Immunisation Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 18 September 2018

(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 21 & 22 February 2019, the record of which will be available in due course.

Record of the Immunisation Subcommittee Meeting held on 18 September 2018

Contents

1. Record of previous minutes

1.1 The Subcommittee noted the minutes from the previous meeting held on 16 May 2018. The Subcommittee reiterated its view about the urgency for funding maternal pertussis vaccination for women earlier than 28 weeks in their pregnancy. The Subcommittee considered this would help improve immunisation coverage in this group and Members urged the Ministry of Health to implement strategies to improve uptake for maternal pertussis vaccination.

1.2 The Subcommittee considered that the minutes were an accurate reflection of the meeting that took place on 16 May 2018.

2. Correspondence and Matters arising

a. Varicella and zoster surveillance

2.1 The Subcommittee noted some correspondence from the Ministry of Health seeking the Subcommittee's view on the Ministry's proposed approach to implementing varicella and zoster surveillance.

2.2 The Subcommittee noted that the Ministry proposed monitoring hospitalisations for varicella and zoster. Members noted that hospitalisations for varicella and zoster are a very small proportion of the number of cases. The Subcommittee considered that if the issue is that immunisation against varicella might cause increased zoster infection in the community, this will be missed by surveillance using hospitalisation data. Members considered that using notifications was suitable for monitoring rare diseases, but not for more common diseases.

2.3 The Subcommittee considered that the Ministry could assess ways of more easily accessing general practice data. The Subcommittee did not support the Ministry of Health's proposed approach to conducting varicella and zoster surveillance by

monitoring hospitalisations. The Subcommittee considered that the Ministry should investigate approaches that used general practice data to obtain surveillance information on the burden of varicella and zoster in the community, if possible. Members noted the Ministry intended to have this surveillance in place from 1 January 2019.

b. Hepatitis B birth dose

2.4 The Subcommittee noted the Ministry of Health's proposed response to the World Health Organisation (WHO) request to review New Zealand's hepatitis B immunisation strategy, outlining that it does not intend to introduce a birth dose of hepatitis B vaccine, despite the WHO recommendation to do so. The Subcommittee noted that it discussed this topic at its May 2018 meeting where it noted that there are "close to zero" hepatitis B infections acquired perinatally in New Zealand.

2.5 The Subcommittee noted that in recent research yet to be published, Peter McIntyre reported that a hepatitis B birth dose boosts pertussis antibodies. Members expressed interest in reviewing this paper following publication.

2.6 The Subcommittee considered that it was supportive of the Ministry of Health's proposed response to the WHO indicating that a birth dose of hepatitis B vaccine is not required and would not be introduced in New Zealand.

2.7 The Subcommittee noted that the Ministry is undertaking work to confirm the quality of antenatal screening and follow-up of babies born to HBsAg+ mothers.

3. MMR Vaccine third dose

Application

3.1 The Subcommittee considered an application from the Ministry of Health Director of Public Health about the use of a third dose of measles, mumps and rubella (MMR) vaccine to prevent and control mumps outbreaks.

Recommendation

3.2 The Subcommittee **recommended** that a third dose of MMR vaccine be funded with a high priority on the Pharmaceutical Schedule with criteria for local mumps outbreaks, on the declaration of a local mumps outbreak by the Medical Officer of Health. The Subcommittee **recommended** PHARMAC seek advice from the Medical Officers of Health to develop an outbreak definition that could be included in the funding criteria.

Discussion

3.3 The Subcommittee noted that from September 2016 to August 2018 there were 1,721 cases of mumps recorded in Auckland. Approximately 50% of cases were in Pacific peoples. Members noted that there was a lack of data about the vaccination status of those affected. The Subcommittee noted that a lot of cases in the Auckland outbreak occurred in areas where there were large populations of Pacific peoples, such as South and West Auckland. Members noted that a large proportion of cases were in people older than school age. Members noted that mumps infection can create inequities for Pacific peoples, particularly from educational exclusion during the infectious period.

3.4 The Subcommittee noted that for the same period (September 2016 - February 2018), Māori accounted for 15% of mumps cases nationally, and make up 15% of the population.

