Record of the Immunisation Subcommittee Meeting held on 8 March 2019

(minutes for web publishing)

Immunisation Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.*

Note that this document is not necessarily a complete record of the Immunisation Subcommittee meeting; the relevant portions of the minutes relating to Immunisation Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Immunisation Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes will be reviewed by PTAC at its meeting on 22 & 23 August 2019, the record of which will be available in due course.

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Present from the Subcommittee:

Sean Hanna (Chair, PTAC member)
Karen Hoare
Osman Mansoor
Stephen Munn (PTAC member)
Edwin Reynolds
Michael Tatley
Nikki Turner
Ayesha Verrall
Tony Walls
Elizabeth Wilson

Apologies:

Stuart Dalziel
Cameron Grant
Lance Jennings

Ministry of Health Observers:

Chris Miller
Niki Stefanogiannis

Present from PHARMAC:
Andrew Oliver
Lindsay Ancelet
John Wyeth
Caroline De Luca
Hannah Hoang

Summary of recommendations

3.3 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule for children 1 year of age with a high priority, with a one year catch up programme for children 1 to 4 years of age.

3.4 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule with a high priority at 14 years of age.

3.5 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule for a one year catch up for adolescents and young adults, with PHARMAC staff to model catch up options for 5 to 21 years of age or 13 to 21 years of age.

3.6 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule with a high priority for individuals 13-25 years of age who are entrants into close living situations with a one year catch up for individuals 13-25 years of age in close living situations.

4.3 The Subcommittee **recommended** that meningococcal B vaccine (MenB) be listed in the Pharmaceutical Schedule with a low priority for infants with a 2+1 dosing schedule, due to the reactogenicity of the vaccine, the need for prophylactic paracetamol administration, the need to add another scheduled visit to the Childhood Immunisation Schedule and the high cost of 4CMenB vaccination.

4.4 The Subcommittee **recommended** that MenB be listed in the Pharmaceutical Schedule with a high priority for special groups (immunocompromised people as defined by the current meningococcal ACWY access criteria) since this group is at risk from all groups of meningococcal disease.

4.5 The Subcommittee **recommended** MenB be listed in the Pharmaceutical Schedule with a medium priority for close contacts of meningococcal B cases and people who have previously had meningococcal disease of any group. The Subcommittee considered that these people are at higher risk of contracting meningococcal disease.

4.6 The Subcommittee **recommended** that MenB be listed in the Pharmaceutical Schedule with a high priority for adolescents and young adults aged 13-25 years in close living situations, with a one year catch up programme. The Subcommittee considered that adolescents and young adults in close living situations have a higher risk of meningococcal disease and reducing nasal carriage in this group will reduce the risk.

5.3 The Subcommittee **recommended** that an additional dose of hexa-valent DTaP-IPV-HepB/Hib at 15 months of age be funded on the Pharmaceutical Schedule instead of the current Hib vaccine with a high priority. The Subcommittee considered that an additional pertussis dose given at the 15 month visit would provide additional protection in the context of the ongoing pertussis outbreak and possible waning immunity before the next pertussis dose is given at 4 years of age.

1. Declared interests

1.1 The Subcommittee was updated on conflicts of interests including perceived and actual conflict of interests, including research and shareholdings in pharmaceutical companies, due to requests for information under the Official Information Act 1982. The Subcommittee was informed that declarations of actual and perceived conflicts were required for appropriate management, as it was important to consider how a conflict may be perceived by the public.

1.2 The Subcommittee members noted their responsibilities for declaring all actual, potential, and apparent conflicts of interest that may arise during the duration of their involvement with PHARMAC and the Subcommittee. Members noted that a new process for the management of perceived and actual conflicts was implemented on 29 September 2017. Members noted that their signed declaration forms, as detailed below, had been reviewed by PHARMAC's Medical Director and the Subcommittee Chair who determined that the conflicts declared were manageable without any specific action required for the meeting.

1.3 Tony Walls declared that he would be an investigator in a Seqirus influenza vaccine trial that will be recruiting patients in 2019.The Chair deemed the interest a conflict, but participation permitted under Board Chair's Standing Permission.

1.4 Sean Hanna, Karen Hoare, Osman Mansoor, Stephen Munn, Edwin Reynolds, Michael Tatley, Nikki Turner, Ayesha Verrall, and Elizabeth Wilson declared that they had no new interests to declare since their most recently signed declaration with PHARMAC.

2. Record of previous minutes

2.1 The Subcommittee noted the previous minutes from the 18 September 2018 meeting.

2.2 The Subcommittee reiterated its view regarding the urgency for funding pertussis vaccination for pregnant women before 28 weeks of pregnancy (January 2018 recommendation with high priority). PHARMAC staff provided a confidential update to Members that consultation on a proposal to widen access to pertussis vaccination for women at any stage of pregnancy is likely to be released soon and is being progressed as soon as possible with an expected implementation date of 1 July 2019.

2.3 The Subcommittee reiterated the very high health need of this population in the current national pertussis epidemic. Members considered that funding of pertussis vaccination for women in pregnancy should be progressed urgently, in the same

way as vaccination for the recent meningococcal outbreak response. The Subcommittee considered PHARMAC should reconsider the implementation date with this in mind.

2.4 The Subcommittee considered that the minutes were an accurate reflection of the meeting that took place on 18 September 2018.

3. Meningococcal ACWY vaccine

Conflicts of interests

3.1 The Chair noted that there were no conflicts of interest for this item.

Application

3.2 The Subcommittee reviewed a paper from PHARMAC staff regarding the funding of meningococcal ACWY (MenACWY) vaccine for: inclusion in the Pharmaceutical Schedule; adolescents aged 13-19 years; and adolescents aged 13-19 years in close living circumstances.

