IMD serogroup B notifications aged 0-24 months in South Australia 2000-24 April 2018: year by age in months at notification

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	20	21	22	23	24
2000		1	2		1								1					1					2
2001							1		1	1						1			1				
2002								1	2													1	
2003			1	1							1			1	1				1				
2004	1		1	1																			
2005					1		1				1	1									1		
2006							1	1		1													1
2007					1	1		1						1									
2008											1	1									1		
2009				2											1				1				
2010						1	1					1		1							1		
2011				1			1		1					1									
2012					2		1						1								1		
2013					1			1						1									
2014						1	1	1		1										2			
2015				1							2		1										
2016																1						1	1
2017						1				1	1						1	1					
2018							1																
	1	1	4	6	6	4	8	5	4	4	6	3	3	5	2	2	1	2	3	2	4	2	4

Table 10: IMD serogroup B notifications in South Australia 2000 to 24 April 2018 in persons who identify as Aboriginal: year by age (in years) at notification

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2000	1	1	1																	
2001								1												
2002	1																			
2003																				
2004																				
2005	1																			
2006	1		1																	
2007				1																
2008		1																		
2009																				
2010	1			1																
2011	1																			
2012																				
2013																				
2014	1			1																1
2015																				
2016		1																		
2017				1																
2018												1								
	7	3	2	4	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1

There were no cases in this time period in those who identify as Aboriginal and are aged older than 19 years

Table 11: IMD serogroup B notifications in South Australia 2000-24 April 2018 in persons who identify as Aboriginal: year by age (in months) at notification – children aged <= 2 years

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	20	21	22	23	24
2000					1								1										1
2001																							
2002									1														
2003																							
2004																							
2005					1																		
2006							1																1
2007																							
2008																					1		
2009																							
2010							1																
2011				1																			
2012																							
2013																							
2014						1																	
2015																							
2016																1							
2017																							
2018																							
	0	0	0	1	2	1	2	0	1	0	0	0	1	0	0	1	0	0	0	0	1	0	2

Table 12: IMD serogroup B notifications in South Australia 2000-24 April 2018: year by age (years) at notification – deaths

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2000																					
2001																					
2002																					
2003																					
2004																					
2005																					
2006																					
2007																					
2008																					
2009																			1		
2010		1																			
2011		1																		1	
2012																			1		
2013																				1	
2014	1																				
2015																					
2016		1																			
2017		1																			
2018	1																				
	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	0

	50	51	52	53	54	56	58	60	61	63	68	72	73	74	75	76	77	80
2000																		
2001																		
2002																		
2003																		
2004																		
2005																		
2006										1								
2007																		
2008																		
2009				1														
2010																		
2011																		
2012																		
2013																		
2014																		
2015			1															
2016																		
2017				1														
2018																		
	0	0	1	2	0	0	0	0	0	1	0	0	0	0	0	0	0	0

No deaths in this time period in those 21-49 years. Age in months of deaths 2010: 22 months; 2011: 13 months; 2014: 6 months; 2016: 16 months; 2017: 18 months; 2018: 6 months

Table 13: Age specific incidence rates of IMD serogroup B for those aged 0-25 years, in South Australia, 2000 to 2017

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0 years	22.3	17.1	17.1	17.3	17.2	22.8	16.8	15.9	10.2	10.1	15.3	15.5	14.8	9.8	19.8	15.0	0.0	15.4
1 years	10.9	11.1	5.7	17.0	0.0	5.7	0.0	5.5	5.3	10.2	10.1	5.1	10.2	4.9	9.7	4.9	9.9	9.7
2 years	16.3	21.7	0.0	5.6	5.6	5.7	5.6	0.0	0.0	0.0	10.2	0.0	10.1	0.0	9.7	4.8	4.9	4.9
3 years	0.0	5.4	10.8	5.4	0.0	0.0	0.0	5.5	0.0	0.0	10.4	5.1	0.0	0.0	5.0	4.8	4.8	4.9
4 years	0.0	5.3	0.0	10.7	0.0	11.1	5.6	0.0	0.0	0.0	0.0	0.0	5.0	0.0	4.9	0.0	0.0	4.8
5 years	0.0	0.0	0.0	0.0	0.0	5.4	0.0	5.5	0.0	0.0	0.0	5.2	0.0	0.0	4.9	0.0	0.0	0.0
6 years	0.0	5.0	0.0	0.0	0.0	5.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7 years	0.0	5.1	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0
8 years	0.0	0.0	0.0	0.0	0.0	5.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
9 years	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10 years	0.0	5.0	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
11 years	5.0	0.0	0.0	14.8	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
12 years	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
13 years	0.0	0.0	0.0	5.0	0.0	0.0	0.0	0.0	0.0	4.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
14 years	0.0	0.0	0.0	0.0	4.9	0.0	0.0	0.0	0.0	4.8	0.0	0.0	0.0	0.0	0.0	0.0	5.2	0.0
15 years	0.0	0.0	4.9	9.9	0.0	0.0	0.0	0.0	0.0	4.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1
16 years	4.8	0.0	9.7	4.9	0.0	4.9	4.8	9.7	0.0	4.8	0.0	0.0	0.0	0.0	4.9	0.0	4.9	5.0
17 years	9.9	0.0	0.0	4.8	0.0	0.0	0.0	4.7	0.0	9.4	4.7	0.0	4.7	4.8	4.8	9.7	4.8	0.0
18 years	5.0	0.0	0.0	0.0	4.7	9.7	4.8	4.7	13.8	13.9	9.2	9.3	18.9	4.6	9.3	23.5	14.2	0.0
19 years	5.1	5.0	4.9	0.0	0.0	0.0	0.0	0.0	13.8	8.8	4.5	4.5	9.1	9.2	13.3	13.5	9.2	9.2
20 years	5.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.6	4.4	4.3	4.4	0.0	13.4	9.0	4.3	0.0	4.5
21 years	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.3	0.0	4.4	8.8	4.4	4.4	12.8	0.0
22 years	0.0	0.0	0.0	5.0	0.0	0.0	0.0	0.0	4.5	0.0	0.0	0.0	8.5	4.3	0.0	4.3	0.0	0.0
23 years	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.5	4.5	0.0	0.0	0.0	0.0	0.0	4.3	4.3	4.3	4.3
24 years	0.0	10.7	0.0	5.4	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
25 years	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	4.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 14: Maximum number of vaccines recommended at each schedule point