3.5 The Subcommittee noted that there were two approaches to consider: a schedule listing that would list the vaccine with criteria that included details of how an outbreak was defined or declared; or alternatively to continue with the current approach that PHARMAC consider each outbreak on a case by case basis. Members noted there were risks to vaccine supply and timeliness of response for each approach.

3.6 The Subcommittee noted that in April 2017, PHARMAC approved the funding of a 3rd dose of MMR vaccine for the management of a mumps outbreak at a school in the Auckland region. The approval was for up to 2,000 doses. The outbreak occurred at a school with 1800 students, and the third dose strategy was considered to prevent the spread of the outbreak for students and teachers. Members noted the criteria used to decide to immunise with a 3rd MMR dose for mumps outbreak control were: high two-dose vaccination coverage (i.e. coverage >90%); intense exposure settings likely to facilitate transmission (e.g. schools, colleges, correctional facilities, congregate living facilities) or healthcare settings; high attack rates (i.e. >5 cases per 100,000 population); and evidence of ongoing transmission for at least two weeks in the target population.

3.7 The Subcommittee noted that many Pacific Island countries do not include mumps vaccination in their Immunisation Programmes, instead offering a measles and rubella (MR) vaccine. Such countries include Fiji, Kiribati, Nauru, Papua New Guinea, Solomon Islands, Tonga, Tuvalu and Vanuatu. Members noted that there is a potential population of mumps-naïve individuals in the Pacific Region and this group may be fuelling the current outbreaks in New Zealand.

3.8 The Subcommittee considered Cardemil et al. N Engl J Med, 2017;377:947-56 which described the interventions during a mumps outbreak the University of Iowa, where 5,000 people were given a third dose of MMR vaccine (MMR3) before the outbreak reached its peak. Members noted that only 103 out of 20,000 university students had not previously received two doses of MMR vaccine (MMR2). The mumps attack rate was substantially lower if a third dose had been given. Members noted that evaluation of the number of years since MMR2 was given suggested a waning of immunity.

3.9 The Subcommittee considered that Cardemil et al. (2017) was supportive of the benefit of administering MMR3 in outbreak settings, but noted that the study was in a very defined population so results could not necessarily be extrapolated to a New Zealand population and setting. Members considered it was reasonable to consider the possibility of waning immunity so a MMR3 would be helpful, and an additional dose for those who have not previously received MMR2.

3.10 The Subcommittee noted that in October 2017, the Advisory Committee on Immunization Practices (ACIP (US)) (Marin et al. MMWR Morb Mortal Wkly Rep 2018;67:33-8) recommended that "persons previously vaccinated with two doses of a mumps virus–containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus–containing vaccine to improve protection against mumps disease and related complications."

3.11 The Subcommittee noted that the US Centers for Disease Control and Prevention (CDC) defines a mumps outbreak as three or more cases linked by time and place. Members considered that this definition was also suitable for use in New Zealand but that there should not be a requirement that the at-risk population have high MMR2 coverage, which was one of the criteria used for the April 2017 Auckland outbreak.

3.12 The Subcommittee considered that the at-risk population estimates provided by PHARMAC staff were reasonable and had used good data sources. The proposed at-risk groups included armed forces personnel living in barracks or quarters, tertiary students living in halls of residence and all school aged children. Members considered that those born before 1981 are not considered as at risk as natural mumps infection confers life-long immunity. Members noted that in an outbreak situation, cases would be geographically isolated, so all subgroup members in that location would be vaccinated.

3.13 The Subcommittee considered there was good quality evidence to support MMR3 for use in outbreaks. Members noted that MMR3 is an unapproved indication but did not consider that this was of concern, however, this would need to be made clear to those administering the vaccine. Members considered that increased immunity to measles and rubella would be an additional benefit from MMR3.

3.14 The Subcommittee considered that if MMR3 was funded for use in outbreak settings, it would be preferable to list it in the Pharmaceutical Schedule with eligibility criteria that allow for the Medical Officer of Health to declare a local outbreak in a defined locality in order for eligible people to receive MMR3. The Subcommittee considered that there could be implications for vaccine stock management if outbreaks were widespread. Members requested the PHARMAC staff seek advice from the Medical Officers of Health (via the Ministry of Health Public Health team) to develop an outbreak definition to be used in declaring a local outbreak. The definition should include geographical location definitions and appropriate age groups. The Subcommittee considered that it should review the draft outbreak definition by email.

