DG Memorandum

New Notice under section 34A of the Medicines Act 1981 authorising off-label administration of COVID-19 vaccines

Date:	23 June 2022
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Phil Knipe, Chief Legal Advisor, Health Legal
From:	Allison Bennett, Acting Group Manager, Public Health System Policy, SS&P
For your:	Decision and signing

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Purpose of report

1. This memo seeks your agreement and signing of a notice, pursuant to new section 34A of the Medicines Act 1981, authorising:

    - the off-label administration of a fourth dose of the Pfizer/BioNTech COVID-19 vaccine (Pfizer vaccine) to provide wide access to the recommended at-risk groups, and
    - the ongoing administration of the third (or booster) dose of the Pfizer vaccine at the reduced three-month dose interval (3 months since completion of primary course) as set out in the previous Epidemic Preparedness (Medicines Act 1981—COVID-19) Immediate Modification Order 2022 (IMO).

Background and context

2. In April 2022 COVID-19 Vaccine Technical Advisory Group (CV-TAG) provided initial advice (attached at appendix 2) on the waning of immunity after a third COVID-19 vaccine dose, and the groups in which waning immunity may occur more rapidly. That advice included recommendations for fourth doses for certain groups, and the dose interval at which a fourth dose should be given.

3. On 16 May 2022 Vaccine Ministers agreed to progress an amendment to the Medicines Act 1981 (the Act) to facilitate the broader roll out of fourth doses of the Pfizer vaccine beyond administration on prescription via authorised prescribers, such as General Practitioners (GPs) (HR 20220797 refers).

4. On 22 June 2022 the Medicines Amendment Bill (No.2) received Royal assent and is now in force.

The Medicines Act 1981 has been amended to allow the Director-General of Health to authorise the administration of COVID-19 vaccines otherwise than in accordance with the approved data sheet

5. The amendment to the Medicines Act 1981 (the Act) enables the Director-General of Health (Director-General) to authorise the administration of a consented COVID-19 vaccine otherwise than in accordance with the approved data sheet for that vaccine by issuing a notice under section 34A of the Act (the Notice).

6. The Director-General may only issue a notice in respect of a COVID-19 vaccine that has already been given consent or provisional consent under sections 20 or 23 of the Act.

7. The Director-General must have regard to the likely therapeutic value of the proposed administration of that COVID-19 vaccine, and the risk (if any) of the proposed administration injuriously affecting the health of any person.

8. The Director-General must be satisfied that the proposed administration of the COVID-19 vaccine is an appropriate measure to manage the risks associated with the outbreak or spread of COVID-19.

9. The Director General may specify by notice published in accordance with the Legislation Act 2019:

    i. who may receive the vaccine;

    ii. the recommended number and frequency of doses;

    iii. the recommended manner of administration; and

    iv. any other circumstances in which the vaccine may be administered.

10. Any person or class of persons permitted by the Act or by regulations to administer the relevant COVID-19 vaccine may administer that vaccine in accordance with a notice issued under section 34A. This means all vaccinators currently administering COVID-19 vaccines as part of the COVID-19 Immunisation Programme are able to administer any vaccines authorised by notice under section 34A.

CV-TAG recommends certain people should receive a fourth dose

11. Further to its initial advice in April 2022, CV-TAG was asked to provide advice on the science rationale, safety and peak body guidance on use of a second booster dose in:

    a) individuals with underlying health conditions that are likely to increase the individual's risk of adverse outcomes from COVID-19
    b) those aged over 50 years
    c) extension of the eligibility for a second booster dose to healthcare workers

12. CV-TAG has recommended the following groups should receive a fourth dose, at an interval of six months since their previous dose:

    a) people aged 65 years and over
    b) Māori and Pacific peoples aged 50 years and over

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c) residents of aged care and disability care facilities [of any age]

d) severely immunocompromised people who received a three-dose primary course and a fourth dose as a first booster (noting this would be a fifth dose for these people)

e) people aged 16 years and over who have a medical condition that increases the risk of severe breakthrough COVID-19 illness (see Table 1 in appendix 3 in attached CV-TAG advice for expanded groups)

f) disabled people aged 16 years and over with significant or complex health needs or multiple comorbidities that increase the risk of poor outcomes from COVID-19.

13. CV-TAG noted that data on increased benefits from healthcare workers receiving a second booster remains marginal and that there is no evidence within the available New Zealand data to suggest healthcare workers (particularly if young and without comorbidities), have a higher risk of acquiring and transmitting infection at their place of work. CV-TAG deferred any specific recommendation related to healthcare workers who do not otherwise fall within the groups recommended above.

14. s 9(2)(g)(i) [redacted]

15. A copy of CV-TAG's most recent advice is attached at appendix 3.

Why a fourth dose is needed to manage the risks associated with the outbreak and spread of COVID-19

16. After the peak of the current COVID-19 outbreak in March 2022, there was a steady decline of cases to the week of 17 April 2022. Following that, the rate of decline has slowed. The weekly COVID-19 case rate was 9.3 per 1000 people for week ending 5 June 2022, which is a decrease on the week prior and consistent with an overall trend downwards, with some variation across regions.

17. Precise case numbers remain uncertain. During the Omicron outbreak, the results of surveillance testing in border workers have been used to approximate the 'true' rate of infection in the community. In the week ending 5 June 2022, border workers had a case rate of 14 per 1000 people compared with 9.3 per 1000 people in the general population. This suggests there are approximately 50 percent more cases in the community than testing data is showing, noting that similar estimates earlier in the outbreak were that there were around twice as many cases as testing data showed.

18. In addition, wastewater testing shows that infection levels may be higher than self-reported cases, as wastewater RNA levels have remained relatively constant since early April.