Recommendation

3.3 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule for children 1 year of age with a high priority, with a one year catch up programme for children 1 to 4 years of age.

3.4 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule with a high priority at 14 years of age.

3.5 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule for a one year catch up for adolescents and young adults, with PHARMAC staff to model catch up options for 5 to 21 years of age or 13 to 21 years of age.

3.6 The Subcommittee **recommended** that a single dose of MenACWY vaccine be listed in the Pharmaceutical Schedule with a high priority for individuals 13-25 years of age who are entrants into close living situations with a one year catch up for individuals 13-25 years of age in close living situations.

Discussion

3.7 The Subcommittee noted that at its May 2018 meeting, it considered a paper from PHARMAC staff assessing the effects of funding a meningococcal C vaccination programme for adolescents and young adults in close living circumstances, infants and adolescents, with catch up programmes. The Subcommittee noted that it requested the PHARMAC staff conduct further analysis for people in close living situations and provide the most recent meningococcal C epidemiology possible.

3.8 The Subcommittee noted that at its September 2018 meeting, it considered a paper from PHARMAC staff providing updated epidemiology and further analysis

of various population options for people in close living situations and the vaccination of infants, toddlers and adolescents. The Subcommittee noted that it recommended that a quadrivalent MenACWY vaccine be listed for toddlers in the second year of life and adolescents with a possible catch up, with a high priority. The Subcommittee noted that it would like to review toddler dosing and possible options for catch up programme following the vaccines commercial process planned for late 2018. The Subcommittee noted that it recommended that meningococcal C only vaccination for childhood vaccination be declined.

3.9 The Subcommittee noted that PHARMAC issued a Request for Proposals (RFP) for the supply of various vaccines in November 2018, including conjugate MenACWY vaccine with the possibility of widened access. Supply of vaccines under any contracts resulting from the RFP would be for commencing supply from June 2020.

3.10 The Subcommittee noted a paper from PHARMAC staff containing further analysis of vaccination options and possible target groups for MenACWY vaccine, incorporating vaccine availability and costs following the vaccines RFP. The Subcommittee noted that PHARMAC sought further clinical advice about groups that would benefit from MenACWY vaccination and the preferred vaccination dosing and scheduling options.

3.11 The Subcommittee noted that in November 2018 there was a declared outbreak of MenW in Northland. The Subcommittee noted that it provided advice to PHARMAC by email recommending a vaccination response to the outbreak and defining the target populations for vaccination. The target groups were children 9 months to 5 years of age and adolescents 14 to 19 years of age. The Subcommittee noted that approximately 14,000 doses of Menactra and Nimenrix vaccines were delivered in Northland from November 2018 to January 2019.

3.12 The Subcommittee considered that vaccination against meningococcal disease is the preferred management strategy as it is a rapidly progressing disease for which antibiotic treatment may not always be provided in time to prevent disability or death. The Subcommittee noted that over the last 5 years, a quadrivalent meningococcal ACWY (MenACWY) vaccine would have covered twice as many isolates of *N. meningitidis* as targeting meningococcal C (MenC) alone. The Subcommittee noted that although the total number of MenACWY cases has remained steady, the number of Men W and Men Y cases had started to increase over the last two years, while the number of Men C cases has remained very low.

3.13 The Subcommittee considered that the patient populations who would benefit most from MenACWY vaccination would be infants, adolescents, Māori and Pacific people, although all age groups have some risk. Non-vaccinees can get some indirect protection through reduction of transmission (herd immunity). This has been shown for MenC and MenA, but there is currently very limited evidence showing herd immunity for MenW.

3.14 The Subcommittee considered that internationally meningococcal disease is rare but serious. The Subcommittee considered that randomised controlled trials (RCTs) are not feasible against disease endpoints because of the large sample

sizes that would be required and because of ethics considerations relating to the high case fatality rate for this disease. For this reason, studies of meningococcal vaccine effectiveness often make use of intermediate endpoints such as measures of immunogenicity, and often consist of observational data.

3.15 The Subcommittee considered an observational report of surveillance data from the first 4 years since the introduction of Men C conjugate vaccine in the UK for all people under 19 years of age in 1999, followed by the introduction of routine infant vaccination for children <1 year (Trotter et al. Lancet 2004;364:365-7). Vaccine effectiveness remained high (90%) for children aged 5 months to 18 years who were vaccinated in the catch up campaign, but vaccine effectiveness fell for children vaccinated in the routine infant immunisation programme. The Subcommittee considered that although this was an observational study, it used a national dataset so would be highly representative and was high quality observational data.

3.16 The Subcommittee considered MenC epidemiology data for the UK both before and up to 10 years after the introduction of its MenC vaccination programme (Campbell et al. Clin Vaccine Immunol. 2010;17:840-7). The Subcommittee noted that the epidemiological data showed the near elimination of MenC disease by 10 years after the introduction of the vaccination programme with the conjugate vaccine. The Subcommittee noted that vaccine effectiveness was shown to fall more than 1 year after completion of the 3-dose infant schedule, but the substantial reduction in MenC disease has been sustained, mainly due to indirect herd immunity effects from the reduction in carriage.

3.17 The Subcommittee noted that in 2015 the UK changed its meningococcal vaccination focus to herd immunity rather than individual protection (antibody responses in the first year of life). The UK currently offers a single dose of Hib/MenC vaccine at 1 year of age and a single dose of MenACWY vaccine (Menveo or Nimenrix brands) at 14 years of age and for new university students 19-25 years of age.