4. Meningococcal ACYW vaccine

Application

4.1 The Subcommittee reviewed a paper from PHARMAC staff with updated epidemiological data regarding an application to fund meningococcal C vaccine and/or meningococcal ACYW vaccine for people in close living situations and universal childhood vaccination of infants, toddlers and teenagers.

Recommendation

4.2 The Subcommittee **recommended** that a quadrivalent meningococcal ACYW vaccine be listed in the Pharmaceutical Schedule for toddlers in the second year of life (1 or 2 dose to be determined) and an adolescent dose and a catch up programme to be determined, with a high priority. The Subcommittee considered that it should review toddler dosing and possible options for a catch up programme following the commercial process due to be run later in 2018.

4.3 The Subcommittee **recommended** that meningococcal C vaccine for universal vaccination be declined.

Discussion

4.4 The Subcommittee noted that at its May 2018 meeting it deferred making a recommendation regarding the funding of meningococcal C vaccination for people living in close living situations and universal childhood vaccination of infants, toddlers, and teenagers, until more recent epidemiological data can be made available. Members noted they had previously reviewed the evidence to support meningococcal vaccination.

4.5 The Subcommittee noted recent epidemiological data (up to August 2018) highlights that most cases of meningococcal disease in New Zealand are due to meningococcal B (MenB), but cases from groups other than B and C are increasing. Members noted that over the last five years, Meningococcal ACYW (MenACYW) vaccine would have covered twice as many isolates of *N. meningitidis* than the meningococcal C (MenC) vaccine. Members noted that the rate of group W and Y cases is increasing relative to group C.

4.6 The Subcommittee noted that the age most at risk of group B cases tends to be concentrated particularly in children under one year of age, but other meningococcal group cases tend to be spread more widely across the age groups. Members noted that the relatively short duration of protection from any meningococcal vaccination means that multiple doses could be required across a person's lifetime to maintain protection against vaccine strains.

4.7 The Subcommittee discussed a number of options for which immunisation visits would be optimal to deliver meningococcal vaccination if MenACYW or MenC was funded. The Subcommittee considered that it would be preferable to give one or two doses in infancy/childhood and a further dose in adolescence. The Subcommittee considered that better herd immunity effects would be gained by starting vaccination

with a MenACYW catch-up campaign followed by routine doses in the second year of life, followed by an adolescent dose. Members noted that adolescent vaccination reduces nasal carriage in the population with the highest carriage rates.

4.8 The Subcommittee noted that group W cases have increased in Australia to a greater extent than in New Zealand, although group W cases have increased in New Zealand in recent years. Members considered it was necessary to regularly monitor surveillance data for meningococcal cases.

4.9 The Subcommittee considered that the population size estimates by PHARMAC staff for people in close living situations, children aged 1-4 years and children under 1 year were reasonable. Members considered that the age distribution of cases favoured vaccination in the second year of life with a quadrivalent vaccine to also get coverage for other strains. Members considered that vaccination of adolescents or catch up campaigns could promote herd immunity, and more data on this was needed.

4.10 The Subcommittee considered that there was stronger evidence for including meningococcal vaccine in the Childhood Immunisation Schedule than for targeting adolescents in close living situations such as university halls of residence, boarding schools or military barracks. The Subcommittee considered that if a national MenC or MenACYW vaccination campaign was introduced, it should ideally include both infants and adolescents, rather than either group separately. The Subcommittee requested that they review the costings of possible meningococcal vaccination programmes, including adolescent catch up, following the commercial process for all vaccines that is scheduled to be released at the end of 2018. Members noted that logistically it would be easiest to deliver adolescent vaccination as part of the Year 11 and 12 Intermediate School programme, although waning efficacy of the vaccine delivered at this age would leave older adolescents less well protected.