19. CV-TAG has noted that there is evidence of waning immunity following the third (or booster) dose. Immunity also appears to wane faster in some populations, such as the elderly and immunocompromised people, who may also have a lower immune response to the vaccines.

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20. Third (booster) doses began to be administered in New Zealand from 29 November 2021, and therefore many people in the recommended groups are now, or soon will be, six months from receiving their third dose as we move through winter.

21. Data from the Omicron outbreak in New Zealand to date shows that hospitalisations and deaths have been higher in the groups recommended by CV-TAG to receive a fourth (second booster) dose. The highest mortality rates have been among those aged 65 years and over. Additionally, we know that Māori and Pacific peoples have been disproportionately affected in the current outbreak to date and are at greater risk of hospitalisation and severe disease from COVID-19, having respectively 2.5-fold and 3-fold higher odds of being hospitalised compared with non-Māori/non-Pacific peoples, and Māori are likely to spend 4.9 days longer in hospital.

22. Immunocompromised people and those with chronic conditions are also at increased risk of severe outcomes from COVID-19 and are more likely to be hospitalised.

23. The goal of the COVID-19 vaccination programme offering a fourth dose in New Zealand is to maintain the population protection already gained through COVID-19 vaccination and prevent severe disease cause by COVID-19. Fourth doses are critical now as we manage the additional risk of seasonal winter respiratory illnesses alongside the likely further COVID-19 spread throughout winter, and with modelling forecasting a second peak of cases during winter or early spring.

24. The BA.4 and BA.5 Omicron subvariants are now emerging in New Zealand and have a clear transmission advantage over the currently dominant BA.2. We therefore expect that as these new subvariants, which also exhibit significant immune escape, will add to case numbers and hospital admissions over winter.

25. Demand is already placing significant pressure on the health system, including both primary care and hospitals. COVID-19 and influenza are both contributing markedly to the overall burden, for example 50 percent of district health boards (DHBs) experienced inpatient occupancy of over 90 percent in recent weeks.

26. Despite the impact of other respiratory illnesses on the health system, COVID-19 continues to require targeted measures due to its substantially higher mortality rate compared to seasonal illnesses such as influenza, and the greater potential severity of its symptoms.

Safety and efficacy of a fourth dose

27. Data are limited on the safety and efficacy of a fourth dose in populations younger than 65 years of age, in healthy individuals, in people with social risk factors, and in pregnant people. This is because in most countries where fourth doses have been made available to date, they have been targeted older and at-risk population groups. Healthy young people (aged under 30) appear to produce a strong immune response to three doses and are considered to have continued good protection from adverse outcomes of COVID-19 infection.

28. A growing body of international evidence is emerging in the form of real world data from those at-risk populations who have already received a fourth dose.

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Effectiveness

29. Studies have shown that the relative vaccine effectiveness of a fourth dose in boosting immunity back to levels similar to those gained from a first booster dose is substantial and sustained against severe disease, hospitalisation and death but less so against infection. A fourth dose may recover the immunity lost from waning, which can provide an important boost over the winter months and during periods of surging infection.

Safety

30. CV TAG has considered the safety profile of fourth doses of the Pfizer vaccine. From the data available so far reported adverse reactions appear to be similar as for primary course and third doses – for most people mild – and more commonly reported in younger age groups than in those over 60 years of age.

31. The growth in the availability of real world data is contributing to studies such as a nationwide study undertaken by the University Hospital Southampton in the UK, published last month, that found fourth doses of the Pfizer COVID-19 vaccine are proving to be both safe and even more effective than third doses at boosting immunity against COVID-19.

Māori and Pacific peoples aged 50 years and over

32. There are important equity considerations in considering access to a fourth dose (second booster). CV-TAG has identified the groups that will most benefit from a fourth COVID-19 vaccination. These groups include Māori and Pacific peoples over 50 years of age.

33. Data from both the Delta and Omicron outbreaks have shown that Māori and Pacific peoples are at greater risk of COVID-19 hospitalisation and severe disease compared to non-Māori and are likely to spend 4.9 days longer in hospital. Māori and Pacific peoples are also more likely to live in multigenerational families and in overcrowded housing conditions, increasing the risk of transmission.

34. Delivery of fourth doses will increase protection against COVID-19 for Māori and Pacific peoples over 50 who are vaccinated. It has the potential to significantly reduce the number of hospitalisations and deaths in recommended groups, including for Māori and Pacific peoples, and to help manage the additional pressure on the health system during the winter season.

Older people over the age of 65 years old, residents (of any age) living in aged care and disability care facilities, and those severely immunocompromised

35. Many countries have begun delivering fourth doses to their elderly and at-risk populations. For example, in March 2022 fourth doses were rolled out in Australia to the following groups:

    a) those aged over-65 years,

    b) patients within residential aged care facilities,

    c) those severely immunocompromised

    d) Aboriginal and Torres Strait Islander people aged 50 and older

    e) people aged 16–64 with a wide range of comorbidities including cancer and diabetes (this group was added in May 2022).

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36. An early study from the delivery of fourth doses in Israel has shown that the risk of infection and severe illness appears to significantly reduce after a fourth dose (approximately 2 to 4 times less likely). The study has shown those aged 60 to 100 years old who have received a fourth dose of Pfizer, have had a 78 percent lower mortality rate from COVID-19 than those who only received a third dose.

People with medical conditions that increase the risk of severe breakthrough COVID-19 illness and those who live with disability with significant or complex health needs or multiple comorbidities

37. These groups have also been identified by CV-TAG as being at increased risk of severe outcomes from COVID-19 infection, with the potential to significantly benefit from a fourth dose to boost immunity through the winter months.