3.18 The Subcommittee considered a nationwide observational study from the Netherlands reported a 99% and 93% decline in MenC invasive disease in the eligible and non-eligible population for vaccination following vaccine introduction in 2002 (1998 to 2001 vs 2002 to 2012) (Bijlsma Clin Infect Dis. 2014;59:1216-21). Indirect protection was responsible for >36% of MenC vaccine impact.

3.19 The Subcommittee considered a phase 3 randomised clinical trial of MenACWY (conjugated to CRM) or MenB (4CMenB) vaccination on nasal carriage rates in 18-24 year olds (Read et al. Lancet 2014;384:2123-31). The Subcommittee noted that MenACWY-CRM reduced carriage of group Y by 39% and groups CWY by 36.2%. 4CMenB reduced carriage rates of groups BCWY by 26.6%. The Subcommittee considered that the reduction in carriage was lower for group W, so there might be less herd immunity effects for W.

3.20 The Subcommittee considered a case-control evaluation of vaccine effectiveness (VE) and duration of protection of a MenACWY diphtheria toxoid conjugate vaccine (MenACWY-D / Menactra) in the United States (Cohn et al. Pediatrics

2017;139:e20162193). The Subcommittee noted that a single dose of MenACWY-D was administered to adolescents between 2006 and 2013. Vaccine effectiveness was calculated at 69% (95% CI:51-80%) across the CYW strains. The Subcommittee noted that MenACWY-D was effective in the first year after vaccination, but effectiveness waned 3 to 8 years after vaccination.

3.21 The Subcommittee considered an observational study of MenACWY conjugated to tetanus toxoid (MenACWY-TT / Nimenrix) in an emergency vaccination programme in the UK targeting adolescents leaving school (with catch up) and new university entrants up to 25 years of age in England (Campbell et al. Emerg Infect Dis. 2017;23:1184-7). The Subcommittee considered that meningococcal epidemiology in the UK showed a cyclic periodicity over 10-15 years. The Subcommittee noted that although cases of MenW had been predicted to increase, there was a 69% reduction from predicted levels after the first year that MenACWY vaccination was introduced, with only 36.6% coverage in the target cohort. The Subcommittee considered that even though there may be a lower level of herd immunity for MenW compared to other meningococcal groups, vaccination appears to be very effective at preventing Men W cases. The Subcommittee noted that 4CMenB vaccination may have had some influence on MenACWY data. The Subcommittee noted data provided by the Ministry of Health that MenW cases in England and Australia approximately doubled year on year before immunisation programmes were introduced. The UK cases started to decline two years after the start of a national immunisation programme for MenW.

3.22 The Subcommittee considered that MenACWY vaccination could provide a health benefit for family, whānau or wider society by reducing the risk of meningococcal outbreaks, which are disruptive to the community and schooling. The Subcommittee considered that meningococcal outbreaks are resource intensive for the health sector to manage. The heightened awareness of meningococcal disease results in increased referrals to DHBs and increased consultations for the worried well.

3.23 The Subcommittee noted that it had considered the impact of meningococcal sequelae on the health sector at its May 2018 meeting, where it noted that there is a 10-20% serious disability rate for people who survive meningococcal disease, with those who experience significant complications requiring ongoing care and support. The Subcommittee noted that MenW has an atypical presentation and a higher case fatality rate than other groups. The Subcommittee considered that the uptake estimates for adolescents in close living situations that it provided at its May 2018 meeting were low in the context of the current public awareness of meningococcal disease and should be revised up to 75%.

3.24 The Subcommittee noted that the UK has about half the rate of meningococcal disease of New Zealand, and other developed countries also have lower incidence rates than New Zealand. The Subcommittee requested that PHARMAC staff consider if modelling data can be used to predict fluctuations in meningococcal disease cases following implementation of a MenACWY vaccine programme.

3.25 The Subcommittee considered an observational study in Brazil evaluating the effect of MenC vaccination of children under 5 years of age in the State of Bahia

with MenC conjugated to TT or CRM (Neisvac-C or Menjugate) vaccination which also included a catch up programme for individuals 10-24 years of age (Macedo et al. Hum Vaccin Immunother. 2018;14:1131-7). The Subcommittee noted that the area that included the catch up programme had reduced incidence of MenC disease in all age groups with virtually no MenC cases after 5 years. The Subcommittee considered that this indicated that the inclusion of an adolescent catch up programme can provide herd protection for MenC, including for infants.

3.26 The Subcommittee considered an Immunisation Advisory Centre meningococcal antigen review (Nowlan 2018;IMAC website). The Subcommittee noted that the antigen review postulated that a single dose of MenACWY vaccine in early or mid-adolescence is likely to provide indirect protection to other age groups of highest risk, with the possible exception of MenW. A mass catch up campaign is the most effective strategy to rapidly gain herd immunity.

3.27 The Subcommittee considered that while indirect protection (herd immunity) is well documented for A and C, particularly where both children and adolescents are targeted, it is not yet established for other serotypes. The Subcommittee considered that there was a lack of data about MenW nasal carriage rates, but considered there may be an individual protective effect and some herd immunity without necessarily achieving significant carriage reduction. Members considered that conjugate MenC vaccination of all individuals under the age of 19, with continued vaccination of infants and at 14 years, would provide approximately 30% herd immunity effect.

3.28 The Subcommittee considered that if a one dose infant schedule was introduced in New Zealand, it would be best to also give an adolescent dose and have a catch up programme for children from 1 to 4 years of age and adolescents from 13 – 21 years of age.

