Memo

The use of Pfizer mRNA COVID-19 vaccine for children aged 6 months to 4 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	24 November 2022
To:	Robyn Shearer, Acting Director-General of Health
Copy to:	Dr Andrew Old, Deputy Director-General, Public Health Agency Dr Nick Chamberlain, National Director, National Public Health Service Dr Nicholas Jones, Director of Public Health, Public Health Agency Astrid Koornneef, Director, National Immunisation Programme (NIP) Alison Cossar, Manager, Public Health Policy & Regulation, Public Health Agency Laurence Holding, Acting Manager, System Enablers, Strategy, Policy & Legislation Andrew Oliver, Senior Therapeutic Group Manager, Pharmac Dave Henderson, Acting Group Manager - Intelligence, Knowledge and Surveillance, Public Health Agency
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the use of the Pfizer-BioNTech COVID-19 vaccine formulated for those aged 6 months and over and less than 5 years of age (referred hereafter as 6 months to 4 years of age).

Background and context

2. The primary course of the Pfizer vaccine formulation for those aged 6 months to 4 years (the 'Pfizer vaccine') is three doses of the 3 µg vaccine (rather than two doses of 10 µg or 30 µg in 5-11 year olds and those 12 years and older, respectively). The interval between these three doses are 3 weeks between first and second dose and at least 8 weeks between the second and third dose.
3. On 15 December 2021, CV TAG recommended the paediatric Pfizer vaccine be offered to all 5- to 11-year-olds in Aotearoa New Zealand, with an 8-week interval between doses, prioritising Māori and Pacific children, children with high-risk pre-existing conditions, and children living with vulnerable people. This decision was made towards the end of the Delta

wave when there were high rates of severe disease from COVID-19, and the benefit of immunisation to reduce infection, transmission and severe disease, outweighed the risks.

4. Pfizer's clinical trial for those 6 months to 4 years of age was intended to assess 2 doses of the 3 µg vaccine, but after pre-specified interim analysis of immunogenicity in a sub-set of participants, Pfizer amended the protocol to add a third 3 µg dose at least two months after the second dose.[1, 2]

5. On 23 May 2022, Pfizer-BioNTech announced that their vaccine for 6-month to 4-year olds demonstrated "strong immune response, high efficacy and favourable safety" following a primary course of three doses. [3] On 17 June 2022, the FDA granted emergency use authorisation for children aged 6 months to 4 years. [4]

6. As at 8 November 2022, Medsafe is assessing an application submitted by Pfizer for the use of the Pfizer vaccine in those aged 6 months to 4 years within New Zealand and a decision is expected in December 2022. The CV TAG recommendations presented here are subject to Medsafe approval.

7. The COVID-19 Vaccine Technical Advisory Group (CV TAG) met on 13 September 2022 and 11 October 2022 to discuss the need for and use of the paediatric formulation of the Pfizer vaccine for children aged 6 months to 4 years. This included feedback on the RfA *"Use of a primary dose of paediatric COVID-19 vaccines for children aged 6 months to 4 years*" (Appendix 2*)*. Please note, any data mentioned in this memo supersedes the data in the RfA.

Evidence informing advice

8. The RfA "*Use of a primary dose of paediatric COVID-19 vaccines for children aged 6 months to 4 years*" (see Appendix 2), details current evidence about paediatric vaccines for children aged 6 months to 4 years. This includes both consideration of New Zealand and international rates of COVID-19 hospitalisation and deaths in young children, immunogenicity and efficacy data that is available and peak body advice. The following is an overview of the evidence.

Severe COVID-19 (deaths, ICU admissions, and hospitalisations) in children in New Zealand

Deaths

9. [redacted]

ICU admissions

10. [redacted]

11. Preliminary analyses conducted by the New Zealand Paediatric Surveillance Unit (NZPSU) [unpublished data] also support the conclusion that COVID-19 infections have resulted in few severe cases in children (requiring intensive care) in New Zealand. Their analysis (data from 1 January 2022 – 30 June 2022) showed [redacted]

Hospitalisations

12. The Ministry of Health has conducted a preliminary analysis of COVID-19-related hospitalisation data for Aotearoa New Zealand in 2022 ("MoH preliminary analysis"). However, due to limitations in the way data are collected and coded, these hospitalisation data (in their raw form) can be misleading, overestimating the true number of admissions for COVID-19, particularly for children under five years of age:

    a. *Infants are under-represented in the dataset*

    The data are for age cohorts defined at 1 January 2022, and no one born after this date is included in these data. This means infants under are under-represented in the dataset given that by the end of the observation period the youngest person in the dataset will be almost 10 months old

    b. *Data sources include NMDS and IP data*

    The hospitalisation data are derived from two sources: the National Minimum Dataset (NMDS) and a feed of in-patient (IP) data from hospitals in Auckland, Canterbury, Southern, Counties Manukau, Waikato, Capital and Coast, Waitematā and Northland. There are limitations to how COVID-19 attributed hospitalisations, and hospitalisations in general, are coded. The NMDS provides national coverage, with extensive information, including whether hospital stays are incidental or contributory/underlying to COVID-19. However, the NMDS is only available after a significant time lag (often 60 days or more). The IP data on admissions is more up-to-date, however are incomplete, do not have national coverage, and are subject to revision as more comprehensive data becomes available.

    c. *Definition of hospitalisation for COVID-19 is broadly inclusive*

    In this dataset, the primary clinical codes along with health speciality codes have been used to determine whether each hospitalisation is related to COVID-19, with attempts made to exclude individuals hospitalised *with*, rather than *for* COVID-19. However, the definition of hospitalisation for COVID-19 tends to remain broadly inclusive in both IP and NMDS, leading to overestimates of hospitalisation risk. For example, hospitalisations for conditions that could appear similar to COVID-19 (e.g. pneumonia), where individuals have had incidental rather than contributory/underlying SARS-CoV-2 infection may be incorrectly classified as 'hospitalisation for COVID-19', because hospital discharge coding cannot differentiate between the two situations.

d. Data has been restricted to 2 or more nights of admission

In these data, children under 5 years of age have a disproportionate number of short hospitalisations (likely to represent less severe illness). For example, those under 5 years of age were around twice as likely to be discharged on the same day as admission than those over the age of 5 (around 50% and a 25% of admissions respectively). Those under five years of age were also around twice as likely to be discharged on or before the day after admission compared to those 5 years or older (around 80% and 40% respectively). Many children may therefore have been assessed at the hospital and sent home (i.e., not admitted to a ward). For this reason, these data are best easier to interpret when restricted to hospitalisations where discharge date is at least 2 days after the admission date (as shown in Table 1).