Additional information and factors for consideration

38. You have carefully considered the latest CV TAG advice and reviewed the summary of evidence in that advice. You have also reviewed: the latest data on New Zealand's Omicron Outbreak, including case numbers and patterns, hospitalisations and deaths and the trends in these; the latest modelling, which projects a further surge in cases through winter; recent whole genome sequencing (WGS) data showing the presence and growing contribution of the BA4 and BA5 Omicron subvariants; and the positions and recommendations of other jurisdictions, including the US CDC.

39. To capitalise on the strength of the protection afforded by a fourth dose (therapeutic value), making the vaccine available to additional groups would benefit both the individual and public from the risks of COVID-19:

- **People aged over 50 years**. Māori and Pacific people have a lower life expectancy and are disproportionally impacted by COVID-19, including poorer outcomes from a COVID-19 infection, so it is appropriate to recommend the vaccine for these groups and to strongly target vaccination delivery to them and other priority groups. In this case, ethnicity is being used as a marker of higher risk (just as age is for over 65s). Many people without pre-existing conditions in the age group 50 to 64 will be of similar risk. We note that the US CDC has now recommended a fourth dose for all people over 50 years, and a number of other countries also do (including South Africa, Chile – both in the Southern Hemisphere – and Denmark) .
- **Healthcare workers**. Currently healthcare workers are experiencing higher rates of infection of COVID-19 infection (1.6%) than border workers (1.1%) who are used as a proxy for the prevalence rate in the general population. This group works in an environment where they are in contact with at-risk people. A fourth dose will provide protection to the healthcare worker and help to preserve health service delivery during this high demand period. Also of note is that the evidence shows a reduction in likelihood of being infected with COVID-19 for at least a few weeks after a second booster dose, and some residual protection from infection beyond that. This will help to reduce the likelihood of health care workers becoming infected and potentially infecting vulnerable people in their care through winter. Due to the higher rates of myocarditis and pericarditis for individuals under 30 years following first and second Pfizer doses, it is not recommended health care

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workers under 30 years of age, who are not also in the other recommended groups, receive a fourth dose until further evidence emerges.

40. It is proposed that you agree to the following groups, in addition to those groups recommended by CV-TAG, to be eligible for a fourth dose of COVID-19 vaccine:

- All people over 50 years
- Healthcare workers 30 years and over.

41. In order to ensure that groups at the highest risk of an adverse outcome, and thus most likely to benefit from a second booster dose, the COVID-19 Vaccination Programme should strongly target efforts towards the population groups recommended by CV-TAG, whilst making it available to all people over age 50 and healthcare workers over 30 years of age.

Crown Law Advice (legally privileged)

s 9(2)(h)

Timing of receiving the fourth dose

46. CV-TAG recommends that the fourth dose should be offered six months after the third dose.

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47. This means a number of people in the target groups would already be eligible for and due a fourth dose, and many more will be due throughout July and into August and September 2022.

48. A fourth dose, if due, should be postponed for three months after COVID-19 infection. Clinical discretion can be applied when considering vaccination prior to three months after infection.

The need for a reduced interval for third doses

49. The new section also provides for the permanent reduction in the dose interval between the primary course and the third (booster) dose. Third (booster) doses (at the reduced three-month dose interval) were previously provided for under the Epidemic Preparedness (COVID-19 – Medicines Act 1981) Immediate Modification Order (IMO).

50. The IMO was a temporary measure and has been revoked with the intention that if this reduced booster interval is still required it can be provided for by a notice issued under new section 34A.

51. As we continue to manage a significant Omicron outbreak in New Zealand and expect a further surge in cases over winter as outlined above, the advice provided to Vaccine Ministers in February 2022 (attached) on the rationale for the reduction in the dose interval for third (or booster) doses to 3-months from completion of a primary course, remains relevant.

52. Nearly 2.7 million third (or booster) COVID-19 vaccine doses have been administered in New Zealand so far, many of those at the reduced 3-month dose interval (since completion of a primary course). Third doses have proven to be effective and safe, including when administered at the 3-month dose interval.

53. Since February, the international evidence has grown regarding vaccine effectiveness against the Omicron variant. The previous advice that COVID-19 vaccine effectiveness reduces more quickly against the Omicron variant than against Delta remains accurate.

54. Whilst the World Health Organisation has urged pharmaceutical companies to focus efforts on developing a longer lasting COVID-19 vaccine, the current vaccines remain our most important tool in the management of COVID-19 in New Zealand. As we head into winter, ensuring that those who are yet to receive their third (or booster) COVID-19 vaccine dose can do so at the reduced 3-month dose interval remains essential to help manage the ongoing outbreak through winter and beyond.

55. Alongside authorising fourth doses for the recommended groups at a 6-month dose interval (between third and fourth doses) the Notice also authorises the ongoing reduced dose interval for third (or booster) doses at 3-months since completion of a primary COVID-19 vaccine course.

56. The Ministry continues to advise that any vaccine dose that people are eligible for and due, be received 3 months after any infection with COVID-19, and guidance on this is set out on the Ministry website.

The Notice outlines

57. The attached Notice authorises the ongoing delivery of third (or booster) doses of the Pfizer COVID-19 vaccine at the reduced 3-months dose interval since completion of a primary COVID-19 vaccine course.

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58. A further Notice will be provided on Monday 27 June 2022 that sets out the authorisation for fourth doses of COVID-19 vaccines to the listed recommended groups.

Next steps

59. Should you agree to the recommendations below, please sign the attached Notice. Officials will ensure that the Notice is published on the Ministry's website and notified in the New Zealand Gazette and the changes will be communicated through the relevant channels. The Minister is also required to present the notice to the House of Representatives.

60. The COVID-19 Vaccination Programme will communicate the eligible groups for the fourth COVID-19 vaccine dose on Monday 27 June and begin delivery on Tuesday 28 June 2022.