3.29 The Subcommittee noted that if MenACWY was added to the immunisation schedule, some changes would need to be made to accommodate the extra vaccine doses required. An additional immunisation visit would be required at 12 months since adding MenACWY to the existing 15 month visit would result in 5 vaccinations being administered at that visit which would not be pragmatically feasible. The Subcommittee noted that a one dose infant and one dose adolescent programme could be given at the 15 month visit and at a school visit, possibly around 14 years of age. The Subcommittee noted that Menactra and Nimenrix are generally well tolerated and not particularly reactogenic. Menactra is currently listed in the Pharmaceutical Schedule for special groups. The Subcommittee considered that either Menactra or Nimenrix would be suitable to list in the Pharmaceutical Schedule, and the product to be considered for listing would be determined from the RFP.

3.30 The Subcommittee considered that MenACWY should be listed in the Pharmaceutical Schedule for children at 1 year of age, with a high priority, with a catch up programme for children 1 to 4 years of age due to the risk and impact of outbreaks, being a difficult disease to diagnose and projected increased rates expected in the next few years based on overseas data. The Subcommittee considered that a national vaccination programme should be considered before

the W rates start to rise dramatically in New Zealand.

3.31 The Subcommittee considered that a single dose of MenACWY should be listed in the Pharmaceutical Schedule with a high priority at 14 years of age with a one year catch up for individuals 5 to 21 years of age due to the risk and impact of outbreaks, being a difficult disease to diagnose and projected increased rates expected in the next few years based on overseas data.

3.32 The Subcommittee considered that a single dose of MenACWY be listed in the Pharmaceutical Schedule with a high priority for individuals 13-25 years of age who are entrants into close living situations with a one year catch up for individuals 13-25 years of age in close living situations due to the risk and impact of outbreaks, being a difficult disease to diagnose and projected increased rates expected in the next few years based on overseas data.

4. Meningococcal B vaccine

Conflicts of interests

4.1 The Chair noted that there were no conflicts of interest for this item.

Application

4.2 The Subcommittee reviewed a paper from PHARMAC staff regarding the funding of meningococcal B vaccine (MenB) for infants with a 2+1 dosing schedule in the Pharmaceutical Schedule, adolescents in close living situations, special groups (immunocompromised) and close contacts of cases.

Recommendation

4.3 The Subcommittee **recommended** that meningococcal B vaccine (MenB) be listed in the Pharmaceutical Schedule with a low priority for infants with a 2+1 dosing schedule, due to the reactogenicity of the vaccine, the need for prophylactic paracetamol administration, the need to add another scheduled visit to the Childhood Immunisation Schedule and the high cost of 4CMenB vaccination.

4.4 The Subcommittee **recommended** that MenB be listed in the Pharmaceutical Schedule with a high priority for special groups (immunocompromised people as defined by the current meningococcal ACWY access criteria) since this group is at risk from all groups of meningococcal disease.

4.5 The Subcommittee **recommended** MenB be listed in the Pharmaceutical Schedule with a medium priority for close contacts of meningococcal B cases and people who have previously had meningococcal disease of any group. The Subcommittee considered that these people are at higher risk of contracting meningococcal disease.

4.6 The Subcommittee **recommended** that MenB be listed in the Pharmaceutical Schedule with a high priority for adolescents and young adults aged 13-25 years in close living situations, with a one year catch up programme. The Subcommittee

considered that adolescents and young adults in close living situations have a higher risk of meningococcal disease and reducing nasal carriage in this group will reduce the risk.

Discussion

4.7 The Subcommittee noted that MenB disease had previously been considered at its February 2015 meeting, when it noted that MenB disease had a higher incidence than Men C disease and recommended that PHARMAC assess the New Zealand epidemiology for similarities in incidence patterns in the UK and Australia.

4.8 The Subcommittee noted that in February 2018, PHARMAC purchased 100 doses of MenB vaccine (4CMenB, Bexsero) as emergency stock that could be used in the event of a MenB outbreak in a multi-occupancy residential setting such as university halls of residence. Bexsero did not have Medsafe approval for use in New Zealand at that time, so a limited quantity was purchased for use under Section 29 of the Medicines Act in the event of an outbreak in a multi-occupancy residential setting. Bexsero gained Medsafe approval in July 2018.

4.9 The Subcommittee noted that it considered a supplier funding application for 4CMenB (Bexsero, GSK) at its May 2018 meeting, prior to Medsafe approval, and recommended funding for infants on the Pharmaceutical Schedule with a 2+1 dosing schedule with a medium priority, and recommended funding for high risk groups and close contacts with a medium priority. The Subcommittee noted that it previously considered the evidence for 4CMenB at its May 2018 meeting, and at this meeting would consider recently published data and provide advice about the implementation of a MenB vaccination programme.

4.10 The Subcommittee noted that the Pharmacology and Therapeutics Advisory Committee (PTAC) considered the supplier funding application for 4CMenB (Bexsero) at its February 2019 meeting following recent Medsafe approval. Timing was also aligned to provide advice for the Request for Proposals (RFP) for the supply various vaccines issued in November 2018. PTAC recommended funding with a medium priority for universal childhood vaccination with an infant 2+1 dosing schedule and funding with a medium priority for adolescents in close living situations.

4.11 The Subcommittee noted that the RFP included the possible option for a MenB vaccine. Supply of vaccines under any contracts resulting from the RFP would be for commencing supply from June 2020.

4.12 The Subcommittee noted a paper from PHARMAC staff containing further analysis of vaccination options and possible target groups for MenB vaccine, incorporating vaccine availability and costs following the vaccines RFP. The Subcommittee noted that PHARMAC sought further clinical advice about groups that would benefit from MenB vaccination and the preferred vaccination dosing and scheduling options.