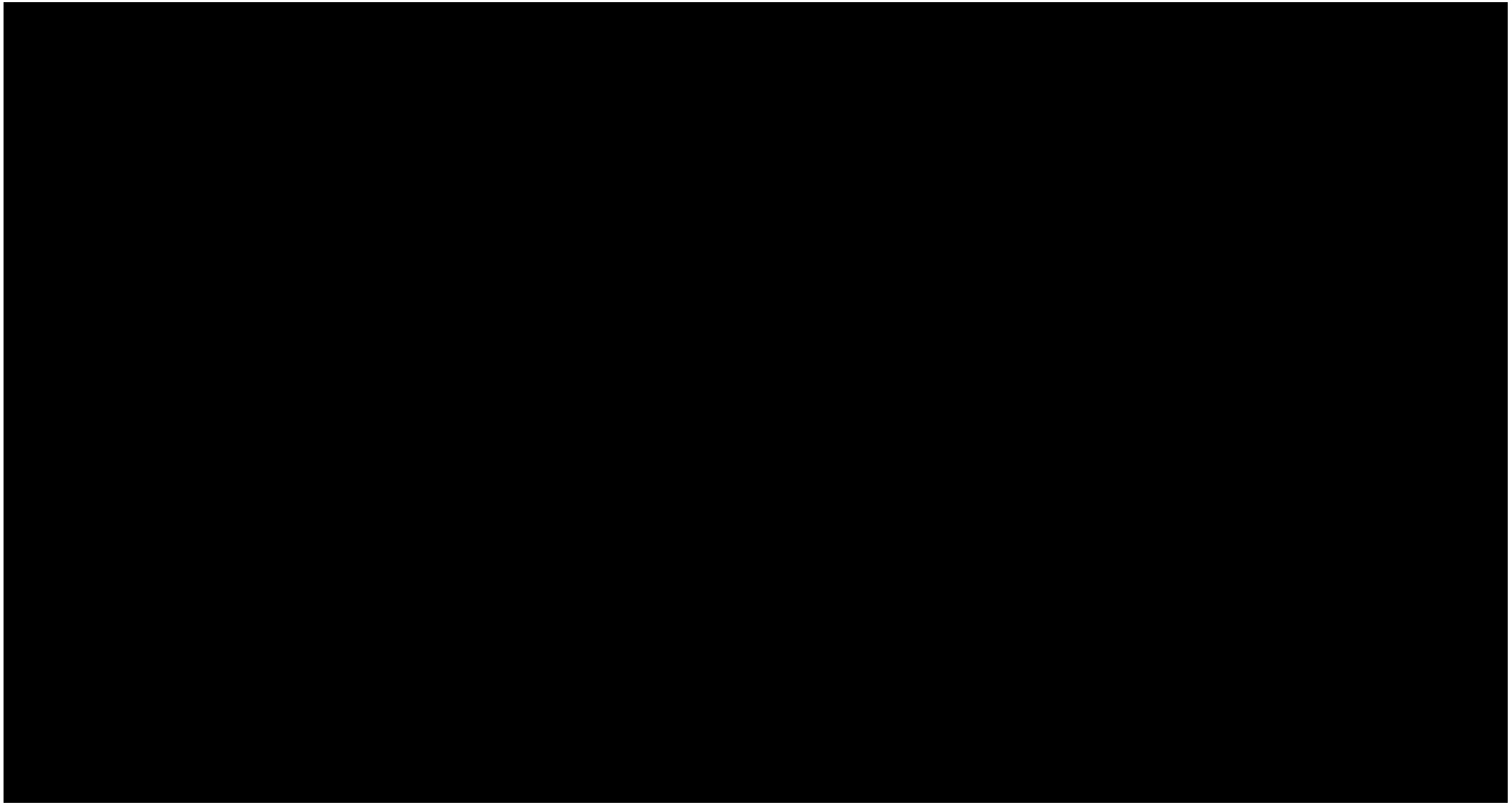
13. The MoH preliminary analysis is presented in Table 1. The data show the risk of COVID-19 related hospitalisation (with discharge date at least 2 days after the admission date) in those under the age of 5 years is similar to that of adults in the 40 - 44 year age group. However, this risk likely still reflects substantial overestimations of hospitalisation in the under 5-year age group due to the limitations described above.

14. Paediatricians on CV TAG have also raised the possibility of incorrect coding of young children who have tested positive for SARS-CoV-2 who have stayed in hospital because of their primary care-giver's hospitalisation rather than their own condition. However, the extent to which this might affect the findings is difficult to assess in this dataset. Further analyses of these data exploring associations with COVID-19 related illnesses (e.g. pneumonia), other positive viral illnesses (e.g. RSV), other diagnoses, severity of hospitalisation, type of admission (e.g. short stay vs. ward) should be considered, as should a review of a sub-set of case notes by a paediatrician. However, these analyses are unlikely to be available for several weeks.

15. In addition to Ministry of health analyses, the COHESION study[1] is currently analysing severity of COVID-19 hospitalisation for various cohorts across New Zealand. These results should be available in the **coming months.**

[1] The *COVID-19 HospitalisEd Patient SeverIty Observational Study NZ* (COHESION) is a national, multi-site, retrospective study, assessing the clinical and demographic predictors of COVID-19 severity in New Zealand in partnership with the University of Otago, Auckland, Waitamata, Waikato, Bay of Plenty, Mid Central, Capital & Coast, Hutt Valley and Canterbury District Health Boards.

Table 1: Preliminary COVID-19 attributable hospitalisation counts (with risk and 95% confidence intervals [CI] per 100,000 of population) ***for stays of 2 or more nights*** *by age group and ethnicity, 01 January to 02 November 2022*



Severe COVID-19 (deaths, ICU admissions, and hospitalisations) in children, International data

16. International data suggests rates of paediatric COVID-19 cases and hospitalisations increased during the Omicron wave. However, despite infection rates being high, data available suggests lower risk of hospitalisation, severe disease and death from Omicron infection as compared to Delta among children aged 6 months to 5 years [5, 6]. US data reported by the CDC found that hospitalisation associated with COVID-19 peaked during the Omicron wave at a rate of 16.1 per 100,000 on 8 January 2022 for 0- to 4-year-olds; a high rate compared to 2.6 per 100,000 in 5–11-year-olds (23.4 in 18–49-year-olds). The cumulative rate per 100,000 in the US is 306.5 and 77.7 respectively. [7] As of 26th November 2022, the CDC has reported that in the United States there have been 270 deaths in children aged 0- 5-months, with 99 of the deaths among children aged 6 to 11-months and 196 in children aged 12 months to 4 years – all contributory to COVID-19. [8] Australia, as of 3 July 2022, has reported 9 deaths from COVID-19 with a national mortality rate of 0.6 per 100,000 in comparison to the population average of 37.9. [9] For more information on international trends, refer to **Appendix 2**.

Vaccine efficacy and immunogenicity

17. Pfizer's Clinical trial had 1,178 6- to 23- month old participants who received at least one dose of the paediatric vaccine (with 32.7% follow up <2 months post-dose three) and 1835 2-4 year old participants who received at least one dose of vaccine (with 34.8% follow up <2 months post-dose three). [1] Control (placebo) groups had around half the number of participants of the vaccinated group (598 and 915 respectively). Limitations of the Pfizer clinical trial include very wide confidence intervals, the addition of a third dose (previously two doses had been trialled) and the median interval for dose 2-3 being significantly longer (16+ weeks) than the 8-week minimum.

18. In the Pfizer clinical trial, the 2–4 year old cohort had vaccine efficacies against symptomatic illness of 30% (first dose only) and 40% (second dose). This did not meet that the pre-specified immune-bridging success criteria in the 2–4 years cohort.

19. Estimated vaccine efficacy (VE) against symptomatic illness after a third dose in the clinical trial was 75.6% (95% CI: −369.1%, 99.6%), in the 6- to 23-month-old cohort and 82.4% (95% CI: −7.6%, 98.3%) in the 2- to 4-year-old cohort. It should be noted that both estimates have very wide confidence intervals (crossing VE of 0%) due to less than 10 COVID-19 cases in either age group (vaccine and placebo cases combined). [1]

20. Exploratory analysis for immunogenicity against Delta and Omicron variants was performed. This noted similar GMT against Delta (Using B.1.617.2) although significantly lower for Omicron (using BA.1 strain). As this was exploratory, the sensitivity of the assay is unknown. [10]

Vaccine Safety data

21. There were no new safety concerns reported in the FDA briefing about Pfizer's placebo-controlled controlled trial on children aged 6 months to 4 years, further to the safety profile of the Pfizer vaccine in the general population.[1] However, safety data about the vaccine on 6 month to 4 year olds remain limited.

