Memo

Decision to use the Pfizer mRNA COVID-19 vaccine for children aged 5-11 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	15 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health
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From:	Dr Ian Town, Chief Science Advisor and Chair of CV TAG
For your:	Information

Purpose of report

1. To summarise the CV TAG recommendations on the decision to use the paediatric formulation of the Pfizer mRNA COVID-19 vaccine ('the Pfizer vaccine') for children who are 5 to 11 years of age.

Background and context

2. In February 2021, CV TAG advice was sought for use of the Pfizer COVID-19 vaccine in people who were 16 years and over, following Medsafe approval. Cabinet agreed that the COVID-19 Immunisation Programme proceed with the roll out of the Pfizer vaccine, and this has been underway since February.
3. In August 2021, CV TAG confirmed support to extend the age of people who can receive the Pfizer vaccine to 12- to 15-year-olds, noting that this would likely lead to a reduction in school closures and disruption to education, and contribute to equitable vaccination coverage in Māori and Pacific peoples.
4. Medsafe is assessing an application submitted by Pfizer for the use of a paediatric formulation of the vaccine in 5- to 11-year-olds within New Zealand. The CV TAG recommendations presented here are subject to Medsafe approval and any listed clinical conditions.
5. The Ministry's Policy team has sought clinical and scientific advice from CV TAG on the use of the Pfizer vaccine for children who are 5- to 11-years of age. This advice will be considered as

part of the Decision to Use Framework, and alongside policy considerations for the sequencing of the COVID-19 Immunisation Programme.

The COVID-19 vaccine in 5- to 11-year-olds

Phase 2/3 trial findings

6. One phase 2/3 randomised control trial was conducted to assess the safety, immunogenicity, and efficacy of two doses of the Pfizer vaccine administered 21 days apart in children aged 6 months to 11 years, with findings published for 5- to 11-year-olds to date [1].

7. In the phase 2/3 trial, participants were randomly assigned in a 2:1 ratio to receive two doses of either the Pfizer vaccine at 10 µg (a lower dose than the 30 µg used in older age groups), or a placebo. A total of 2268 children were assigned to receive the Pfizer vaccine (1517 children) or placebo (751 children) [1].

8. The trial was run across 81 sites in the US, Spain, Finland and Poland. Overall, 52% were male, 79% were White, 6% were Black, 6% were Asian, and 21% were Hispanic or Latinx. The mean age was 8.2 years; 20% of children had coexisting conditions (including 12% with obesity and approximately 8% with asthma), and 9% were SARS-CoV-2–positive at baseline. Demographic characteristics were similar between the 5- to 11-year-old and 16- to 25-year-old Pfizer recipients who were included in the immuno-bridging subset, apart from younger age and the percentage of Black and Hispanic or Latinx in the 5- to 11-year-old group (6% and 18%, respectively) being lower than in the 16- to 25-year-old group (12% and 36%, respectively) [1].

Safety and reactogenicity

9. In the 5- to 11-year-olds, as in other age groups, the Pfizer vaccine had a favourable safety profile, with side effects generally comparable to those observed in 16- to 25-year-olds who received the standard 30 µg doses [1].

10. Safety evaluations included assessment of reactogenicity events reported by a parent or guardian using an electronic diary for 7 days after each dose. Data on unsolicited adverse events, including confirmed diagnoses of myocarditis or pericarditis, were collected from the first dose through 1 month after the second dose. Data on serious adverse events will be collected from the first dose through 6 months after the second dose [1]. At data cut-off, the median follow-up was 2.3 months [1].

11. Most local reactions were mild to moderate, lasting 1-2 days. Injection-site pain was the most common local reaction, occurring in 71-74% of Pfizer recipients. Fatigue and headache were the most frequently reported systemic events. In general, systemic events were reported more frequently after the second dose than first dose. As compared with adults and adolescents in the pivotal trial, 5- to 11-year-olds reported a higher incidence of injection-site redness (15 to 19%, vs. 5 to 7%) and swelling (10 to 15%, vs. 5 to 8%), but a generally lower incidence of systemic events, including fever (3 to 7%, vs. 1 to 20%) and chills (5 to 10%, vs. 6 to 42%) [1-3].

12. From the first dose through to one month after the second dose, adverse events were reported by 10.9% of Pfizer recipients and 9.2% of placebo recipients. Slightly more Pfizer recipients (3.0%) than placebo recipients (2.1%) reported adverse events that were considered by the investigators to be related to the vaccine or placebo [1].