4.13 The Subcommittee noted recent epidemiological data (up to January 2019) that highlighted that the proportion of meningococcal cases due to each serotype has

changed since 2016, with the emergence of more group W and Y cases and fewer cases due to groups C and B. MenB still accounts for the majority of New Zealand cases. The Subcommittee noted that the literature describes a case fatality rate of 10% for invasive meningococcal disease, but the Subcommittee considered that that this would be closer to 4-6% in New Zealand. The Subcommittee considered that case fatality rates vary by strain, expected to be lower for B, intermediate for C and higher for W.

4.14 The Subcommittee noted that from 1991 – 2007, New Zealand experienced a prolonged epidemic of MenB, driven by a single subtype (B: P1.7-2,4), resulting in 6,128 cases and 252 deaths. The MeNZB vaccine was introduced from 2004 – 2008 to manage the epidemic. Disease notifications that were already declining, declined more rapidly. The Subcommittee noted that the immune response to the vaccine was short-lived and it is not expected that anyone previously vaccinated with MeNZB would have sustained immunity to MenB.

4.15 The Subcommittee considered that invasive meningococcal disease disproportionately affects Māori and Pacific people, with these populations exhibiting four times higher rates across all age groups compared to the non-Maori/non-Pacific population. The Subcommittee considered that socioeconomic status and household crowding were factors in the increased rates in these groups. The Subcommittee considered that although there was evidence of a herd effect for MenACWY vaccines, there was no documented herd immunity effect from the New Zealand MenB vaccination programme.

4.16 The Subcommittee noted that the supplier recommends prophylactic paracetamol 30 minutes prior to administration of 4CMenB, followed by two more doses of paracetamol six hours apart to manage the known reactogenicity of the vaccine, particularly fever so as to reduce unnecessary medical intervention. Paracetamol is not currently recommended to be administered for childhood vaccinations, so this would potentially represent an additional cost and increase in primary care workload to manage this. The Subcommittee considered that if prophylactic paracetamol was not administered, there would be a risk of children presenting at ED and being worked up for high fever. Members noted that immunisation rates for the 6 week visit were below the Ministry of Health's 95% target, and any issues with the reactogenicity of 4CMenB could adversely affect coverage. The Subcommittee considered that the evidence on prophylactic paracetamol administration on other vaccines administered at the same visit remains uncertain.

4.17 The Subcommittee noted a surveillance report of the short-term safety profile of 4CMenB during a mass meningococcal vaccination campaign in Canada targeting approximately 60,000 individuals ≤20 years of age (De Serres et al. Vaccine 2018;36:8039-46). The Subcommittee noted that the 7-day reactogenicity profile was similar to that seen in earlier clinical trials, but indicated frequent adverse events following immunisation which resulted in school absenteeism and medical consultations. The Subcommittee noted that the incidence of fever on days 1-2 was highest in children under 2 years of age, with 0.6% reporting a temperature ≥40ºC.

4.18 The Subcommittee noted a phase 3b randomised controlled trial investigating the

immunogenicity and safety of 4CMenB and MenACWY-CRM vaccines (Marcias Parra et al. Vaccine 2018;36:7609-17). The Subcommittee noted that co-administration of the two meningococcal vaccines was non-inferior to single immunisation in infants.

4.19 The Subcommittee considered a study using data from a phase 3b multicentre clinical trial, evaluating the strain coverage of 4CMenB administered with a 2+1 or 3+1 dosing schedule (Biolchi et al. Hum Vaccin Immunother. 2018; doi: 10.1080/21645515.2018.1537756). The Subcommittee noted that in line with the approved dosing schedule, 4CMenB is administered as a 3+1 schedule in some countries, but the UK uses a 2+1 schedule. The Subcommittee noted that the study reported that to the immunogenicity of a 2+1 schedule appears non-inferior to a 3+1 infant vaccination schedule.

4.20 The Subcommittee noted a prospective surveillance study assessing adverse reactions to 4CMenB in children up to 18 months of age following the introduction of routine infant 4CMenB immunisation in the UK (Bryan P et al. Lancet Child Adolesc Health 2018;2:395-403). The Subcommittee noted that over the surveillance period from September 2015 to May 2017, approximately 1.29 million children aged 2-18 months received a combined 3 million doses of 4CMenB. There were 902 reports of suspected adverse reactions, of which 366 (41%) were related to local reactions and 364 (40%) were related to fever.

4.21 The Subcommittee considered that MenB epidemiology shows the bimodal burden of disease with peaks for children under 5 years of age and people 15-20 years of age. The Subcommittee considered that 4CMenB offers a relatively short duration of protection, with a primary schedule protecting children to 5 years of age, but a booster would be required by about 15 years of age to protect those 15-20 years of age.

4.22 The Subcommittee noted that if 4CMenB was added to the childhood immunisation schedule, some changes would need to be made to accommodate the extra vaccine doses required. The Subcommittee considered that with a 2+1 dosing schedule, doses would be administered at 6 weeks, 3 months and in the second year of life. This would require an additional immunisation visit, probably at 12 months, since adding 4CMenB to the existing 15 month visit would result in 5 vaccinations being administered at that visit. The Subcommittee noted that Bexsero is approved for use in children from 2 months of age but considered that vaccination from 6 weeks was appropriate as infants under 1 year of age are the group most affected by meningococcal disease.

4.23 The Subcommittee noted PHARMAC estimates of the group sizes and uptake assumptions for the groups under consideration. The Subcommittee considered that the uptake in adolescents and young adults in close living situations could be up to 75%, given the recent media attention and focus on meningococcal disease.