22. The safety data from the trial showed that the risk of local adverse effects was lower in those aged 6 months to 4 years compared to those aged 5 to 11 years (who received a 10 µg dose in previous studies).[1] This is likely due to the lower dose of mRNA administered to the 6

months to 4 years age group. However, fever was reported more frequently and with higher severity in those aged 6 months to 4 years compared to 5-11 year olds (who received the 10 µg dose). [1]

23. Serious adverse events (SAE) were reported at similar frequencies in the vaccinated and the placebo groups. In the 6-23 months cohort, 3.1% reported SAE after vaccination and 2.3% after placebo. [1] In the 2-4 years cohort SAE were reported in 0.7% of individuals after vaccination and 0.9% after placebo. [1] The most commonly reported SAEs were respiratory illnesses, gastrointestinal illness, or infections that occur commonly in this age group. Two SAEs (pyrexia and pain in the extremity) reported by the same participant (in the 2- 4 years old group) were considered at least possibly related to vaccination by the study investigator. The remainder of the SAEs were not considered by the study investigator or by FDA to be related to vaccination, given the time to onset after vaccination and/or plausible alternate aetiology. Full details of SAEs are available in the FDA briefing document. [1]

24. The FDA briefing on the Pfizer clinical trial states that no cases of myocarditis/pericarditis or vaccine-related anaphylaxis were reported in either age group (6-23 months, and 2-4 years) through the data cut off.[1] There was no safety data available in subpopulations such as immunocompromised children or previously infected children. [1]

Peak body advice

Australia

25. On 3 August 2022, the Australian Technical Advisory Group on Immunisation (ATAGI) recommended that COVID-19 vaccination for children aged 6 months to 4 years be limited to children with severe immunocompromise, disability, and those who have complex and/or multiple health conditions which increase the risk of severe COVID-19. [11]

26. ATAGI does not currently recommend vaccination for children aged 6 months to 4 years who are not in the risk categories for severe COVID-19. [11] Australia's recommendation is for 2 primary doses of the paediatric formulation of Moderna COVID-19 vaccine (Spikevax), except for those with severe immunocompromise who require 3 primary doses, with an eight-week interval. [11]

Canada

27. On 14 July 2022, the National Advisory Committee on Immunisation (NACI) in Canada made recommendations about the use of the Moderna vaccine (Spikevax) in those aged 6 months to 5 years.[12] They provided a "discretionary NACI recommendation" that a complete vaccination series with the Moderna Spikevax (25 mcg) COVID-19 vaccine may be offered to children aged 6 months to 5 years who do not have contraindications to the vaccine, with a dosing interval of at least 8 weeks between the first and second dose. A "discretionary" recommendation suggests the need for consultation with a healthcare provider prior to vaccination. There is also a "discretionary NACI recommendation" that children aged 6 months to 5 years who are moderately to severely immunocompromised may be immunised with a primary series of three doses of the Moderna Spikevax (25 mcg) vaccine, using an interval of 4 to 8 weeks between each dose. NACI also strongly recommended that the Moderna Spikevax should not be routinely given concurrently (i.e., same day) with other vaccines (live or non-live).

Recent changes in policy

28. Recently, with a reduction in COVID-19 cases and less severity in disease from Omicron in children, many countries have started to dial back efforts to vaccinate children against COVID-19. However, majority of these changes have been in relation to vaccinating children aged 5 and above. For example, in England, children turning 5 after August 2022 will no longer be eligible for COVID-19 vaccination, with the exception of those at risk for severe disease. [13] Children aged 5-11 in Sweden, with the exception of those at risk for severe disease, are also no longer eligible. [14] Denmark has also halted vaccinations for those under the age of 18. [15]

Recommendations

29. CV TAG met on 13 September 2022, 11 October 2022 and 8 November 2022 to discuss whether the paediatric Pfizer vaccine should be offered or made available to children aged 6 months to 4 years.

30. CV TAG noted that:

a. After the waves of SARS-CoV-2 infections seen in New Zealand since late 2021, there is likely to be a high proportion of children under 5 years of age who have already been exposed to COVID-19.

b. After consideration of the data available (including the substantial limitations around the hospitalisation data, and the very few deaths and cases of PICU/ICU admission) CV TAG considers the risk of severe illness due to SARS-CoV-2 to be very low in children under the age of five.

c. There is insufficient data to suggest that vaccination of children would have any benefit on community transmission.

d. Vaccine efficacy and effectiveness data is scarce in this age group. Additionally, cases occurring in the clinical trial in 6 month – 4 year olds were accrued during February 2022 through April 2022. Although this is during a period of Omicron-variant circulation, there may be differences in efficacy against the lineages circulating in early 2022 compared to that against current and future lineages.

e. There is limited data on safety of the paediatric Pfizer vaccine in children under the age of five.

f. There are currently no efficacy data or safety available in sub-populations such as immunocompromised children or previously infected children. [1] This limits understanding of whether three doses of the paediatric formulation of the Pfizer vaccine (for children aged 6 months to 4 years) are effective against COVID-19 for severely immunocompromised children, or those with complex medical issues, or whether additional doses may be required (as recommended for older age groups that are severely immunocompromised).

g. There are only a small number of children aged 6 months to 4 years that would qualify under the severely immunocompromised category.

h. There is low vaccine uptake among younger children in New Zealand, particularly among Māori and Pacific children. Only 15% of Māori children aged 5-11 have completed a primary course of the COVID-19 vaccine, as compared to 19% of Pacific children and 37% of Non-Māori and Non-Pacific children in the same age group. [16]

i. Internationally, the uptake of the paediatric vaccine from those aged 6 months to 4 years has been very low. In the US, the CDC has reported less than 5% of children aged 6 months to 4 years have received the COVID-19 vaccine.

j. There are existing limitations on the availability and supply of the paediatric formulation of the Pfizer vaccine (for children aged 6 months to 4 years) , and the vaccine will not be available in New Zealand in 2022. The Moderna vaccine is a potential option to support the supply of paediatric vaccines.

31. CV TAG recommended that:

a. COVID-19 vaccination for children aged 6 months to 4 years is NOT needed in otherwise healthy children.

b. The paediatric primary course Pfizer vaccine (3 dose series) should be **available** for children aged 6 months to 4 years that are severely immunocompromised, or who have complex and/or multiple health conditions which increase the risk of severe disease from COVID-19 (following the Starship Child Health table of underlying comorbidities provided in **Appendix 1)**.

c. The paediatric formulation of the Pfizer vaccine (for children aged 6 months to 4 years) should be administered at a schedule in line with the Medsafe datasheet (a three-dose course, with intervals of 3 or more weeks between first and second dose, and 8 or more weeks between the second and third dose). The specific interval adopted within the programme should be considered and decided after approval by Medsafe and following discussion with National Immunisation Programme (NIP) clinical advisors.

d. The paediatric formulation of the Pfizer vaccine for children aged 6 months to 4 years can be administered before, after, or at the same time as other vaccines in this age group

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

Signature _____ Date: 24 November 2022

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

Signature _____ Date: 24 November 2022

Te Tumu Whakarae mō te Hauora

Acting Director-General of Health

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Appendix 1

Starship Clinical Guidelines: COVID-19 disease in children [17]

Note: only the risk factors listed by Starship that relate to "children with underlying co-morbidities" form this list.

Risk factors for severe disease in children: Co-morbidities

- Chronic lung disease including bronchiectasis, cystic fibrosis, BiPAP for OSA
- Non-repaired congenital heart disease, acquired heart disease or congestive heart failure
- Poorly controlled asthma (regular symptoms occurring in a usual week that affect the patient's quality of life and includes anyone with an admission in the last 2 years or anyone with 2 or more courses of steroids in the last two years)*
- Obesity (BMI ≥95th centile for age)
- Diabetes (insulin-dependent)
- Chronic kidney disease (GFR <15 ml/min/1.73m2)
- Severe cerebral palsy (or neurodevelopmental disorder)
- Complex genetic, metabolic disease or multiple congenital anomalies
- Trisomy 21/Downs Syndrome
- Primary or acquired immunodeficiency
- Haematologic malignancy and post-transplant (solid organ or HSCT in last 24 months)
- On immunosuppressive treatment including chemotherapy, high-dose corticosteroids, biologics or DMARDS

*https://www.nzrespiratoryguidelines.co.nz/uploads/8/3/0/1/83014052/arf_nz_child_asthma_guidelines_update_30.6.20.pdf

Appendix 2

Request for Advice (RfA)

This form contains the details relevant to the questions posed to the Science and Technical Advisory (STA). STA will respond to the request using this form which will also be stored in STA content management system for future reference.

This form, or parts of it, may also be forwarded to other relevant parties as appropriate.