Recommendations

It is recommended that you:

1.	note	the Medicines Amendment Act (No 2) 2022 commenced on 23 June 2022	Noted
2.	note	the amendment inserts a new section 34A that empowers the Director-General of Health to authorise, by Notice, the use of a consented COVID-19 vaccine otherwise than in accordance with the approved data sheet	Noted
3.	note	to issue a notice under new section 34A, as Director-General you: (a) must be satisfied that the proposed administration of the COVID-19 vaccine is an appropriate measure to manage the risks associated with the outbreak or spread of COVID-19; and (b) must have regard to the likely therapeutic value of the COVID-19 vaccine, and its risk (if any) of injuriously affecting the health of any person.	Noted
4.	note	as Director-General you can only use the power in section 34A in relation to COVID-19 vaccines that already have consent, or provisional consent, under section 20 or 23 of the Act	Noted
5.	note	you must also have regard to the likely therapeutic value of the COVID-19 vaccine, and its risk (if any) of injuriously affecting the health of any person	Noted
6.	note	CV-TAG's June 2022 advice, attached to this memo	Noted

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7.	note	CV-TAG has recommended the following groups receive a fourth dose of the Pfizer/BioNTech COVID-19 vaccine, at an interval of six months since their last dose of a COVID-19 vaccine: • people aged 65 years and over • Māori and Pacific peoples aged 50 years and over • residents of aged care and disability care facilities • severely immunocompromised people who received a three-dose primary course and a fourth dose as a first booster (noting this would be a fifth dose for these people) • people aged 16 years and over who have a medical condition that increases the risk of severe breakthrough COVID-19 illness (see Table 1 in appendix in attached CV TAG advice for expanded groups) • disabled people aged 16 years and over with significant or complex health needs or multiple comorbidities which increases the risk of poor outcomes from COVID-19	Noted
8.	agree	to include these groups in the Notice as being eligible for a fourth dose and to also include in the Notice the following groups as eligible for a fourth dose: • all people aged over 50 years • healthcare workers aged over 30 years	Yes
9.	note	individuals in the groups noted above at paragraph 12 are at increased risk of severe outcomes from COVID-19 infection, with the potential to significantly benefit from a fourth dose to boost immunity through the winter months.	Noted
10.	agree	you are satisfied that authorising the administration of fourth doses fourth doses of the Pfizer/BioNTech COVID-19 vaccine to anyone in groups noted above at paragraphs 12 and 40 at an interval of not less than six months since their last dose of a COVID-19 vaccine is an appropriate measure to manage the risks associated with an outbreak or spread of COVID-19	Yes
11.	agree	you are satisfied that the likely therapeutic value of a fourth dose to anyone in groups noted above at paragraphs 12 and 40 outweighs the risk, if any, of a fourth dose injuriously affecting the health of any person in those groups.	Yes

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12.	authorise	pursuant to section 34A of the Medicines Act 1981 the administration of fourth doses of the Pfizer/BioNTech COVID-19 vaccine to anyone in the groups noted above at paragraphs 12 and 40 at an interval of not less than six months since their last dose of a COVID-19 vaccine	Yes
13.	agree	that the COVID-19 Vaccination Programme target efforts to recommended high risk groups whilst making it available to healthcare workers over age 30 and all people over 50 years of age	Yes
14.	note	that any person or class of persons permitted by the Act or by regulations to administer the vaccine may administer the vaccine in accordance with the Notice	Noted
15.	note	section 5 of the Medicines Amendment Act 2022 revoked the Epidemic Preparedness (COVID-19 – Medicines Act 1981) Immediate Modification Order that allowed for the reduced (3-month) dose interval between the primary course and the third (booster) dose for anyone aged 18 years or older	Noted
16.	note	authorising a booster dose at a reduce interval is appropriate in the current COVID context as there are benefits in ensuring maximum immune protection over the winter period	Noted
17.	agree	you are satisfied that authorising the administration of third dose of the Pfizer/BioNTech COVID-19 vaccine to anyone aged 18 years or older at least three months after they had their second dose of the Pfizer/BioNTech COVID-19 vaccine is an appropriate measure to manage the risks associated with an outbreak or spread of COVID-19	Yes
18.	agree	you are satisfied that the likely therapeutic value of a third dose of the Pfizer/BioNTech COVID-19 vaccine to anyone aged 18 years or older at least three months after they had their second dose of the Pfizer/BioNTech COVID-19 vaccine outweighs the risk, if any, of a third dose at this reduced dose interval injuriously affecting the health of any person in those groups.	Yes
19.	authorise	pursuant to section 34A of the Medicines Act 1981, the administration of third doses of the Pfizer/BioNTech COVID-19 vaccine to anyone aged 18 years or old at an interval of not less than three-months since completion of a primary COVID-19 vaccination course, on the 23 June 2022.	Yes

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20.	approve and sign	the Notice attached in Appendix One which outlines the above proposed changes.	Yes
21	note	that a separate Notice providing the eligible groups will be provided for your signature on Monday 27 June 2022	Noted
22	note	that the COVID-19 Vaccination Programme will communicate the eligible groups for the fourth COVID-19 vaccine dose on Monday 27 June and begin delivery on Tuesday 28 June 2022	Noted

Signature

Date: 23 June 2022
Dr Ashley Bloomfield
Director-General of Health
Te Tumu Whakarae mō te Hauora

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Appendix One

Notice under Section 34A of the Medicines Act 1981 authorising off-label administration of COVID-19 Vaccine – interval between second and third doses

Pursuant to section 34A of the Medicines Act 1981, I, Dr Ashley Bloomfield, Director-General of Health, make this Notice.

A third dose of Pfizer/BioNTech (Comirnaty, Tozinameran, BNT162b2) vaccine may be administered to any person who—

a) is aged 18 years or older; and
b) received their second dose of the Pfizer/BioNTech (Comirnaty, Tozinameran, BNT162b2) vaccine at least 3 months before the date on which the third dose is administered to that person.