4.24 The Subcommittee noted that the UK Joint Committee on Vaccination and Immunisation (JCVI) considered a supplier application for 4CMenB which included a number of revisions suggested by the JCVI to improve the cost effectiveness. These revisions included the use of a quality of life adjustment factor of 3, a

proportion of litigation costs associated with meningococcal disease in the NHS and inclusion of quality of life losses to family members. With the incorporation of these factors, the JCVI concluded that the vaccine could be cost effective at a very low vaccine price. The Subcommittee noted that none of these economic evaluation practices are in accordance with economic evaluations carried out by PHARMAC.

4.25 The Subcommittee considered the reactogenicity of the vaccine, the need for prophylactic paracetamol administration and the need to add another scheduled visit to the Childhood Immunisation Schedule could significantly impact the successful implementation of a meningococcal B vaccine programme and noted concerns regarding the impact on the wider success of the childhood immunisation schedule. The Subcommittee also noted the very high cost of 4CMenB vaccination and high cost of implementation to support such a programme.

4.26 The Subcommittee requested to review the epidemiological data for meningococcal B cases for each month of life for children under the age of 1 year to better inform appropriate timing for vaccination.

4.27 The Subcommittee considered that adolescents and young adults aged 13-25 years in close living situations would be at an increased risk of contracting meningococcal B disease. Members considered that there was no evidence that vaccination with 4CMenB provided any herd immunity.

4.28 The Subcommittee considered that immunocompromised people, as defined by the current meningococcal ACWY access criteria, as well as close contacts of meningococcal B cases would be at an increased risk of contracting meningococcal disease and would have a high health need.

4.29 The Subcommittee considered that the special group and close contact eligibility criteria for MenB should be same as for MenACWY vaccine with the following proposed criteria:

Any of the following:

1. Maximum of three doses for infants under one year of age or maximum of two doses for people aged one year or older meeting any of the following criteria:
    a) for patients pre- and post splenectomy and for patients with functional or anatomic asplenia, HIV, complement deficiency (acquired or inherited), or pre or post solid organ transplant; and a booster every 5 years; or
    b) close contacts of meningococcal cases; or
    c) for patients who have previously had meningococcal disease; or
    d) for bone marrow transplant patients; or
    e) for patients following immunosuppression*.

*Immunosuppression due to steroid or other immunosuppressive therapy must be for a period of greater than 28 days.

5. Vaccine RFP 2019

Conflicts of interests

5.1 Tony Walls declared that he would be an investigator in a Seqirus influenza vaccine trial that will be recruiting patients in 2019.The Chair deemed the interest a conflict, but participation permitted under Board Chair's Standing Permission.

Background

5.2 The Subcommittee considered a paper from PHARMAC staff regarding the Request for Proposals (RFP) for various vaccines and influenza vaccines, outlining a number of possible changes to funded vaccines that could occur from July 2020 as a result of the RFP.

Recommendations

5.3 The Subcommittee **recommended** that an additional dose of hexa-valent DTaP-IPV-HepB/Hib at 15 months of age be funded on the Pharmaceutical Schedule instead of the current Hib vaccine with a high priority. The Subcommittee considered that an additional pertussis dose given at the 15 month visit would provide additional protection in the context of the ongoing pertussis outbreak and possible waning immunity before the next pertussis dose is given at 4 years of age.

Discussion

Adult diphtheria and tetanus vaccine

5.4 The Subcommittee noted that Adult diphtheria and tetanus vaccine (ADT Booster) is currently funded in the Pharmaceutical Schedule and listed on the National Immunisation Schedule at 45 and 65 year old visits and is also used ad hoc for tetanus boosters for tetanus prone wounds. The Subcommittee considered that many people were receiving more tetanus boosters than required over their lifetime. The Subcommittee considered that the funding of a tetanus containing vaccine for people 45 years old could be amended to remove the need to vaccinate all 45 year olds and instead enable a catch up dose at 45 years of age for those who have not previously had at least 4 previous tetanus doses. Members noted that would target the need of tetanus vaccination appropriately. The Subcommittee noted that providers cannot claim the immunisation benefit for vaccine administration for 45 and 65 year olds.

5.5 The Subcommittee considered if a different vaccine could be used to provide an adult tetanus vaccine to help manage costs. The Subcommittee considered that Boostrix (vaccine containing diphtheria, tetanus and pertussis) would be a suitable replacement for ADT Booster in the Pharmaceutical Schedule for the following groups:

1. Patients aged 45 who have not had 4 previous tetanus doses
2. Patients aged 65 years old
3. Previously unimmunised or partially immunised patients
4. Revaccination following immunosuppression
5. Boosting of patients with tetanus-prone wounds

5.6 The Subcommittee considered that messaging about any change in tetanus containing vaccine needs to clearly explain that the change is related to price and availability of adult diphtheria and tetanus vaccine and not for a clinical reason. There is no evidence that using adult pertussis as a booster vaccine reduces overall disease in a community. However, Members also noted that increasing pertussis immunity in this age group may be advantageous in the current pertussis epidemic setting.

5.7 Members noted that some people may choose not to accept vaccination for tetanus if the vaccine also contained pertussis, however this potential risk could be managed with appropriate messaging and implementation support.

5.8 The Subcommittee considered that PHARMAC should seek external advice from an immunologist regarding the most appropriate alternative tetanus containing vaccine that could be used for testing for primary immunodeficiency diseases.

Haemophilus influenzae B vaccine

5.9 The Subcommittee noted that *Haemophilus influenzae* B (Hib) vaccine is included in the Pharmaceutical Schedule and National Immunisation Schedule as part of a hexa-valent vaccine at 6 week, 3 month and 6 month visits. It is also included in the Schedule as a Hib only vaccine at the 15 month infant visit.