4.11 The Subcommittee noted that the Immunisation Advisory Centre (IMAC) has recently completed a meningococcal antigen review. The Subcommittee requested that PHARMAC staff consider the antigen review and bring information back to the next Subcommittee meeting.

5. Fluad

Application

5.1 The Subcommittee reviewed a funding application from Seqirus (NZ) Ltd to list a trivalent adjuvanted influenza vaccine (MF59-adjuvanted), on the National Immunisation Schedule for people aged 65 years and over.

Recommendation

5.2 The Subcommittee **recommended** that the application to list the Fluad MF59 adjuvanted influenza vaccine in the Pharmaceutical Schedule be declined.

Discussion

5.3 The Subcommittee noted a systematic review of the safety and immunogenicity of Fluad with a non-adjuvanted seasonal influenza vaccine in elderly people (Frey et al. Vaccine 2014;32:5027-34). This study showed non-inferiority of the trivalent adjuvanted vaccine (aTIV) compared with trivalent non-adjuvanted vaccine (TIV). Members noted that although aTIV generated higher antibody responses at Day 22 than TIV against all homologous and heterologous strains, superiority was not established. Reactogenicity was higher in the aTIV group, but reactions were mild to moderate and transient.

5.4 The Subcommittee noted an unpublished meta-analysis conducted by the applicant. The meta-analysis included all RCTs comparing aTIV (Fluad) versus TIV for immunogenicity measures, seroconversion rate and geometric mean titre ratio (GMTR). Members noted that the study concluded that aTIV was superior to TIV for all three strains (A/H1N1, A/H3N2 and B). aTIV also demonstrated cross-reactivity against drifted strains. Members noted that a meta-analysis of RCTs comparing aTIV to quadrivalent influenza vaccine (QIV) found no statistical difference between treatment groups for immunogenicity measures of homologous strains.

5.5 The Subcommittee noted an unpublished indirect treatment comparison conducted by the applicant. The indirect comparison used the results of the meta-analysis and pivotal studies. Members noted that aTIV was reported to be non-inferior to QIV for all outcomes. aTIV was reported to be statistically superior to QIV for seroconversion against the A strains in both the meta-analysis results and pivotal trial comparisons. aTIV was also statistically superior to QIV in the meta-analysis GMTR results for A/H1N1 and B/VIC strains, as well as in the GMTR analyses of the pivotal studies. Members considered that the indirect comparison was of poor quality, with heterogeneity of included studies which should therefore not have been combined.

5.6 The Subcommittee noted a review of the safety of MF59 adjuvanted influenza vaccine (Black S. Vaccine 2015;33 Suppl 2:B3-5). Members noted a theoretical concern about the potential for immunisation with the squalene based adjuvant to induce autoantibodies, although no changes in anti-squalene IgG or IgM antibodies were observed post-vaccination.

5.7 The Subcommittee noted an observational non-interventional prospective study (Villa et al. Am J Epidemiol. 2013;178:1139-45) which concluded that similar safety profiles were observed for both MF59-adjuvanted and non-adjuvanted influenza vaccines in subjects aged 65 years and over.

5.8 The Subcommittee noted an unpublished systematic literature review conducted by the applicant which identified three studies comparing the effectiveness of aTIV with TIV. Members noted that the three studies showed a relative vaccine effectiveness (VE) range of 25-63% for aTIV compared to TIV. No studies were identified that compared the effectiveness of aTIV with QIV.

5.9 The Subcommittee noted a systematic review that assessed the effectiveness of aTIV in the elderly (Domnich et al. Vaccine 2017;35:513-20). A pooled analysis of four case-controlled studies showed a VE range of 30-61% against hospitalisation

for pneumonia/influenza among elderly adults living in the community. Members noted that relative to TIV, the VE for aTIV tended to be higher but it was not possible to conduct a meta-analysis on these studies.

5.10 The Subcommittee noted a 2017 literature review conducted by the Canadian National Advisory Committee on Immunization (NACI) which concluded that there is insufficient evidence that Fluad is effective at reducing the risk of hospitalisation for influenza and influenza complications in the elderly compared to those who received TIV.