Title	Use of a primary dose of paediatric COVID-19 vaccines for children aged 6 months to 4 years		
Subject	Information on the use of a primary dose of paediatric COVID-19 vaccines for children aged 6 months to 4 years		
Reference No.	0534	Date Received	25/07/2022
Requestor	COVID-19 Vaccine Technical Advisory Group (CV TAG)	Date Due	TBC
Advisor	[redacted]	Date Completed	11/10/2022 (amended date 3/11/2022)
Peer reviewed by	[redacted]		
Advice issued to	CV TAG		
Approved by	Dr Ian Town, Chief Science Advisor		
Deliverables	Review of evidence and international guidance		

6.

8.

Request Outline

Background/Context

To date, New Zealand has implemented a predominantly Pfizer-based COVID-19 immunisation programme. Cabinet approved use of the Pfizer vaccine to protect 5–11-year-olds in New Zealand on 21 December 2021. This followed advice from the COVID-19 Vaccine Technical Advisory Group (CV TAG), and Medsafe approval. On 22 March 2022, CVTAG recommended that children aged 5–11 years who are severely immunocompromised should be offered a third primary dose of the paediatric Pfizer vaccine.

CV TAG has not, to date, provided official advice about COVID-19 vaccines for children under the age of 5. Since mid-June 2022, an increasing number of jurisdictions have now authorised COVID-19 primary course vaccinations for children aged 6 months to 4 years (this term is used throughout to mean those 6.0 months to 4.99 years of age).

CV TAG is seeking information to inform recommendations about the administration of a paediatric primary course vaccine in New Zealand for children aged 6 months to 4 years.

Questions

- What safety and efficacy data are available for introducing a primary course of the paediatric COVID-19 vaccines for children aged 6 months to 4 years?
- Which COVID-19 vaccine platform has the best profile (in terms of efficacy and safety) for children aged 6 months to 4 years?
- Which countries have recommended a primary course of the paediatric COVID-19 vaccines for children aged 6 months to 4 years?
- What is the recommended interval between each dose of the primary course of the paediatric COVID-19 vaccines for children aged 6 months to 4 years?
- What are some key considerations for administering a primary course of the paediatric COVID-19 vaccine among children aged 6 months to 4 years?

Intended application of advice

To inform recommendations for a paediatric primary course of COVID-19 vaccines for children aged 6 months to 4 years.

What are the implications and considerations of this advice on Te Tiriti o Waitangi and equity?	The current objective of the COVID-19 vaccine immunisation programme is to protect individuals from severe disease outcomes and to reduce the impact of the virus on the healthcare system. Equity and Te Tiriti are relevant to assessing who is impacted by a recommendation of COVID-19 primary course vaccination for children under the age of 5. Given these groups are more likely to have severe outcomes as a consequence of SARS-CoV-2 infection, it is important they are prioritised. Māori and Pacific peoples are more vulnerable to severe disease and hospitalisation due to COVID-19, and therefore a pathway for Māori and Pacific children, particularly if immunocompromised is of significant importance.

Response to Request for Advice

Key points

- National and international data indicate increasing rate of paediatric COVID-19 cases seen during the Omicron wave. However, data available indicates a low risk of severe COVID-19 disease and/or death for children under the age of 5.
- Moderna and Pfizer are currently trialling COVID-19 paediatric vaccines among children aged between 6 months and 4 years (this term is used throughout to mean those 6.0 months to 4.99 years of age).
- The US, Canada and Australia have now authorised COVID-19 vaccines for children in this age group.
- The Moderna vaccine is a two-dose primary vaccination (25 µg doses, 1 month apart), whereas the Pfizer is a three-dose series (3 µg each, intervals of 3 weeks between first and second dose and at least 8 weeks between the second and third dose).
- The Pfizer vaccine for those aged between 6 months and 4 years is up for evaluation by the Medical Assessment and Advisory Committee by mid-October. The paediatric Moderna vaccine on the other hand, is not up for consideration, and has not been authorised for children aged 6-11 years in New Zealand.
- Available data on efficacy and safety suggest that both vaccines induce a strong immune response, are well tolerated, with mild to moderate side effects.
- Key considerations for vaccine approval include current regulations, vaccine uptake and vaccine schedules.

Background

During the Omicron wave, there was an increasing number of paediatric COVID-19 cases seen nationally and internationally. Since December 2021, children aged 5-11-years have been eligible for a primary course of the paediatric COVID-19 Pfizer vaccine. This followed advice from the COVID-19 Vaccine Technical Advisory Group (CVTAG), and Medsafe approval. Since 22 March 2022, CVTAG has also recommended that children aged 5–11 years who are severely immunocompromised should be offered a third primary dose of the paediatric Pfizer vaccine.

No advice to date has been provided on COVID-19 vaccines for **children under the age of 5**. Throughout this document, the term "6 months to 4 years" of age is used inclusively (that is, to include those 6.0 months to 4.99 years of age).

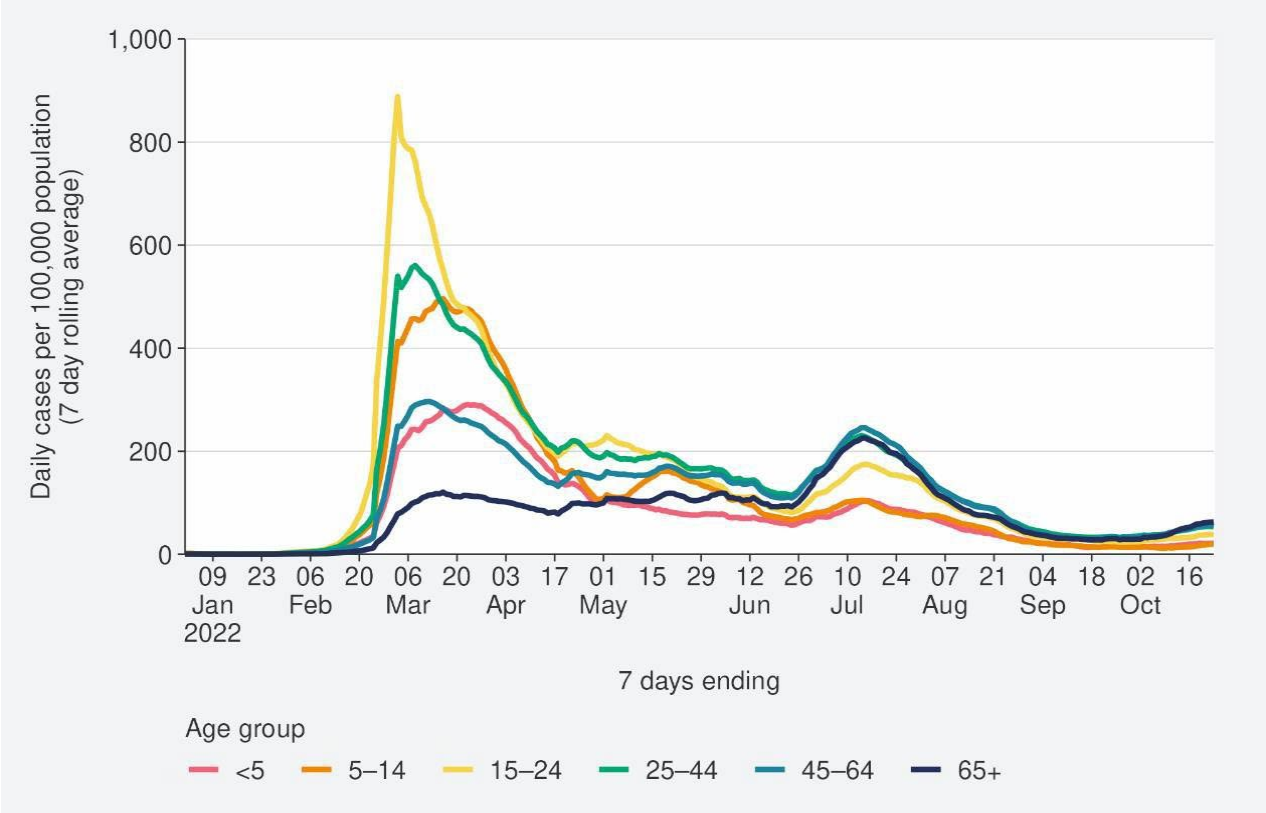
The number of jurisdictions which have authorised the use of a primary course of COVID-19 vaccine to children aged 6 months to 4 years continues to increase. In June 2022, the United States (US) Federal Drug Agency (FDA) granted emergency use authorisation (EUA) to Pfizer and Moderna's vaccines for children aged 6 months to 4 years. [1] On 19 July 2022, Australia's Therapeutic Goods Administration (TGA) provisionally approved a paediatric dose of the Moderna vaccine for children aged six months to six years. [2] On 3 August 2022, the Australian Technical Advisory Group on Immunisation (ATAGI) recommended COVID-19 vaccination for children aged 6 months to 4 years with severe immunocompromise, disability, and those who have complex and/or multiple health conditions which increase the risk of severe COVID-19.[3] More information on Jurisdictions is detailed in **Paediatric COVID-19 vaccination in** other jurisdictions below.