5.10 The Subcommittee considered that the hexa-valent vaccine could be used as a replacement for the Hib only vaccine at the 15 month visit and any catch up vaccinations required for children. As the hexa-valent vaccine is not approved for use in older children and adults, the Hib only vaccine would need to remain listed for older children, adolescents and adults at high risk (see below) who can not receive a combined vaccine. The Subcommittee considered the eligibility criteria for the Hib only vaccine could be amended as follows for this scenario (amendments in bold and strikethrough):

One dose for patients meeting any of the following:

~~1. For primary vaccination in children; or~~

2. An additional dose (as appropriate) is funded for (re-)immunisation for patients **10 years of age and older** post haematopoietic stem cell transplantation, or chemotherapy; functional asplenic; pre or post splenectomy; pre- or post solid organ transplant, pre- or post cochlear implants, renal dialysis and other severely immunosuppressive regimens; or

3. For use in testing for primary immunodeficiency diseases, on the recommendation of an internal medicine physician or paediatrician.

5.11 The Subcommittee considered that it would be important to retain flexibility regarding the Hib only vaccine market as there was potential for future scheduling changes from other vaccines, such as introducing a 12 month visit if meningococcal vaccines were to be added to Pharmaceutical Schedule, that would likely impact on the use of the Hib only vaccine in the Childhood Immunisation Schedule.

Hepatitis B

5.12 The Subcommittee noted the ongoing stock issues with the currently contracted hepatitis B vaccine. The Subcommittee noted the preferred supplier of Hepatitis B vaccine and had no comments regarding the proposed change for this vaccine.

Pneumococcal vaccines

5.13 The Subcommittee noted that PCV10 pneumococcal vaccine (Synflorix) is currently listed to provide the primary course of pneumococcal vaccination in children. PCV13 (Prevenar) is currently listed for use in high risk people. Both PCV10 and PCV13 are administered with a 3+1 dosing schedule. The Subcommittee noted that at its September 2018 meeting it recommended that New Zealand could move from a 3+1 to a 2+1 dosing schedule for PCV10 or PCV13, and also considered that PCV13 with a 2+1 dosing schedule would be suitable for high risk groups.

5.14 The Subcommittee considered that its previous recommendations to move to a 2+1 schedule for PCV10 and PCV13 remained appropriate. The Subcommittee considered that the doses for a 2+1 PCV10 schedule should be administered with primary doses at 6 weeks and 3 months, with the booster given at the toddler visit.

5.15 The Subcommittee considered that there was a health need to continue listing PCV13 for special groups of patients at increased risk of contracting pneumococcal disease, particularly as PCV10 is not approved for use in adults. The Subcommittee considered that the current number of four PCV13 doses for the special groups of immune compromised patients (criteria 3) remained appropriate. The Subcommittee considered the eligibility criteria for PCV13 be amended as follows (additions in bold, deletions in strikethrough):

Any of the following:

1. One dose is funded for high risk children (over the age of 17 months and under 18 years) who have previously received ~~four~~ **three** doses of PCV10; or
2. Up to an additional ~~four~~ **three** doses (as appropriate) are funded for high risk children aged under 5 years for (re-)immunisation of patients with any of the following:
    a. on immunosuppressive therapy or radiation therapy, vaccinate when there is expected to be a sufficient immune response; or
    b. with primary immune deficiencies; or
    c. with HIV infection; or
    d. with renal failure, or nephrotic syndrome; or
    e. who are immune-suppressed following organ transplantation (including haematopoietic stem cell transplant); or
    f. with cochlear implants or intracranial shunts; or

g. with cerebrospinal fluid leaks; or

h. receiving corticosteroid therapy for more than two weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater; or

i. with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy); or

j. pre term infants, born before 28 weeks gestation; or

k. with cardiac disease, with cyanosis or failure; or

l. with diabetes; or

m. with Down syndrome; or

n. who are pre-or post-splenectomy, or with functional asplenia; or

3. Up to an additional four doses (as appropriate) are funded for (re-)immunisation of patients 5 years and over with HIV, for patients pre or post haematopoietic stem cell transplantation, or chemotherapy; pre- or post splenectomy; functional asplenia, pre- or post- solid organ transplant, renal dialysis, complement deficiency (acquired or inherited), cochlear implants, or primary immunodeficiency; or

4. For use in testing for primary immunodeficiency diseases, on the recommendation of an internal medicine physician or paediatrician.

Meningococcal C conjugate vaccine

5.16 The Subcommittee noted that meningococcal C conjugate vaccine (Neisvac-C) is currently listed for high risk patients and approved for use in children from 8 weeks of age as well as adolescents and adults. Infants under 12 months of age require 2 doses.

5.17 The Subcommittee considered that MenACWY vaccine (Menactra) is suitable for all high risk patients from 9 months of age to adult, so meningococcal C conjugate vaccine (Neisvac-C) should remain listed only for children from 8 weeks to 8 months of age. The Subcommittee considered the eligibility criteria for meningococcal C conjugate vaccine be amended as follows (additions in bold, deletions in strikethrough):

Children under 9 months of age.
Any of the following:

1. Up to three doses ~~and a booster every five years~~ for patients pre- and post splenectomy and for patients with functional or anatomic asplenia, HIV, complement deficiency (acquired or inherited), or pre or post solid organ transplant; or
2. ~~One dose~~ **Three doses** for close contacts of meningococcal cases; or
3. ~~A maximum of two~~**Three** doses for bone marrow transplant patients; or
4. ~~A maximum of two~~**Three** doses for patients following immunosuppression*.