Dated this 23rd day of June 2022.

DR ASHLEY BLOOMFIELD, Director-General of Health.

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Explanatory note from the Ministry of Health:
This advice has since been updated to better reflect evidence about safety during pregnancy.

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

Second booster update: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	22 June 2022
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Astrid Koornneef, Director, National Immunisation Programme (NIP) Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Jim Miller, Acting Director of Public Health
From:	Dr Dan Bernal on behalf Dr Ian Town, Chief Science Advisor
For your:	Consideration

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Purpose of report

1. To provide COVID-19 Vaccine Technical Advisory Group's (CV TAG) advice on the science rationale, safety and peak body guidance on use of a second booster dose in:
    a. individuals with underlying health conditions that are likely to increase the individual's risk of adverse outcomes from COVID-19 and/or
    b. those aged over 50 years and/or
    c. extension of eligibility for a second booster dose to healthcare workers.

Background and context

2. On 8 November 2021 MedSafe updated the provisional approval for the Pfizer vaccine to state: *"a booster dose of Comirnaty may be administered intramuscularly at least 6 months after completion of the primary course in individuals aged 18 years of age and older"*.
3. On 17 June 2021 MedSafe further updated the provisional approval for the Pfizer vaccine to include *"A booster dose of Comirnaty may be given at least 6 months after the primary course for people 12 years of age and older"*.
4. Pfizer have not yet submitted an application to MedSafe for approval of any further doses.
5. On 01 February 2022, CV TAG recommended that a booster dose of the COVID-19 vaccine should be given sooner after the primary course to all eligible people aged 18 years and over, including immunocompromised individuals and pregnant persons.
6. The Ministry of Health provided advice to Cabinet and it was agreed that eligibility for a first booster dose would commence from 3 months after the second (or third primary) dose.
7. As cases of COVID-19 climb globally due to outbreaks of the Omicron variant, and evidence has emerged on the waning of protection, some jurisdictions have rolled out second booster

doses to populations who remain at highest risk of severe breakthrough disease despite receiving a first booster dose. Defining populations most at-risk of severe breakthrough COVID-19 differs across jurisdictions but includes people with various combinations of comorbidities, age and in a few jurisdictions, healthcare workers.

8. In discussion with the Prime Minister and other ministers, the Director-General of Health has requested a further update on the science rationale and safety of a second booster dose, in addition to advice provided by international peak bodies around guidance of second booster doses. The Director-General has also asked for advice on consideration of extending eligibility criteria of a second booster dose to anyone over 50, those with underlying health conditions, and healthcare workers.

9. CV TAG previously met on the 01 March and 22 March 2022 to discuss the waning of protection after first booster doses, and the need for second booster doses.

    a. CV TAG noted that:

        i. There is evidence of waning of protection following the first booster dose. Protection also appears to wane faster in some populations, e.g., the elderly. People with other health conditions or comorbidities are at an increased risk of poor outcomes also, and may have a lower immune response to vaccines, though evidence is still emerging on the need for a further dose.

        ii. Booster doses began to be administered from 29 November 2021, and therefore the numbers of people who are now four months from receiving their first booster dose, are steadily increasing in late June as we approach winter.

        iii. The influenza immunisation programme commenced in April, and there is a risk of increased burden on the healthcare system from what increasingly appears to be a record high influenza season from May 2022 with SARS-CoV-2 also circulating. Research from 305,000 people in hospital in the UK with COVID-19 between February 2020 and December 2021 found 6,965 people recorded as having another respiratory infection alongside COVID-19, 227 (3%) of which were influenza. The researchers estimated that people with COVID-19 and influenza combined were 2.4 times more likely to die and four times more likely to end up on a ventilator than if they only had COVID.[1]

        iv. Data on the reactogenicity, safety, immunogenicity, and efficacy of a second Pfizer booster dose is currently limited to three studies from Israel, which studied the immunogenicity and safety among healthcare workers and the elderly. A second booster of the Pfizer vaccine appears to be safe and effective at restoring protection against COVID-19, including Omicron but is a reactogenic vaccine, with 78.6% (95%CI: 71.2-84.8) of people who received a second booster dose reporting a local adverse event, and 42.9% (95%CI: 35-50.7) systemic adverse events. Most of these were mild and resolved quickly.

        v. Some countries have begun rolling out second booster doses, with intervals varying from four to six months after the first booster dose.

        vi. The goal of the COVID-19 vaccination programme and offering a second booster dose in New Zealand is to prevent severe disease caused by SARS-CoV-2.

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

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1. Māori and Pacific peoples have been disproportionately affected in the current outbreak.
2. Māori and Pacific peoples are at greater risk of COVID-19 hospitalisation and severe disease, having respectively a 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 [2, 3].
3. Māori and Pacific peoples are more likely to live in multigenerational families housing in overcrowded conditions, increasing the risk of transmission [4, 5].

viii. MedSafe are yet to approve the use of Pfizer as a second booster dose, and therefore these recommendations require MedSafe approval.

ix. Data is limited on the safety and efficacy of a second booster dose in populations younger than 65 years of age, in healthy individuals, in people with medical or social risk factors, and in pregnant people. Young people (aged under 30) produce a strong immune response to three doses, have a low baseline risk of severe disease and continue to be well protected.

b. CV TAG recommended that:

i. A second booster dose be offered to:

1. People aged 65 years and over
2. Māori and Pacific peoples aged 50 years and over
3. Residents of aged care and disability care facilities
4. Severely immunocompromised people who received a three-dose primary course and a fourth dose as a first booster (noting this is a fifth dose for these people).