Impact of COVID-19 in young children in New Zealand

Age related COVID-19 case rates

As of 5 August 2022, there have been 70,331 reported cases of COVID-19 in children aged between 0 and 4 years. Children aged 0 to 9 have comprised of 10.3% of COVID-19 reported cases in New Zealand (last reporting from 8 August 2022).

COVID-19 cases by age group and status



Ethnicity

Recent COVID-19 cases from the BA.4/5 wave, indicate children between the ages of 0-4 seem to have much lower rates of COVID-19 infection reported as compared to older age groups (albeit similar rates seen for children aged 5-14). Moreover, the lowest case rates reported (by age and ethnicity) out of any cohort were among those aged 0-4 of Pacific Peoples ethnicity and 5-14 of Māori ethnicity (2.9 and 3.0 per 1,000 population respectively). This is likely an underestimate, as it is based on case reporting.

Hospitalisations, ICU admissions and deaths

1. The Ministry of Health has conducted preliminary analysis of COVID-19-related hospitalisation data for Aotearoa New Zealand in 2022 ("MoH preliminary analysis"). However, these hospitalisation data (in its raw form) could be misleading, particularly for children under the age of five, due to the following limitations in data collection and coding:

    a. The hospitalisation data are derived from two sources: the National Minimum Dataset (NMDS) and a feed of in-patient (IP) data from hospitals in Auckland, Canterbury, Southern, Counties Manukau, Waikato, Capital and Coast, Waitematā and Northland. There are limitations to how COVID-19 attributed hospitalisations, and hospitalisations in general, are coded. The NMDS provides national coverage, with extensive information, including whether hospital stays are incidental or contributory/underlying to COVID-19. However, the NMDS is only available after a significant time lag (often 60 days or more). The IP data on admissions is more up-to-date, however are incomplete, do not have national coverage, and are subject to revision as more comprehensive data becomes available.

    b. In this dataset, the primary clinical codes along with health speciality codes have been used to determine whether each hospitalisation is related to COVID-19, with attempts made to exclude individuals hospitalised *with*, rather than *for* COVID-19. However, the definition of hospitalisation for COVID-19 tends to remain broadly inclusive in both IP and NMDS, leading to overestimates of hospitalisation risk. For example, hospitalisations for conditions that could appear similar to COVID-19 (e.g. pneumonia), where individuals have had incidental rather than contributory/underlying SARS-CoV-2 infection may be incorrectly classified as 'hospitalisation for COVID-19', because hospital discharge coding can not differentiate between the two situations

    c. In these data, children under 5 years of age have a disproportionate number of short hospitalisations (likely to represent less severe illness). For example, those under 5 years of age were around twice as likely to be discharged on the same day as admission than those over the age of 5 (around 50% and a 25% of admissions respectively). Those under five years of age were also around twice as likely to be discharged on or before the day after admission compared to those 5 years or older (around 80% and 40% respectively). For this reason these data are best easier to interpret when restricted to hospitalisations where discharge date is at least 2 days after the admission date.

    d. The data are for age cohorts defined at 1 January 2022, and no one born after this date is included in these data. This means infants under are underrepresented in the dataset given that by the end of the observation period the youngest person in the dataset will be almost 10 months old.

2. The MoH preliminary analysis is presented in Table 1 despite these limitations. The data show the risk of COVID-19 related hospitalisation (with discharge date at least 2 days after the admission date) in those under the age of 5 years is similar to that of adults in the 40 - 44 year age group. However, this risk likely still reflects substantial overestimations of hospitalisation in the under 5-year age group due to the limitations described above. Paediatricians in CV TAG have also raised the possibility of incorrect coding of young children who have tested positive for SARS-CoV-2 who have stayed in hospital because of their primary care-giver's hospitalisation rather than their own condition. However, the extent to which this might affect finding is difficult to assess in this dataset. Further analyses of these data exploring associations with COVID-19 related illnesses (e.g. pneumonia), other positive viral illnesses (e.g. RSV), other diagnoses, severity of hospitalisation, type of admission (e.g. short stay vs. ward) should be considered, as should a review of a sub-set of case notes by a paediatrician. However, these analyses are unlikely to be available for several weeks.

[redacted]

The COHESION study is currently analysing severity of COVID-19 hospitalisation for various cohorts across New Zealand. These results should be available in the **coming months.**

Analysis conducted by the New Zealand Paediatric Surveillance Unit (NZPSU) [unpublished] also support the notion that COVID-19 infections have had a very mild impact on children in New Zealand. [redacted]

[redacted]

International data trends in cases rates, hospitalisation and death from COVID-19 in children

Increasing rate of paediatric COVID-19 cases and hospitalisations during the Omicron wave

In the US, seroprevalence studies report that the majority of children have been infected with COVID19. A study using data collected between September 2021 and February 2022 reported that approximately 3 out 4 children aged 0-11 years have antibodies that show previous infection with SARS-CoV-2. [12] Another study estimates that out of all confirmed cases of COVID-19, five times as many children aged 0-4 years were hospitalised during the Omicron wave (Dec, 2021) than from the Delta wave [13]. In UK, paediatric admissions began to rise from 26 December 2021, with a 3-fold increase in 2 weeks.[14]. The rise of COVID-19 associated hospitalisation was most rapid among children under 5 years, and highest in infants aged under 1 year. This was based on a period of 90% Omicron prevalence.

Although infection rate seems high, current data suggests lower risk of hospitalisation, severe disease and death from Omicron infection, as compared to Delta, among children under 5.

More than 200 deaths of 0 – 4-year-olds have been reported in the US due to COVID-19 since Jan 2020, and this accounts for 1.7% of all deaths in this age group. [15] However, a US study of children under 5 years found a significantly lower risk for severe clinical outcomes in the 3-day time-window following initial Omicron infection diagnosis compared to Delta. [16] Risk for an ED visit was 18.83% (vs 26.67%), hospitalisation was 1.04% (vs 3.14%), ICU admissions was 0.14% (vs 0.43%), and mechanical ventilation was 0.33% (vs 1.15%).
In UK, a clinical case review of a small number of Omicron admissions in infants found those admitted were not severely unwell. [14, 17] UK data during the Omicron wave (14 December 2021 to 6 January 2022) indicate less severe outcomes in children aged under 1 year compared to previous waves.[18] In this wave period, 12.7% required oxygen use compared to 22.5% in the first wave of the pandemic. 16% required admission to intensive care (vs 14%), 3.9% required use of mechanical ventilation (vs 5.8%), 1.3% required use of non-invasive ventilation (vs 7.2%), and mean length of stay was 1.9 days (vs 6.6 days).

There are some presenting illnesses among some paediatric COVID-19 cases causing concern:

A study from the US states that paediatric acute upper airway infection (UAI) cases have increased during the Omicron variant surge, with many developing severe disease.[19] The retrospective cohort study suggests that Omicron replicates more efficiently in the conducting airways, increasing the risk of a croup phenotype in children as they have smaller airways.