Schedule point	Current number of individual funded/recommended vaccines at each schedule point (based on probable NIP childhood and adolescent schedule from 01 July 2018).				Meningococcal B program in SA	Total (if Men B program implemented in SA)		
	No. of vaccines recommended/funded				No. of vaccines recommended	No. vaccines recommended/funded		
	Vaccine	Injection - no. of doses		Oral - no. of doses	Injection - no. of doses	Injection - no. of doses		Oral - no. of doses
		NIP Childhood	NIP Childhood, NIP ATSI, NIP MAR, SA Influenza < 5 yrs			NIP Childhood	NIP Childhood, NIP ATSI, NIP MAR, SA Influenza < 5 yrs	
Birth	Hep B	1	1			1	1	0
6 weeks (2 months)	Infanrix Hexa, Rotarix, Prevenar 13	2	2	1	1	**3**	**3**	1
4 months	Infanrix Hexa, Rotarix, Prevenar 13	2	2	1	1	**3**	**3**	1
6 months	Infanrix Hexa, Prevenar 13, Influenza	1	3		1	**2**	**4**	0
12 months	MMR, Prevenar 13, Nimenrix, Hepatitis A, Influenza, Hepatitis B	3	6		1	**4**	**7**	0
18 months	MMR-V, DTPa, Hib, Influenza, Hepatitis A	3	5			3	5	0
48 months	DTPa, Pneumococcal, Influenza	1	3			1	3	0
Year 8	HPV, dTpa	3	3			3	3	0
Year 10	Bexsero				2	2	2	0
	Trumenba				2 to 3*	2 to 3*	2 to 3*	0
Year 11	Bexsero				2	2	2	0
	Trumenba				2 to 3*	2 to 3*	2 to 3*	0
Year 12 to < 21 years of age	Bexsero				2	2	2	0
	Trumenba				2 to 3*	2 to 3*	2 to 3*	0

MAR = medically at risk; ATSI = Aboriginal and Torres Strait Islander; NIP = National Immunisation Program

* For individuals at increased risk of IMD

Table 15: Potential [redacted]

YEAR	TOTAL COST BY YEAR		
	[redacted]	[redacted]	[redacted]
*2018	[redacted]	[redacted]	[redacted]
#2019	[redacted]	[redacted]	[redacted]
2020	[redacted]	[redacted]	[redacted]
2021	[redacted]	[redacted]	[redacted]
2022	[redacted]	[redacted]	[redacted]
2023	[redacted]	[redacted]	[redacted]
2024	[redacted]	[redacted]	[redacted]
2025	[redacted]	[redacted]	[redacted]
2026	[redacted]	[redacted]	[redacted]
2027	[redacted]	[redacted]	[redacted]
2028	[redacted]	[redacted]	[redacted]
2029	[redacted]	[redacted]	[redacted]
^2030	[redacted]	[redacted]	[redacted]
2031	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

[redacted]

* Infant and Childhood catch-up programs commence [redacted]

Infant, Year 11 and Year 12 to less than 21 years of age catch up programs commence [redacted]

^ Year 10 catch up program end

Table 16: Estimated cost of evaluation and safety surveillance of the SA MenB vaccine program

Study 1: Evaluation of infant & Adolescent Program.		FTE	**2019**	**2020**	**2021**	**2022**	oncost included
[redacted]							
Study 2: Vaccine effectiveness		FTE	**2019**	**2020**	**2021**	**2022**	
[redacted]							
Study 3: Vaccine safety		FTE	**2019**	**2020**	**2021**	**2022**	
[redacted]							

Table 17: Overall Cost per Program Element

Program		**Estimated Cost**			**Total cost of each program**
Program Name	Term of Program (years)	Vaccine		Program Costs*	
Meningococcal B Program: Infant	Annual (ongoing)	[redacted]	[redacted]	[redacted]	[redacted]
Meningococcal B Catch Up Program: Childhood	1.25	[redacted]	[redacted]	[redacted]	[redacted]
Meningococcal B Catch Up Program: Year 10	12	[redacted]	[redacted]		[redacted]
		[redacted]		[redacted]	[redacted]
		[redacted]	[redacted]		[redacted]
Meningococcal B Catch Up Program: Year 11	1	[redacted]	[redacted]		[redacted]
		[redacted]		[redacted]	[redacted]
		[redacted]	[redacted]		[redacted]
Meningococcal B Catch Up Program: Year 12 to less than 21 years of age	1	[redacted]	[redacted]		[redacted]
		[redacted]		[redacted]	[redacted]
		[redacted]	[redacted]		[redacted]

*Program costs calculated for first five years of the program and include costs associated with a Communication Strategy, Program Implementation, Program Evaluation, Vaccine Effectiveness Direct Costs and Vaccine Safety & Surveillance mechanisms. Costs are extrapolated based on the term of the program, except the Meningococcal B Program: Infant as this is ongoing.

For more information

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