ii. In general, the second booster dose should be offered from six months after a first booster dose. However, in the context of high influenza circulation and the need to also maximise influenza vaccine uptake, CV TAG believe it is appropriate to reduce the interval between the first and second booster doses to 4 months and allow COVID-19 vaccines to be given at the same time as the influenza vaccine. In this context, CV TAG also recommends bringing the age range eligibility for the funded influenza vaccine down to align with the age ranges recommended for the COVID-19 second booster vaccines.

iii. A second booster dose, if due, should be postponed for three months after SARS-CoV-2 infection. People can be advised that following infection after the first booster dose, protection is increased but clinical discretion can be applied when considering vaccination prior to 3 months after infection. This may be appropriate for those individuals at highest risk of severe disease from COVID-19 re-infection and impaired immune responses.

iv. The influenza, MMR, HPV, diphtheria/tetanus/pertussis combination vaccine (Boostrix), and other vaccines may be administered before, after, or at the same time as the Pfizer COVID-19 vaccine, without concern for the spacing of the vaccinations. The only exception to this advice is for the live-attenuated shingles

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vaccine (Zostavax) where a 7-day interval, before or after administering Pfizer COVID-19 vaccine, is advised.

Evidence informing advice

Waning of immunity after a first booster dose

10. Data from the United Kingdom and United States show that vaccine effectiveness (VE) against symptomatic infection and severe disease caused by Omicron wanes over time.

    a. There is significant global data to show that vaccine effectiveness (VE) against symptomatic infection and severe disease caused by COVID-19 wanes over time. Data from the UKHSA also shows that 2-4 weeks after a booster dose of the Pfizer vaccine, VE against symptomatic COVID-19 caused by Omicron is approximately 65% and moderately retains effectiveness with a VE of 45% from 10-14 weeks after the booster. [2]

    b. A CDC study found the VE for Pfizer against Omicron *hospitalisation* after three doses wanes from 91% (95% CI: 88–93) at ≤2 months to 78% (95% CI: 67–85) at ≥4 months.[6] This trend is broadly in line with the UK Health Security Agency (UKHSA), who found VE after three doses of Pfizer against *hospitalisation* wanes from 85-90% at 2-4 weeks to approximately 75% at 10-14 weeks (~2-3 months).[7]

11. *Pace of waning and at-risk groups:* A number of studies evaluating antibody titres have shown that protection does not wane at the same pace for everyone, and appears to wane faster for the elderly, and for some people with other health conditions their immune response to the vaccine is lower. [8-11]

    a. Immunogenicity data suggests that cancer, transplant, dialysis patients, and those on immunosuppressant therapy have a reduced response to a first dose of vaccine which can improve with a second dose,[12-19] although the response may still not be optimal, with both reduced antibody and T cell responses. [20-28]

    b. A (non-peer reviewed) study of antibody responses following the second dose of Pfizer has been conducted using data from the UK's national COVID-19 Infection Survey. This study found that antibody responses can last for over a year, though they declined more rapidly in older people, males, and those with underlying health conditions. The greatest antibody half-life was observed among those previously infected by SARS-CoV-2. [29]

Safety, reactogenicity and efficacy of a second booster dose

12. Data on the reactogenicity, safety, immunogenicity, and efficacy of a second booster dose are predominantly from studies conducted in Israel, with a small number recently published from the UK.

    a. Another study of Israeli healthcare workers aged 18 years and over evaluated a fourth dose of Pfizer or Moderna administered after three Pfizer doses. The study population were 1,050 eligible healthcare workers with no known history of SARS-CoV-2 infection, who received the third dose of Pfizer at least 4 months earlier.[30] Of 1050 eligible, 154 and 120 (274 total) were enrolled to receive Pfizer and Moderna, respectively, and compared to 426 age-matched controls. Primary endpoints were safety and immunogenicity, and secondary endpoints were vaccine efficacy in preventing SARS-CoV-2 infections and COVID-19 symptomatic disease. 18.3% (95% CI: 11.9-24.2%) of participants that received a Pfizer second booster had breakthrough infection compared

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with 25.0% (95% CI: 17.3-30.1%) of the control group who had only had three doses. In the majority of cases (65-72%) symptoms were mild (without fever of ≥38°C).[30]

b. A preprint prospective observational study comparing the short-term effects of the first and second Pfizer boosters, was conducted in Israel. A total of 2,019 participants aged from 19 to 89 years, with a median age of 52 years, were issued a smartwatch (to record physiological measurements) and filled in a daily questionnaire on systemic reactions to the vaccine. 30% (615 participants) received a second booster during the study period. Receivers of the second booster experienced a considerable increase in heart rate and heart rate variability-based stress within 48 hrs of administration. However, this was transient and returned to baseline levels after 72 hrs. Comparison to those that received the first booster, revealed no significant difference in physiological measures between the second and first booster. 67.7% of participants that received the second booster, did not report any symptoms which is comparable to the 65.8% after the first booster. The most frequently reported reactions (i.e., fatigue, headache, muscle pain, fever, and cold) were similar after the first and second booster doses. [31]

c. A study conducted in the UK as part of the COV-BOOST trial, evaluated the effect of a fourth dose of the Pfizer vaccine on participants aged 30 years or older. 31 participants had previously received three doses of Pfizer as part of the trial, with a median age of 67.2 years old, before receiving a fourth dose of Pfizer. The median interval between the third and fourth doses was 208 days (29.7 weeks). Anti-spike IgG concentrations increased 11-fold 14 days after the fourth dose, showing a strong antibody response to the fourth vaccine. Furthermore, similar T-cell responses were seen, suggesting that a fourth dose of the Pfizer vaccine provides a substantial boost to both humoral and cellular immunity. [32]