5.11 The Subcommittee noted the Australian Technical Advisory Group on Immunisation (ATAGI) considered that aTIV is superior to TIV in some scenarios, particularly where influenza A/H3 is the dominant strain. ATAGI considered this potential benefit could offset the potential loss of the additional B strain included in QIV, for people over 65 years of age. The Subcommittee noted that ATAGI considered there was substantial uncertainty about the magnitude of incremental effectiveness compared to TIV and there is an absence of head to head studies with QIV.

5.12 The Subcommittee noted that aTIV is indicated for people aged 65 years and over, while QIV is indicated for children and adults. Members considered that funding an influenza vaccine for a specific age group would add complexity to vaccine stock management and increase vaccine storage needs, requiring additional fridge space for influenza vaccine over the peak months.

5.13 The Subcommittee considered that there was a high health need for influenza vaccination in the elderly. The Subcommittee noted that it considered the health need of elderly and high risk patients at its May 2018 meeting.

5.14 The Subcommittee considered that while there was evidence of aTIV effectiveness compared to TIV, there were limited head to head studies and no head to head studies with QIV. Members considered that the reactogenicity of the aTIV formulation was of concern as this can discourage the elderly from being vaccinated. Members considered that there was not sufficient evidence to support the use if aTIV at this time. The Subcommittee considered that it would like to review data comparing aTIV to high dose TIV vaccine in people aged 65 years and over, as well as data for aTIV use in immunocompromised people, especially local data if possible, should these become available. The Subcommittee noted that aQIV is in development and considered it would like to consider this product in the future.

6. Synflorix

Application

6.1 The Subcommittee reviewed a clinical data update from GSK (NZ) Ltd for pneumococcal conjugate vaccine, 10-valent adsorbed (Synflorix).

Recommendation

6.2 The Subcommittee **recommended** that it would be a suitable option for New Zealand to move from a 3+1 to a 2+1 dosing schedule for PCV10 or PCV13.

Discussion

6.3 The Subcommittee noted the updated data from the supplier included information relating to the effectiveness of PCV10 against cross-reactive serotype 19A and the effectiveness of a 2+1 dosing schedule.

6.4 The Subcommittee noted that Deceuninck et al. (Vaccine 2015;33:2684-9) reported PCV10 vaccine efficacy (VE) against serotype 19A, in children aged 2 – 59 months with a 2+1 dosing schedule, of 71% (CI 24-89%) for PCV10 and 74% (CI 11-92%) for PCV13.

6.5 The Subcommittee noted that Domingues et al. (Lancet Respir Med 2014;2:464-71) reported VE with PCV10 to be 83.8% (95% CI 65.9-92.3) against vaccine serotypes and VE 82.2% (CI 10.7-96.4) against serotype 19A.

6.6 The Subcommittee noted that a study in Finland (Jokinen et al. PLos One 2015;10(3)e0120290) reported a 62% (CI 20-85 reduction in the population incidence of invasive pneumococcal disease (IPD) caused by 19A over three years following the introduction of PCV10.

6.7 The Subcommittee noted the SAGE 2017 PRIME systematic review recommended the use of either PVC10 or PCV13 in a 3+0 or 2+1 dosing schedule starting as early as 6 weeks of age. SAGE recommended a minimum interval of 4 weeks and a maximum of 8 weeks in the primary series for the 2+1 schedule, with a booster dose 9-18 months thereafter. Members noted that SAGE found that both PCV10 and PCV13 have substantial impact against pneumonia, vaccine-type invasive disease and carriage. There is at present no evidence of different net impact on overall disease burden between the two products. SAGE considered that PCV13 may have additional benefit in settings where disease attributable to serotypes 19A or 6A is significant. Members noted that SAGE recommended that sustained high quality sentinel and population based surveillance for pneumococcal disease and carriage be implemented, ideally indefinitely but no shorter than 5 years, following full PCV introduction in order to quantify long term impact and monitor serotype changes.