Multisystem Inflammation Syndrome (MIS-C) is being seen in children after a SARS-CoV-2 infection with no alternative diagnosis. This is categorised as severe illness, with multisystem organ involvement, fever and inflammation. Although relatively uncommon, MIS-C can present approximately 2-6 weeks following acute infection and generally requires intensive care treatment, with 1-2% of patients dying [15, 20][15, 20][16, 21][16, 21][16, 21][15, 20][15, 20][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21][16, 21](16, 21)[15, 20][15, 20]. Although not expressively stated, current reporting does indicate the highest rates of MIS-C detected in US had been during the Delta Wave (i.e. October 2020 to March 2021), as opposed to the more recent Omicron wave (December 2021 to March 2022) [15].

Long COVID symptoms have also been reported among children, with those aged 0-5 being more likely than those without infection to experience symptoms such as fatigue, loss of smell and loss of taste 4 weeks after infection. Evidence on prevalence of long COVID among young children is limited by inability of younger children to verbalize symptoms, few studies including children, lack of control groups and symptoms frequently occurring in children without known COVID-19 infection. [15]

- A large study of an uninfected and unvaccinated population of children investigated severe outcomes among 1,147 children aged 0-11 years who were hospitalised between 5 February and 28 February 2022 (a BA.2-dominant period). Severity of BA.2 infection among hospitalized children who had no past COVID-19 infection or vaccination was not mild. [21] ○ Children hospitalised during the BA.2 dominant period had higher likelihood of ICU admissions, mechanical ventilation and oxygen use.
    - ○ BA.2 was reported to be more neuropathogenic than previous SARS-CoV-2 variants, influenza and parainfluenza viruses, resulting in more seizures.

Current COVID-19 vaccines available for children under the age of 5

The following table details current COVID-19 vaccination eligibility for children across different age groups in New Zealand. **Note: age categories are different between Pfizer-BioNTech and Moderna COVID-19 vaccines:**

Pfizer		Moderna	
Age Group	Eligible for vaccination in NZ*	Age Group	Eligible for vaccination in NZ*
6 month –4 years	No	6 month –5 years	No
5-11 years	Yes	6-11 Years	No
12-17 years	Yes	12-17 years	Yes

*As of 9 August 2022

Pfizer (Cominarty, BNT162b2)

Details of the current paediatric primary course Pfizer vaccine are;

- a three-dose course of 3 µg each (compared to two doses of 10 µg in 5-11 and 30 µg doses for individuals aged 12 years or more).
- an interval of 3 weeks between first and second dose and at least 8 weeks between the second and third dose.

In December 2021, following advice from the independent data monitoring committee, Pfizer announced that the ongoing clinical trial of the Pfizer COVID-19 vaccine in children aged 6 months through to 4 years would be amended from 2 doses to evaluate a third 3 µg dose at least two months after the second dose of the two-dose series. This decision was made to provide higher levels of protection for this group. [4] The current estimated primary completion date is June 2024. [5] Pfizer amended the protocol from 2 doses to a third 3 µg dose at least two months after the second dose of the two-dose series following analysis of the post-Dose 2 safety and effectiveness data The median interval for dose 2-3 was significantly longer (16+ weeks) than the eight week minimum detailed in the amended protocol for administration. The FDA briefing noted concern over the need for a third dose at 11 weeks after the second dose as this is a large period of time before the children are considered protected from vaccination. [6]

In February 2022, Pfizer announced plans to extend their rolling submission to the US FDA for amendment of the EUA to include children aged 6 months to 4 years. FDA advisors backed the use of three doses of Pfizer for children aged 6 months to 4 years and the schedule was approved for use in the US in the week of the 13 June 2022.

The data submitted to support the EUA was from an ongoing Phase II/III trial (C4591007). Only data analysed before the 29 April 2022 was included in the EUA, this encompassed safety data from 1,678 children under 5 years old. The trials was a randomised, double blinded trial with 2:1 (placebo control: vaccination). [6]

The trial split the participants into two cohorts by age, 6 - 23 months and 2 - 4 years. For the 2- to 4year-old cohort had a vaccine efficacy against symptomatic illness of 30% (first dose only) and 40%
(second dose). Patients with a history of past SARS-CoV-2 infection were not excluded from the study.
Safety and effectiveness data was collected following the second dose for both age groups. This measured neutralising geometric mean titres (GMTs) and seroresponse rates were assessed against a reference strain. Following analysis of safety and effectiveness data after the first two doses, the protocol was amended to include a third primary dose. After the third dose the trials end points and success criteria were met. [6]

The efficacy against symptomatic illness after a third dose was 75.6% (95% CI: -369.1%, 99.6%) in the 6 - 23-month cohort and 82.4% (95% CI: -7.6%, 98.3%) in the 2 - 4-year-old cohort. This produced a combined efficacy in children aged 6 months to 4 years of 80.4% (95% CI: 14.1%, 96.7%). However there is uncertainty around estimates as shown by wide confidence intervals. Pfizer/BioNTech data is only available up to five months after vaccination.[7]

The FDA briefing on the Pfizer clinical trial did not report on the incidence of myocarditis/pericarditis in this age group. In addition, there was no safety data available in subpopulations such as immunocompromised children or previously infected children. [7]

There is limited evidence on breadth of immunity from vaccines in this age group. Reliable data on hybrid immunity is limited. While there is likely still some benefit against

symptomatic infection from vaccination it may not be sufficient to overcome vaccination risk in children under five.

Overall, Pfizer noted that the three doses in 6-month- to 4-year-olds elicited a strong immune response (discussed below with clinical results) and was well tolerated, presenting mild to moderate side effects. [6].

Moderna (Spikevax, mRNA-1273)

Details of the primary course vaccine:

- a two-dose primary vaccination (25 µg doses, 1 month apart).
- This is again a lower dose than provided to adults (100 µg/dose). [8]

On 23 March 2022, Moderna announced positive interim data from the Phase II/III trial in children aged 6 months to <2 years and 2 years to <6 years. Based on these data, Moderna submitted a request for authorisation of a 25 µg two-dose primary course of mRNA-1273 for children aged 6 months to <6 years of age to the US FDA, EMA, and other global regulators. FDA advisors backed the use of two doses of Moderna for children aged 6 months to 5 years and it was approved for use in the US in the week of the 13 June. [8] Since then, Canada, Australia, Israel and Argentina have approved Spikevax in this age group. [9-11] The paediatric dose is formulated in the same way as that for older children and adults but contains a lower concentration of the active ingredient. Children aged six years and older can already receive two doses of the vaccine administered 28 days apart.

The two-dose schedule means that the primary course is completed in approximately 1/3 of the time frame required to complete the Pfizer primary course.
Moderna submitted clinical data from the KidCOVE trial supporting the use of vaccine in children aged 6 months to under 5 years. This was a randomised, observer blind, placebo control study designed to evaluate the safety, immunogenicity and tolerability of the vaccination. Data from approximately 6,700 children was included in the FDA submission. Data was separated by the following age groups:

- 6 months – 23 months
- 2 years – under 6 years

[8]

Safety, Immunogenicity and Efficacy of Vaccines

Reactogenicity and Safety

Both mRNA vaccines (Pfizer and Moderna) appear to be well tolerated among children aged 6 months through to 4 years, although Moderna may be more reactogenic. Overall, rates of serious adverse events were low. Although these studies were too small to identify the risk of myocarditis / pericarditis, post-authorisation surveillance suggests it declines with younger age after peaking in late adolescents / young adults. Overall, the vaccines have been deemed safe, although the very low risk of serious side effects should be put into context with the very low of risk severe COVID-19 in these age groups.