13. *Safety and Reactogenicity:* In the trial of healthcare workers, most adverse events (AEs) were reported as mild and resolved within 2 days post booster dose. No serious AEs or hospital admissions were reported. Active reporting of local AEs were common, and for Pfizer 78.6% (95% CI: 71.2-84.8) of second booster dose recipients reported an adverse event. Among Pfizer second booster dose recipients, more were reported by younger participants: 88% (95%CI: 80.6-95.3) compared with 69.6% (95% CI: 59.4-79.7) in those >60 years of age. Solicited systemic AEs were reported by 42.9% (95% CI: 35-50.7) of Pfizer second booster dose recipients. Systemic adverse events resolved within 2 days. The most common systemic AE reported was fatigue followed by myalgia and headache. Fever was relatively uncommon and usually resolved within 24-36 hours in either group. [30]

14. To date, no safety data have been reported separately (from first booster doses) for second booster doses. The most recent UK government report, with data to May 25th 2022 [33], states "review of third and booster dose reports does not raise any new safety concerns", and, in relation to myocarditis and pericarditis "the reports after booster doses are extremely rare and there is no indication that these events are more serious after boosters". [33] No data about safety of a second booster dose are available yet from the USA. Surveillance data for the first booster dose show "for myocarditis, the findings are consistent with those observed with primary series vaccination, but the risk appears to be lower following the first booster dose compared to dose 2 of primary series". [34]

15. There is particularly limited safety data on second boosters for those under the age of 30, with most safety and reactogenicity studies focusing on older age groups [32, 35]. It is also important to note that a smaller proportion of this age group are eligible for a second

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booster (given older populations worldwide have been prioritised for first booster uptake). Safety concerns remain high for those under the age of 30, given higher rates of myocarditis and pericarditis for younger age groups following the first and second Pfizer dose [36, 37].

16. *Effectiveness:* Almost all studies report second booster doses as vaccine effectiveness (VE) relative to a first booster dose only. Effectiveness of a second booster dose can therefore be interpreted as "there are x% fewer cases of infection/symptomatic infection/severe disease (as applicable) in those who received a second booster dose than in those who continued without this additional dose". All studies were conducted in the Omicron variant dominant period, and therefore reflect effectiveness against the Omicron variant.

17. Relative effectiveness of a second booster dose is substantial and sustained (within the period where data available) against severe disease, but shorter lived against infection:

    a. Severe disease

        i. Severe disease (e.g. oxygen saturation of <94%) with or without hospitalisation: Weekly estimates of relative VE between 58% and 77% from 2-6 weeks after second booster dose with no signs of waning by the 6th week. Adjusted rate of severe disease in the fourth week after the fourth dose was 1.6 cases per 100,000 person-days (95% CI: 1.2-2.0) compared to 5.5 (95% CI: 5.2-2.9) in the three-dose group. [38]

        ii. Hospitalisation: Relative VE 68% in first month (1-4 weeks after vaccination) which correlated to a risk reduction of 180.1 (95% CI: 142.8-211.9) hospitalisation events per 100,000 persons. [39] Second and third studies (which included deaths and hospitalisations) estimated relative VE at 78% 1-3 weeks after the second booster and at 87% 7-10 weeks after, [40] and 40% (time since second booster unclear). [41]

        iii. Death: Relative VE 76% in first month which correlated to a risk reduction of 23.4 (95% CI: 11.8-34.6) COVID-19-related deaths per 100,000 persons. [39]

        iv. Mechanical ventilation or death among those already hospitalised with COVID-19: Relative VE 49%. [42]

    b. Symptomatic infection

        i. Relative VE 43-55% in first month (approximately 1-4 weeks after vaccination) in 2 studies. [30, 39] Another study estimated relative at VE 31% (time since second booster unclear). [41]

    c. Infection

        i. Relative VE 30-45% in first month (7-30 days after vaccination) in 2 studies. [30, 39] Another study estimated relative at VE 19% (time since second booster unclear). [41]

        ii. Weekly estimates of relative VE between 33-50% in the period 2-6 weeks after the second booster, declining to 10% by 8 weeks in one study. [38] Another study estimated relative VE at 55-65% in the 2-6 weeks after the second booster with a decline to 22% by 10 weeks. [43]

18. *Limitations:* More data is required to understand the relative effectiveness of a second booster against infection and severe disease, as the sample sizes for many of these studies are small. Effectiveness estimates are significantly lower than efficacy against infection post-third (first booster) dose and suggest that current mRNA vaccines may produce a "peak"

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response after the third dose, but further doses may only recover the immunity lost over time owing to waning. Despite this, the second booster dose could be beneficial for people at higher risk of severe illness, particularly during periods of surge and rising infections, while emphasising the urgency of next generation development. [44]

19. *Equity considerations:* In addition to equity considerations outlined above (Para 8a vii), it is important to take into account the following factors for targeting younger age groups (those aged 50+) for Māori and Pacific populations:

    a. While New Zealand in general has an ageing population, the age structures for Māori and Pacific people are relatively young. Māori and Pacific people on average have a much lower life expectancy, compared to the rest of the New Zealand population. The average life expectancy at birth was 73.4 years for Māori males in 2017–2019, compared to 80.9 years for non-Māori males. [45]

    b. Māori and Pacific people face disproportionately higher levels of co-morbidities, and that these conditions have emerged at earlier ages, affecting both quality and quantity of life. [46]

    c. These disparities include, higher prevalence of conditions linked to exacerbating the impact of COVID-19, such as chronic pulmonary, liver or renal disease. [46]

    d. Lower access to healthcare, also results in many Māori and Pacific people with co-morbidities remaining undiagnosed.

20. Although the initial Omicron peak has passed, New Zealand is currently experiencing a 'long tail' of COVID-19, with risk of COVID-19 infection remaining high. Individuals that have previously reduced their social contact due to being at a higher risk of severe COVID-19, may be increasing their level of social contact due to a sense of lower risk and the peak having already occurred. It can be argued that the risk of COVID-19 infection is increasing, with a combination of waning immunity (due to being in excess of 3 months since prior booster), multiple variants circulating with higher immune escape and infectivity (i.e. BA.2.12.1, BA.4 and BA.5) and the potential of a further peak due to these variants.