Note: children under ~~seven years~~**nine months** of age require two doses 8 weeks apart, a booster dose **with Meningococcal ACWY vaccine** three years after the primary series and then five yearly.

*Immunosuppression due to steroid or other immunosuppressive therapy must be for a period of greater than 28 days.

Varicella vaccine

5.18 The Subcommittee noted that varicella vaccine is listed for a single dose for infants given at 15 months and also for special groups of patients at an increased risk of varicella infection. The Subcommittee considered that some special group patients could be children between 9 and 12 months of age and that it was important that varicella vaccine remained available for use in this group.

5.19 The Subcommittee considered that it would like to discuss the introduction of a second varicella dose at a future meeting.

Measles mumps, rubella and varicella vaccine

5.20 The Subcommittee noted that MMR and varicella vaccinations are given as separate vaccines: MMR is given at 15 months and 4 years; and a single dose of varicella is given at 15 months. The Subcommittee noted that at its July 2017 meeting it considered the combined MMRV vaccine could be used to accommodate a two-dose varicella regime in the future. Members noted that in Australia the separate MMR and varicella vaccines are administered during the same visit at the age of one year, which then permitted later vaccination with the combined MMRV product.

5.21 The Subcommittee considered that administering MMR and varicella as separate vaccine remains appropriate. Members considered that in the future, New Zealand could consider a similar approach to Australia, administering MMRV as the second MMR dose to accommodate a second varicella dose without increasing the number of injections. The Subcommittee considered that it is necessary to continue listing a separate varicella vaccine for special groups of patients at an increased risk of varicella infection.

Measles mumps and rubella vaccine

5.22 The Subcommittee noted that MMR vaccine is listed with a maximum of two doses for primary vaccination in children, revaccination following immunosuppression or for any individual who is susceptible to measles, mumps or rubella. A maximum of three doses are listed for children who had their first dose prior to 12 months of age.

5.23 The Subcommittee considered that either Priorix or MMR II brands of vaccine would be suitable to be the sole supply brand for MMR vaccine and both brands had been used previously in New Zealand.

Poliomyelitis vaccine

5.24 The Subcommittee noted that inactivated polio vaccine is listed for partially vaccinated or previously unvaccinated individuals, or for revaccination following

immunosuppression. The polio antigen is also given as a component of the hexa-valent vaccine administered in the infant immunisation schedule and as a component of the DTaP-IPV vaccine at the 4 year visit.

5.25 The Subcommittee considered that an inactivated polio-containing vaccine is required for catch up of partially vaccinated or previously unvaccinated individuals and revaccination following immunosuppression. The Subcommittee considered that Infanrix-IPV would not be a suitable alternative as it is not approved for use in adults. Members noted that Boostrix-IPV would be a suitable alternative, however this was not currently part of the Schedule.

Influenza vaccine

5.26 The Subcommittee noted that one possible option regarding the supply of influenza vaccine could be to award sole supply to the Seqirus Afluria Quad brand of quadrivalent inactivated influenza vaccine. The Subcommittee noted that Afluria Quad is currently Medsafe approved for use in people aged 5 years and older. An indication extension to use in infants from 6 months has been approved by the US FDA and is currently under evaluation by the TGA in Australia, with approval expected in March 2019. The supplier proposed that an application would be made to Medsafe once TGA approval is obtained.

5.27 The Subcommittee noted that there had been a change to the manufacturing process to address the previous concerns with using this vaccine in young children. Members noted this related to cases of fever and febrile seizures in young children reported during the 2010 Southern Hemisphere influenza season with Seqirus' trivalent inactivated influenza vaccine. The Subcommittee considered that Afluria Quad would be suitable to be awarded sole supply, including for use in children from 6 months years of age, if the paediatric indication extension was approved by Medsafe. The Subcommittee considered that Seqirus would need a risk mitigation plan for coverage of children from 6 months of age if the paediatric extension was not approved by Medsafe.

Immunisation schedule considerations

5.28 The Subcommittee noted that following a clinical advice meeting in November 2017, the Ministry of Health created a draft immunisation schedule that could accommodate an additional pertussis dose at the 15 month visit and the inclusion of meningococcal vaccines, if these were funded. The draft schedule included a new 12 month visit to allow for the addition of meningococcal vaccines. The Subcommittee considered that it strongly supported adding a dose of hexa-valent DTaP-IPV-HepB/Hib at the 15 month visit, particularly as there is an ongoing pertussis outbreak and an additional dose would overcome possible waning of immunity prior to the next pertussis dose at 4 years of age. The 15 months Hib only dose would no longer be required in this case so there would still only be 4 injections administered at this visit (DTaP-IPV-HepB/Hib, PCV10, MMR and Varicella).

5.29 The Subcommittee noted that maternal pertussis vaccination rates are low and considered that with the ongoing pertussis outbreak the current three infant doses

of pertussis should continue. The Subcommittee considered that if maternal pertussis vaccination rates were to increase in the future, consideration could be given to reducing the number of infant pertussis doses in the primary course. The Subcommittee considered that it should keep monitoring pertussis rates and reviewing this issue.

5.30 The Subcommittee considered that PCV should not be administered at the same visit as MenACWY, so this would need to be considered in the scheduling of doses between a 15 month visit and a new 12 month visit, if Men ACWY vaccine was funded for toddlers. Members considered that MenACWY should be given at least 4 weeks after PCV, and DT containing vaccine should be given at the same visit as MenACWY. A second dose of Men ACWY vaccine would not be required if an adolescent dose was also offered.

5.31 The Subcommittee considered that it would like the dialogue about the primary dose schedule and timing of doses to continue with the Ministry of Health.