[1] **Pfizer**

The Pfizer clinical trial submitted safety data from its placebo-controlled trial on children aged 6 months to 4 years. Serious adverse effects (SAE) were reported in similar frequencies in the vaccinated and the placebo groups. In the 6-23 months cohort, 3.1% reported SAE after vaccination and 2.3% after placebo. The most reported SAE included respiratory illnesses, gastrointestinal or infections, all of which are common within this age group. Among the 2-4 years cohort, 0.7% reported SAE after vaccination and 0.9% after placebo. [6] Compared to all other age groups, the risk of SAEs was lower in the 6 month to 4 years age group (likely due to the lower dose of mRNA). [6]

This clinical trial did not indicate any new safety concerns compared to the safety profile of vaccination in older people. [6] Limitations leading to risk in vaccinating 6 month - 4-year-olds include uncertainties about:

- incidence of myocarditis/pericarditis in this age group
- safety data available in subpopulations (i.e., immunocompromised children or previously infected children). [6]

Moderna

KidCOVE is a randomised, placebo-controlled study by Moderna that is testing the safety and effectiveness of the Moderna (mRNA-1273) vaccine on more than 6000 children in United States and Canada. The study results shared so far, indicate that the vaccine was tolerated by the 6 month to 5 year olds age group, in a consistent way to all other age groups, including adults. Adverse effects were mainly mild or moderate, with more reported following the second dose than the first. Less than 0.2% of participants were reported to have fevers over 40˚C following vaccinations. No new safety concerns were raised, with no reports of myocarditis /pericarditis, MIS-C or deaths. [8]

Efficacy and Immunogenicity

Both vaccines are mRNA based and have the potential to generate antibody levels like those induced in young adults following vaccination. These levels are considered to be protective although this is speculative as the link between antibodies and level of protection is unknown across all age groups. Current data does point to three doses of Pfizer being more efficacious than two doses of Moderna, however, this is with a high degree of uncertainty, particularly on severe COVID-19. While the efficacy data for both vaccines, in tandem with the primary immunobridging (comparison of antibody titres to adult cohorts) endpoints, suggests the vaccines will provide protection, the exact **magnitude and duration remains unknown**.

Pfizer

In the Pfizer clinical trial, the 2–4 year old cohort had vaccine efficacies against symptomatic illness of 30% (first dose only) and 40% (second dose). This did not meet that the pre-specified immunebridging success criteria in the 2–4 years cohort.

Preliminary analysis of efficacy against symptomatic illness after a third dose was reported as follows:

- 6 - 23-month cohort: 75.6% (95% CI: -369.1%, 99.6%)
- 2 - 4-year-old cohort: 82.4% (95% CI: -7.6%, 98.3%)
- Combined analysis of both age groups: 80.4% (95% CI: 14.1%, 96.7%).

Exploratory analysis for immunogenicity against Delta and Omicron variants was performed. This noted similar GMT against Delta (Using B.1.617.2) although significantly

lower for Omicron (using BA.1 strain). As this was exploratory, the sensitivity of the assay is unknown. [6]

There are limitations with the Pfizer clinical trial, including very wide confidence intervals and the Median interval for Pfizer dose 2-3 being significantly longer (20+ weeks) than the 8 weeks for approval. Not all cases for Pfizer 2 doses were attributable to Omicron.

Moderna

Moderna's clinical trial among those aged 6 months to <2 years and 2 years to <6 years is ongoing and the only information currently available for this age group is from press releases. In March 2022, Moderna stated that "In both age groups, two doses of 25 µg provided similar immunogenicity to the 100 µg two-dose primary series in adults ages 18 to 25 years, meeting the non-inferiority criteria and immunobridging, and indicating that the benefit of mRNA-1273 conferred to adults ages 18 to 25 are also conferred to children and infants as young as 6 months. SARS-Cov-2-neutralizing antibody geometric mean ratio (GMR) comparing the response in children 6 months to under 2 years to the response in young adults from the Phase 3 COVE study was 1.3 (95% CI: 1.1, 1.5) and was 1.0 (95% CI:
0.9, 1.2) for the 2 to under 6 years age group. This also predicts protection from COVID-19 and severe
COVID-19 disease down to 6 months of age."

In March 2022, Moderna stated that "The Omicron SARS-CoV-2 variant predominated in the U.S. during the KidCOVE study in these younger age groups. The secondary endpoint of vaccine efficacy confirms statistically significant, but lower efficacy against COVID-19 infection as expected during the Omicron wave and consistent with adult observational data. Using the Phase 3 KidCOVE study COVID-
19 definition, vaccine efficacy in children 6 months to 2 years was 43.7% and vaccine efficacy was 37.5% in the 2 to under 6 years age group. In this case, statistically significant is defined as a lower bound on the 95% confidence interval which is greater than 0. The majority of cases were mild, and no severe COVID-19 disease was observed in either age group. The absence of any severe disease, hospitalization or death in the study precludes the assessment of vaccine efficacy against these endpoints." [8]

Vaccine uptake

Vaccine uptake by age and ethnicity, New Zealand

Age Group:	**12-17**			**5-11**		
Ethnicity:	*Māori*	*Non-Māori Non-Pacific*	*Pacific Peoples*	*Māori*	*Non-Māori Non-Pacific*	*Pacific Peoples*
Dose 1%	92	97	95	36	63	49
Dose 2%	87	95	92	15	37	19

There has been lower COVID-19 vaccine uptake among younger children in New Zealand, particularly among Māori and Pacific children. Only 15% of Māori children aged 5-11 have completed a primary course of the COVID-19 vaccine, as compared to 19% of Pacific children and 37% of Non-Māori and Non-Pacific children in the same age group. [22] This is similar to data seen internationally where vaccine uptake is low among

children and adolescents, as compared to adults, with uptake declining with each dose. In the US, the CDC has reported less than 5% of children in the 6-month- to 5-yearage group have received the COVID-19 vaccine. Similar hesitancy has been seen by parents of children in the 5- to 11-year-old age group, where only approximately 36% of American children are fully vaccinated. Experts speculate that parents are in less of a rush to vaccinate children due to a perceived less threat to them from COVID-19 compared to older or immunocompromised people.[23]

Regulatory changes

Currently, Pfizer remains the 'preferred' COVID-19 vaccine in New Zealand for all age groups 5 years and above. Moderna has not yet been authorised for children aged 6-11 years in New Zealand. It will require changing course to recommend Moderna as opposed to Pfizer as the 'preferred' COVID-19 vaccine for children aged 6 months to 4 years. If this direction is sought, it will need to be accompanied by clear and strong messaging to avoid public confusion and needless apprehension.

Paediatric COVID-19 vaccination in other jurisdictions

United States

On 15 June 2022, the FDA panel endorsed both Moderna and Pfizer COVID-19 vaccines for use in children aged 6 months to 4 years. FDA authorized emergency use of Moderna for individuals 6 months -17 years and Pfizer for children aged 6 months to 4 years. This was endorsed by the FDA's Vaccine and Related Biological Products Advisory Committee who voted unanimously to recommend the use of either vaccines which they deemed to be safe and effective in young children against COVID-19. A preference was not expressed for either vaccine. [1] Current regulations were taken into consideration, including that only a primary course had been approved for Moderna (for those aged 5+), when three doses were needed for those aged 6 months to 4 years, whereas a booster for Pfizer was already approved for those aged 5+.

Australia

On 19 July 2022, Australia's Therapeutic Goods Administration (TGA) provisionally approved a paediatric dose of the Moderna vaccine for children aged six months to six years. The TGA experts considered data from the KidCOVE trial, noting that "vaccines for younger children will provide protection from the most severe outcomes of COVID-19, such as hospitalisation and death". [2]

On 3 August 2022, ATAGI recommended COVID-19 vaccination for children aged 6 months to <5 years with severe immunocompromise, disability, and those who have complex and/or multiple health conditions which increase the risk of severe COVID-19.[3] **Summary of Recommendations include:**

- ATAGI recommends COVID-19 vaccination for **children aged 6 months to <5 years** with severe immunocompromise, disability, and those who have complex and/or multiple health conditions which increase the risk of severe COVID-19. These include children with the following or similar conditions:

- Severe primary or secondary immunodeficiency, including those undergoing treatment for cancer, or on immunosuppressive treatments as listed in the ATAGI advice on 3rd primary doses of COVID-19 vaccine in individuals who are severely immunocompromised;
- Bone marrow or stem cell transplant, or chimeric antigen T-cell (CAR-T) therapy; ○ Complex congenital cardiac disease;
- Structural airway anomalies or chronic lung disease; ○ Type 1 diabetes mellitus;
- Chronic neurological or neuromuscular conditions; or
- A disability that requires frequent assistance with activities of daily living, such as severe cerebral palsy or Down Syndrome (Trisomy 21).