6.8 The Subcommittee considered that the evidence supporting the use of a PCV10 2+1 dosing schedule was of good strength and quality. The Subcommittee considered that the evidence for similar efficacy of PCV10 and PCV13 was of good strength and quality. Members noted that ESR IPD quarterly surveillance reports to June 2018 showed an increase in total invasive pneumococcal disease (IPD) notifications since 2015. IPD notifications caused by serotype 19A in children under 5 years of age have decreased since a peak in the year ended June 2012, and notifications for children under 2 years of age due to 19A have declined markedly in the same period.

6.9 The Subcommittee noted a number of studies related to PCV10 vaccination in high risk groups.

6.10 Asplenia: Szenborn Vaccine 2017;35:5331-8 reported that in children aged 2-17 years given a single dose for those already primed or two doses in those not primed, antibody concentrations for vaccine serotypes and vaccine related serotypes 6A and 19A were at least 94.4%.

6.11 Sickle cell disease: Sirima (Pediatr Infect Dis J. 2017;36:e136-e150) reported that immune responses after age-appropriate vaccination in children aged under 2 years did not appear to be influence by sickle cell disease.

6.12 HIV: Madhi 2012 Poster presented at ESPID reported that the immunological response after each dose in HIV positive children or exposed in utero compared to HIV negative or not exposed in utero after each dose. Cohen et al. (Lancet Global Health 2017;5:PE244-E245) reported PCV13 with a 2+1 schedule had a VE against vaccine serotype was 85% (CI 37-96%) in non-HIV children and VE 91% (CI -35-100%) in HIV infected children.

6.13 Leukaemia: Crawford et al. (Pediatr Infect Dis J. 2015;34:e9-15) reported PCV10 vaccination given during chemotherapy provided a satisfactory serum immune response for 7 of the 10 vaccine serotypes.

6.14 The Subcommittee considered that the evidence supporting PCV10 with a 2+1 dosing schedule in high risk groups was of low strength and quality. Members considered that PCV13 with a 2+1 dosing schedule would suitable for high risk groups.

6.15 The Subcommittee considered that it would be a suitable option for New Zealand to move from a 3+1 to a 2+1 dosing schedule for PCV10 or PCV13, which would reduce the number of vaccinations required at one immunisation visit. The Subcommittee considered that there was no change to its previous recommendation that PCV10 could be considered to have overall comparable clinical benefit to PCV13, apart from high risk groups where there is not sufficient evidence to support this. Members noted that PCV10 is not licenced for use in people aged over 5 years, so PCV13 would still be required for this group.

7. Infanrix-Hexa

Application

7.1 The Subcommittee reviewed a clinical data update from GSK (NZ) Ltd for DTAP-HBV-IPV/Hib (Infanrix-Hexa) vaccine.

Discussion

7.2 The Subcommittee noted that Infanrix Hexa is listed on the National Immunisation Schedule as a 3+0 primary schedule at 6 weeks, 3 months and 5 months of age. The Subcommittee noted GSK supplied information on a 2+1 schedule with Infanrix Hexa administered at 6 weeks, 3 months and 12 months, or 3 months, 5 months and 12 months. Members noted this would shift the third dose of Infanrix Hexa to 12 months removing the need for a separate Hib dose at 15 months, and allowing for either DTaP or Tdap to be given at 4 years of age instead of DTaP-IPV.

7.3 Members noted GSK also provided information on a 3+1 schedule with 3-dose Infanrix Hexa plus Infanrix IPV/Hib booster. The primary schedule would be administered at 6 weeks, 3 months, 5 months and the DTaP booster in the second year of life (Infanrix IPV/Hib). Members noted this would allow the introduction of a

toddler pertussis booster without increasing needle burden, as the current 15 month IPV booster would no longer be required.

7.4 The Subcommittee noted that it considered the dosing schedule for infant pertussis vaccination at its July 2017 meeting, where it considered that maternal immunisation rates would need to be improved before New Zealand could move the 6 week dose to 2 months in line with a number of other countries.