13. No vaccine-related serious adverse events were noted in the clinical trial; however, the trial was too small to detect rare side effects such as myocarditis. Three serious adverse events were reported from two participants (postinjury abdominal pain and pancreatitis in a placebo recipient and arm fracture in a Pfizer recipient). None of these were considered to be related to the vaccine or placebo. No deaths or adverse events leading to withdrawal were reported [1]. No cases of severe COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C) were reported—a condition associated with COVID-19 where body parts can become inflamed [1, 4]. Lymphadenopathy was reported in 10 Pfizer recipients (0.9%) and 1 placebo recipient (0.1%). No myocarditis, pericarditis, hypersensitivity, or anaphylaxis in Pfizer recipients was reported. Four rashes in Pfizer recipients (observed on the arm, torso, face, or body, with no consistent pattern) were considered to be related to vaccination; the rashes were mild and self-limiting, and onset was typically 7 days or more after vaccination [1].

14. No safety data are yet available from the large-scale roll out of the Pfizer vaccine to 5- to 11-year-olds in the USA, though will likely be available by late December 2021 or early January 2022.

Immunogenicity and efficacy

15. Immune responses in the single clinical trial conducted were assessed one month after the second dose of the Pfizer vaccine were equivalent to those in 16- to 25-year-olds. Children aged 5-11 receiving two 10 µg doses had a similar, statistically non-inferior, neutralising antibody responses with a geometric mean titre (GMT) of 1,197.6 (95% CI: 1,106.1, 1,296.6) vs 1,146.5 (95% CI: 1,045.5, 1,257.2) for ages 16-25 [1].

16. Vaccine efficacy against symptomatic NAAT-confirmed COVID-19 at 7 days or more after the second dose (to a median follow up of 2.3 months at data cut-off) was assessed. Among participants without evidence of previous SARS-CoV-2 infection, symptomatic COVID-19 was reported in three recipients of the Pfizer vaccine and in 16 placebo recipients, producing a vaccine efficacy of 90.7% (95% CI, 67.7 to 98.3) [1].

CV TAG Recommendations

17. CV TAG discussed the use of the Pfizer COVID-19 vaccine in children aged 5-11 years at meetings between October and December 2021 and consulted with Māori paediatricians and Māori general practitioners at two meetings in December 2021.[1]

18. CV TAG noted:

    a. **The direct and indirect impacts on children.** Children who have COVID-19 will commonly have few or only mild respiratory symptoms. COVID-19 in this age group is rarely severe or fatal [5, 6], and the rate of severe COVID-19 disease in this age group is the lowest of any age group. However, there is a very small but real risk of MIS-C (described above) at this age which has occurred more frequently among ethnic minorities in the US [4, 7]. A very small proportion of children also experience

[1] CV TAG discussed use of the Pfizer vaccine in the 5-11 age group on: 19 October, 2 November, 9 November, 23 November, 30 November, 7 December, and 14 December.

persistent illness and ongoing symptoms, though evidence about its incidence is limited.

b. In the current Delta outbreak in New Zealand (data to 19 November 2021), children aged 5-11 made up 14.9% of cases (1,003/6,714). Eight of these children were hospitalised but none were admitted to ICU. Of those who were hospitalised, all but one had a pre-existing condition and three were in hospital for less than six hours. As a comparison, between 16 June and 13 November 2021 in Sydney, 14,154 cases (19.4%) were aged 0-11 years and not eligible for vaccination. Of these cases, 632 were hospitalised, 9 were in ICU, and 0 patients died. It was not mentioned whether any of these cases had pre-existing conditions or comorbidities. The Sydney data further demonstrates that COVID-19 is relatively mild in most young children as despite accounting for 19.4% of cases in Sydney since 16 June, they account for only 5.9% of hospitalisations, 0.6% of ICU admissions, and no deaths [8].

c. Children living with pre-existing conditions or comorbidities, from disadvantaged backgrounds, or those living within a lower socioeconomic status have a greater risk of severe disease from COVID-19 [7, 9-11].

d. Even though the direct effects of infection are generally less severe in children, this should not diminish the significance for those who have experienced worse outcomes [6]. Alongside the direct risks and impacts to health and individuals, COVID-19 also has indirect impacts for children on mental health, wellbeing, education and social development, and these are worsened by lockdowns and school closures [7, 12-14].

e. **Children do play a role in transmission however it is significantly smaller than for adults**. Transmission within education settings has occurred but is limited and is more likely to occur between adults [15-17]. Transmission in households is much more common [18, 19]. The benefit of vaccination on onward transmission in households could be lower than in other settings due to the ongoing and close nature of exposure [20, 21], but this is not confirmed. The effect of vaccination of children on household transmission is unknown.