- The recommendation is for 2 primary doses, except for those with severe immunocompromise who require 3 primary doses. The recommended interval between each dose is 8 weeks.
- A paediatric formulation of the Moderna COVID-19 vaccine (Spikevax) was provisionally approved by the Therapeutic Goods Administration (TGA) on 19 July 2022 for use in children aged 6 months to 5 years and can be used for children aged 6 months to <5 years in the above categories.
- ATAGI reiterate the previous recommendation that all children aged **5 years or older** are recommended to receive a two-dose course of COVID-19 vaccine [Pfizer or Moderna].
- ATAGI does not currently recommend vaccination for children aged 6 months to <5 years who are **not** in the above risk categories for severe COVID-19. These children have a very low likelihood of severe illness from COVID-19. However, this is under ongoing consideration based on data on the disease burden and epidemiology, vaccine supply, emerging data on vaccine use in this age group, and availability of new COVID-19 vaccines for this age group.
- Parents of eligible children aged 6 months to <5 years recommended for vaccination should seek COVID-19 vaccination as soon as they are able to secure a vaccination clinic appointment. **ATAGI's guidance takes into account:**

- The very low risk of severe COVID-19 (e.g. hospitalisation due to COVID-19) in healthy children aged 6 months to <5 years. This age group is one of the least likely age groups to require hospitalisation due to COVID-19. Among the small number who are hospitalised or who die due to COVID-19, underlying medical conditions or immunocompromise are frequently present.
- A relatively low rate of paediatric inflammatory multisystem syndrome (PIMS-TS) following COVID-19 in children aged 6 months to <5 years compared to other older children, which has further declined with the Omicron variant compared to ancestral SARS CoV-2 strains.
- A clinical trial which included approximately 5500 children aged 6 months to 5 years and showed that the Moderna COVID-19 vaccine provided modest protection against infection (vaccine efficacy 35-52%) with the Omicron variant after two doses (25 mcg per dose). Safety data from the trial reported patterns of vaccine-related adverse events commonly seen in other age groups after mRNA vaccination, although fever was more common in this age group compared to older children and adults. Most side effects were mild to moderate and lasted

approximately 1-2 days. Children in this trial who had evidence of a previous SARS-CoV-2 infection were more likely to have side effects after vaccination.

- The vaccine efficacy data were against infection with early Omicron variants and there may be differences in efficacy against the currently circulating SARS-CoV-2 subvariants BA.4 and BA.5. Modest efficacy against infection also suggests protection will predominantly be against severe illness rather than infection, although there were insufficient episodes of severe illness in this clinical trial to assess this specific outcome.
- Data on benefits in children with complex medical issues or severe immunocompromise are currently limited, but vaccination is recommended based on first principles and evidence of benefit in other age groups.
- Up to one in four children in this age group had a fever following vaccination with Moderna vaccine, with higher rates seen in those with a history of previous COVID-19. As fever in this age group can sometimes result in medical review and/or investigations, and occasionally trigger a febrile convulsion, the side effect profile for this vaccination needs to be considered in the risk-benefit discussion.
- There is insufficient evidence to suggest that vaccination of infants and children would impact community transmission.
- ATAGI notes that there are currently constraints on the global availability and domestic supply of the Moderna vaccine for children aged 6 months to <5 years, which may persist until an alternative brand, variant-based or bivalent vaccines become available for this age group.
  Vaccine supply was one, among many, considerations in the ATAGI advice for this age group.
  [3]

Canada

On 14 July 2022, the Moderna Spikevax (25 microgram [mcg] dose) mRNA COVID-19 vaccine was authorized in Canada for use in pediatric populations under the age of 5 years. The National Advisory Committee on Immunisation (NACI), in Canada, issued the following recommendations:

For children 6 months to 5 years of age (which is the age group in which the Moderna Spikevax 25 mcg primary series vaccine is authorized):

1. NACI recommends that a complete series with the Moderna Spikevax (25 mcg) COVID-19 vaccine may be offered to children 6 months to 5 years of age who do not have contraindications to the vaccine, with a dosing interval of at least 8 weeks between the first and second dose. **(Discretionary NACI Recommendation)**
2. NACI recommends that children 6 months to 5 years of age who are moderately to severely immunocompromised (Appendix 1) may be immunized with a primary series of three doses of the Moderna Spikevax (25 mcg) vaccine, using an interval of 4 to 8 weeks between each dose. **(Discretionary NACI Recommendation)**
3. NACI recommends at this time that the Moderna Spikevax (25 mcg) COVID-19 vaccine primary series for children 6 months to 5 years of age should not routinely be given concurrently (i.e., same day) with other vaccines (live or non-live). **(Strong NACI recommendation).** [24]

Israel

On 6 July 2022, the Israeli Ministry of Health authorised COVID-19 vaccines for children ages 6 months to 5 years. The vaccine is **recommended** for toddlers between the ages of 6 months and 5 years if they are at-risk for underlying diseases (e.g. obesity, diabetes, chronic heart and lung diseases, chronic kidney disease, and neurological disorders such as convulsions). Among other factors associated with increased morbidity in toddlers are immunosuppression (congenital or acquired), toddlers up to one year of age, and toddlers whose birth was premature or requiring a feeding tube.

Moreover, the Ministry of Health **allows all parents to vaccinate their children** (even if they have no underlying diseases), which provides an important layer of protection against serious illness and the long-term effects of COVID-19.

Recommendations included that those who **recovered from COVID-19** aged six months and older can get vaccinated if at least 3 months have passed since the date of recovery or the date of their positive result on a serologic test.

In the Pfizer vaccine, three doses are administered, the first and second doses separated by 21 days, and the second and third doses separated by 56 days.
Two doses of the Moderna vaccine are administered 28 days apart. [25]

Other Regions

Recently, with a reduction in COVID-19 cases and severe disease in children, many countries have started to ease the efforts to vaccinate children against COVID-19. However, majority of these changes have been in relation to vaccinating children aged 5 and above. For example, in England, children turning 5 after August 2022 will no longer be eligible for COVID-19 vaccination. [26] Children aged 5-11 in Sweden, with the acceptation of those at risk for severe disease are also no longer eligible. [27] Denmark has also halted vaccinations for those under the age of 18.[28]

Next Steps	CV TAG memo issued to Director-General.

In the development of this work, the following parties have been consulted with:	The COVID-19 Vaccine Technical Advisory Group The Intelligence, Knowledge & Surveillance Group at the Public Health Agency

Resources used:		
Ministry of Health Policies and Procedures	☐ Yes ☒ No	
External Health Scientific organisations	☒ Yes ☐ No	
Internal Ministry of Health Advice	☒ Yes ☐ No	
External Expert Advice	☒ Yes ☐ No	
Literature Review	☒ Yes ☐ No	

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Appendix 1

Immunocompromised list form ATAGI

Moderately to severely immunocompromised includes individuals with the following conditions:

- Immunocompromised due to solid tumour or hematologic malignancies or treatments for these conditions
- Solid-organ transplant and taking immunosuppressive therapy
- Hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Immunocompromise due to chimeric antigen receptor (CAR) T cell therapy targeting lymphocytes
- Moderate to severe primary immunodeficiency with associated humoral and/or cell-mediated immunodeficiency or immune dysregulation
- HIV with AIDS-defining illness or TB diagnosis in last 12 months before starting vaccine series, or severe immune compromise with CD4<200 cells/uL or CD4%<15%, or without HIV viral suppression
- Recent treatment with the following categories of immunosuppressive therapies: anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids, alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive • Chronic kidney disease on dialysis

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