7.5 The Subcommittee noted that a Ministry of Health Immunisation Schedule review meeting in November 2017 recommended that the current pertussis series timing of three doses given at ages 6 weeks, 3 and 5 months be retained until more evidence is available on the effects and duration of possible blunting from pertussis immunisation during pregnancy. The Subcommittee considered an option of implementing a 2+1 pertussis schedule with doses at 6 weeks, 3 and 12 months. Members considered that high coverage would be required to make this schedule effective and considered that current coverage rates would be high enough to implement this schedule. The Subcommittee considered that prospectively planned pertussis surveillance should be implemented before such a change was made, to provide some baseline data (in addition to the notification data, which does not capture all cases). Members noted that changes the schedule would also impact the scheduling of other vaccines, such as rotavirus vaccine.

7.6 The Subcommittee noted the EPIC study (Radke et al. Vaccine 2017;35:177-83) supported the use of a 3+1 dose schedule with DTaP-HBV-IPV/Hib plus a DTaP-IPV-Hib booster.

7.7 The Subcommittee considered an option of moving to a 3+1 pertussis schedule. Members considered that a 3+1 schedule was a good option which would allow removing IPV from the 4 year old dose and would defer the need for a further pertussis dose at 4 years of age. However, the Subcommittee considered that there was no compelling reason to change the dose schedule and it should only be implemented if there were benefits to the timing of the Immunisation Schedule.

7.8 The Subcommittee noted that if meningococcal B vaccine 4CMenB was introduced into the childhood Immunisation Schedule in the future, it would be recommended that paracetamol be given before vaccination to reduce the pain and fever associated with 4CMenB administration. If 4CMenB was added to the Schedule, it would likely be given at the same as a pertussis dose. The Subcommittee noted four studies (Primula et al. Lancet 2009;374:1339-50, Falup-Pecurariu et al. Human Vaccines and Immunotherapeutics 2017;13:649-60, Wysocki et al. Vaccine 2017;35:1926-35, and Prymula et al. Human Vaccines and Immunotherapeutics 2014;10:1993-2004) reporting on the use of paracetamol in association with DTaP-HBV-IPV/Hib. Members considered that the data was complex with different findings in different studies. The Subcommittee considered that current evidence does not support the administration of paracetamol with DTaP-HBV-IPV/Hib, but this would need to be reconsidered if 4CMenB was added to the childhood immunisation schedule.

8. TdaP Booster

Application

8.1 The Subcommittee reviewed a clinical data update from Seqirus (NZ) Ltd for the diphtheria tetanus and acellular pertussis (TdaP-Booster) vaccine.

Discussion

8.2 The Subcommittee noted correspondence from Seqirus (NZ) Ltd, including a clinical data update for TdaP-Booster (diphtheria, tetanus, pertussis) vaccine, which had been considered and recommended for decline by the Subcommittee at its October 2015 meeting. The application was further considered by the Subcommittee at its October 2016 meeting, where it considered that the evidence for the use of a TdaP-Booster during pregnancy was weak and there was not enough evidence to recommend its specific use in pregnancy compared to other vaccine options.

8.3 The Subcommittee noted that McMillan et al Obstet Gynecol 2017;129:560-73 reviewed 21 studies in 2017 and concluded that administering TdaP vaccine during the second or third trimester of pregnancy is not associated with clinically significant harms for the foetus or neonate. The Subcommittee noted that Walls et al BMJ Open 2016;6:e009536 investigated the safety of TdaP vaccine for infants exposed during pregnancy. There were no significant differences in birth weight, gestational age at birth, congenital anomalies or infant growth as compared with baseline population data. No cases of pertussis occurred in this cohort despite high rates of disease in the community. The Subcommittee noted that Kroeger et al. in Plotkins Vaccines 2018;96-120 reported that it is now generally accepted that immunisation during pregnancy with vaccines containing inactive toxoids is not expected to be associated with any increased risks to the foetus. The Subcommittee considered that while McMillan et al. (2017), Walls et al. (2016) and Kroeger et al. (2018) were new evidence they had not reviewed before, these studies looked at the use of a different vaccine in pregnant women. Members noted that no clinical studies had been performed with TdaP-Booster that included pregnant or breastfeeding women. Members considered that no new evidence had been provided specifically for the use of TdaP-Booster in pregnant women.

8.4 The Subcommittee considered that there was still insufficient evidence to recommend the use of TdaP-Booster vaccine in pregnancy compared to other vaccine options that are currently available.