f. **There are a number of equity considerations which are important to consider**:

   i. Māori and Pacific children have been disproportionately affected in the current outbreak. To 19 November 2021, Māori made up 52% of cases in 5- to 11-year-olds, and Pacific children have made up 30% of cases among 5- to 11-year-olds.

   ii. Māori and Pacific adults are at greater risk of COVID-19 hospitalisation and severe disease. Māori and Pacific adults have respectively 2.5-fold and 3-fold higher odds of being hospitalised compared to non-Māori, and Māori are likely to spend 4.9 days longer in hospital [22, 23].

   iii. Māori and Pacific children are more likely to live in multigenerational families housed in overcrowded conditions, increasing the risk of transmission. The younger age structure of the Māori population also means that a larger proportion are currently unable to be vaccinated and remain susceptible to infection and transmission, with a risk of onwards transmission to whānau and communities [24, 25], though the risk of transmission from children is lower than from adults.

iv. The vaccine rollout in adults resulted in inequities for Māori and Pacific adults, and the rollout for Māori and Pacific children aged 5-11 will need close consideration and more tailored implementation. This emphasises the need for culturally appropriate messaging and Māori-led initiatives. Whānau-based approaches to the 5-11 rollout may also improve uptake among Māori adults.

v. According to a Horizon Research survey, 72% of those who care for 5- to 11-year-olds would allow their child to receive the COVID-19 vaccine, however this was lower among Māori caregivers at 51% [26]. However, we note that the Māori adult rate of uptake and the Māori childhood immunisation rates are much higher than 51%. Given this we believe with a correctly tailored programme, high rates of immunisation in tamariki Māori are achievable.

g. **The paediatric formulation of the vaccine has been approved for emergency use and rolled out in the USA, Canada, and Israel**. The Advisory Committee on Immunization Practices (ACIP) made an interim recommendation for the emergency use of the Pfizer vaccine in children aged 5-11 years in the United States for prevention of COVID-19 [6, 27]. This was unanimously supported by the Committee. In making this recommendation, ACIP considered the importance of COVID-19 as a public health problem, as well as benefits and harms, parents' values and preferences, acceptability, feasibility, resource use, and equity for use of the vaccine among children [6, 27]. ACIP additionally stated: "children from racial and ethnic minority groups have experienced a disproportionately high incidence of COVID-19 as well as secondary impacts of the COVID-19 pandemic such as reduced in-person learning"[6]. These comments have high relevance for New Zealand given the similar effects of the pandemic on Māori and Pacific peoples as described above.

h. **In Australia, the Therapeutic Goods Administration (TGA)** provisionally approved the Pfizer vaccine as safe and effective for use among this age group on 5 December [28]. ATAGI recommends all 5–11-year-olds be vaccinated with an 8-week interval between doses, and that those at risk of severe disease, Aboriginal and Torres Strait Islanders, and children in crowded conditions or outbreak areas be prioritised [29].

i. **Data are still accumulating from the real-world rollout of vaccines in 5- to 11-year-olds, and there is currently limited safety data available post-second dose**. Some adverse events in other age groups (e.g. myocarditis) have only become apparent following widespread rollout, and as noted above the trials in young children are too small to be able to detect rare side effects. Further data on potential side effects from the vaccine rollout in this age group in other countries will become progressively available.

j. **On coadministration and other vaccines,** there is limited evidence on the safety and immunogenicity of coadministration of the Pfizer vaccine with other vaccines in all populations, however based on first principles of vaccinology it is likely to be safe and effective, particularly in younger age groups.

k. **The wider National Immunisation Schedule** has been facing challenges for some time with declining vaccination rates since before COVID-19, and are particularly marked for Māori and Pacific infants and children. Catch-up campaigns for the MMR, HPV and Tdap vaccines were further delayed by COVID-19 and lockdowns. There is a risk that rolling out the Pfizer vaccine in this age group could further adversely impact the wider immunisation programme through diverting public health resources. This

could increase the risk of outbreaks of other infectious diseases. The risk of a significant measles outbreak is of particular concern once the international borders re-open. Vaccination rates are lowest among Māori, and therefore there are equity concerns that there will be greater risk in this population. However, there is also the opportunity to increase coverage with other vaccines with a thoughtfully implemented COVID-19 vaccination programme in this age group.

l. **On dosing intervals,** there are no data available about extending the interval between doses of the paediatric formulation of the Pfizer vaccine, however, emerging data in adults suggests that the immune response is likely improved by extending the dosing interval [30, 31]. This is consistent with basic principles of vaccinology and immunology which suggests that immune responses are generally better with longer intervals. There may also be a connection between shorter intervals and increased reactogenicity or adverse events, and one pre-print paper on individuals aged 12 and over has shown a statistically significant increase in myocarditis if the second dose was given at a shorter interval of less than 30 days [32]. Australia and Canada have recommended an 8-week interval between doses for 5-11-year-olds, noting this may improve immunogenicity and reduce side effects. Having a longer interval would also allow greater time to monitor international safety data.

m. **On vaccine requirements,** there is a significant risk that use of vaccination mandates or certificates in this age group will result in exclusion and an inability to fully participate in schooling and extracurricular activities. This is likely to inequitably impact communities who are already experiencing disadvantage and where current vaccine coverage is poor. Concerns regarding possible stigmatisation and exclusions could be addressed in ways that do not necessarily influence the decision to use. For example, there could be a policy decision that children cannot be denied access to locations/events on the basis of vaccination status, which could be operationalised by not issuing vaccine certificates for this age group.

19. **CV TAG recommended:**

    a. **Two doses of the paediatric Pfizer vaccine be offered to all 5-11-year-olds in Aotearoa New Zealand, with an 8-week interval between doses.**

    b. Māori and Pacific children, children with high-risk pre-existing conditions, and children living with vulnerable people should be prioritised for vaccination and tailored programmes developed.

    c. On the schedule between doses:

        i. The interval between doses can be shortened in limited circumstances to a minimum of 3 weeks, such as prior to the initiation of significant immunosuppression or international travel.

        ii. Children who turn 12 after their first dose should follow the authorised schedule which uses the paediatric primary formulation (10 µg). They should not be offered the adolescent/adult formulation (30 µg) of the Pfizer COVID-19 vaccine.

        iii. Children in this age group who experience a clinically significant adverse event after their first dose should be carefully reviewed by a specialist clinician. An individual risk:benefit assessment should be made on whether to administer the

second dose. Children in this age group are not obliged to receive a second dose if not clinically appropriate.

d. The paediatric Pfizer vaccine can be administered before, after, or at the same time as other vaccines in this age group.

e. The adolescent/adult Pfizer vaccine formulation (30 µg) should not be used in children aged 5-11 years.

f. Mandates, vaccine certificates or vaccine targets **must not** be used or required for this age group, and children in this age group should not be denied access to locations or events based on their vaccination status. There should be no unintended consequences in terms of participation if children in this age group are not vaccinated, and any use of mandates, certificates or targets that may formally or informally encourage inappropriate exclusion from activities. Exemptions from vaccination should therefore also not be required for this age group. We recommend specific public education campaigns about why children should not be excluded from activities, in order to reduce the risk of informal exclusions.

g. Specific consideration must be given to promoting and improving vaccine access to groups that have experienced disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care, especially for Māori and Pacific peoples. This could be achieved through using the broad geographic accessibility of pharmacies and expanding school-focused strategies. Whānau centred approaches should be considered within these environments to improve primary vaccination and booster rates in the adult population.

h. Emphasis must be given to using the rollout of the COVID-19 vaccine as an opportunity to improve delivery and uptake of the wider National Immunisation Schedule, and large-scale events with whānau-based approaches should be organised to aid catch-up campaigns for other vaccines. The coverage of the childhood National Immunisation Schedule should be closely monitored to ensure that the COVID-19 vaccination rollout for this age group does not adversely impact on the uptake of other important childhood vaccines.

i. In making vaccination available, it should not be solely relied upon and other public health measures in schools and other educational settings should be strengthened, including ensuring good ventilation and filtration of air indoors, use of masks, physical distancing, and promotion of children staying at home if sick.

20. CV TAG will continue to monitor all relevant information (including vaccine efficacy data against emerging variants of concern and emerging evidence on the duration of immunity) and will update their recommendations as further evidence becomes available.

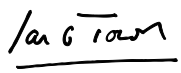
    a. New Zealand and international safety data will be carefully monitored, and the recommendations here will be reassessed by CV TAG in February 2022 prior to second doses being given to any 5–11-year-olds in Aotearoa New Zealand.

    b. Advice for severely immunocompromised children who may need a third primary dose will be reconsidered once further evidence emerges on the need, safety, and efficacy.

Recommendations

It is recommended that you:

2.	Note this advice has been received.	Yes/No



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Signature _____ Date:
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