International recommendations from peak bodies and rollout of second booster doses

21. Given the potential for waning immunity following a first booster, particularly against severe disease (as measured by hospitalisation), some countries have begun recommending the administration of a second booster dose to elderly populations or individuals at increased risk of severe disease or exposure.

    a. *Australia:* The Australian Technical Advisory Group on Immunisation (ATAGI) issued recommendations about second booster doses on 25 March 2022. ATAGI recommended an additional booster dose of COVID-19 vaccine to increase vaccine protection before winter for selected population groups who are at greatest risk of severe illness from COVID-19 and who have received their primary vaccination and first booster dose (link). These groups are:

        i. Adults aged 65 years and older

        ii. Residents of aged care or disability care facilities

        iii. People aged 16 years and older with severe immunocompromise (as defined in the ATAGI statement on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised)

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iv. Aboriginal and Torres Strait Islander people aged 50 years and older.

b. After continuing to review evidence on the need for other population groups, ATAGI recommended on 25 May 2022, a second booster dose for people at higher risk of severe illness from COVID-19, who have already had their first booster dose 4 months ago. (link)

c. The second booster is **additionally recommended** for people aged 16-64 of increased risk who have:

   i. A medical condition that increases the risk of severe breakthrough COVID-19 illness (see **Table 1** in appendix for expanded groups)

   ii. People with disability with significant or complex health needs or multiple comorbidities which increases risk of poor outcomes from COVID-19.

d. The following groups are currently **not recommended** to receive an additional booster dose:

   i. Healthy people aged 16 to 64 years, who do not have a risk factor for severe COVID-19, as their risk of severe illness after their first booster dose is likely to remain very low.

   ii. People from occupational groups, such as healthcare workers, who do not have any other comorbidity that increases their risk of severe COVID-19

   iii. Women who are pregnant without any other comorbidity that increases their risk of severe COVID-19.

e. *Australia*: Victorian Premier Daniel Andrews has signalled his intention to push the federal government to supply a fourth dose for all healthcare workers in hospitals across Victoria, following a recent spate of COVID-19 outbreaks in hospitals by infected staff. (link)

f. *Israel***:** In January 2022, Israel began administering a fourth dose of the Pfizer vaccine to people aged over 60 years and at-risk populations who had received a third dose at least 4 months earlier. An Israeli hospital is also conducting a trial of the second booster dose in healthcare workers. (link) Early data from Israel's rollout of a second booster dose is presented below. On 22 January 2022, Israel's vaccine advisory committee recommended that those aged 18 and over be offered a fourth vaccine dose at least five months after their third dose or after recovering from the disease. (link). Israel's Ministry of Health has since approved use of a fourth dose in healthcare workers and those who are at high risk of exposure to COVID-19 in their line of work. (link)

g. *UK***:** The Joint Committee on Vaccination and Immunisation (JCVI) has advised an additional spring booster dose be given for the most vulnerable individuals in the population. (link) As a precaution, a further booster dose is advised 6 months after the last vaccine dose for adults aged 75 years and over, older residents in a care home, and individuals aged 12 years and over who are immunosuppressed.

h. *Ireland*: Media reports have mentioned that the National Immunisation Advisory Committee (NIAC) is currently considering a second booster for those aged 65 and under, after advising in April that people aged over 65 and those who are immunocompromised should get their second booster dose. (link)

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i. *US*: Pfizer applied for authorisation to the US FDA on 15 March 2022 for adults 65 years and over, (link) and the US FDA has been reviewing data to authorise a second booster dose of vaccines from Pfizer and Moderna. (link) On 29 March 2022, the FDA authorised second boosters for peopled aged 50 and over, and immunocompromised people. (link)

j. *Europe:* According to a joint statement released by the European Medicines Agency and the European Center for Disease Prevention and Control, people over the age of 80 should receive a fourth booster dose of mRNA vaccine due to their weakened immune system, decreased response to vaccination, and increased risk of serious disease. (link)

k. *Spain:* Spain will offer a fourth dose of a COVID-19 vaccine to its entire population, most likely at the end of the year, Health Minister Carolina Darias said on June 16th 2022. (link)

l. *Chile*: Media reports have stated that from 7 February 2022, eligibility for a fourth dose will be extended to people aged over 55 years who had a third vaccine dose at least 6 months prior. (link) The fourth vaccine regimen has not been specified.

m. *Colombia:* Colombia's vaccine advisory committee recommended a second Covid-19 booster dose for people aged 12-49, but only under medical order. The second booster shot, or a fourth vaccine dose, is currently available for immunocompromised people, those with transplants and comorbidity, as well as seniors over 50 years old. (link)

n. *Hungary*: In January 2022, Hungary made a fourth COVID-19 vaccine shot available to people who ask for it, after a consultation with a doctor, to combat growing Omicron infections. (link)

o. *South Korea*: In February 2022, populations that are at increased risk of severe disease (the elderly and immunocompromised) or at increased risk of exposure (healthcare workers) became eligible for a fourth dose, however authorities are not currently considering expanding it more widely. (link)

p. *South Africa*: On 03 June 2022 the national health department announced that from 07 June 2022 all people over the age of 50 years are eligible to receive a second booster dose of Pfizer. (link)

Recommendations

22. CV TAG met on 21 June 2022 to update and further discuss their recommendations for second booster doses.

23. CV TAG noted:

    a. There is an increasing need for second boosters, given waning immunity from the first booster.

    b. There is limited data to date on the safety profile of the second booster, particularly among younger people

    c. The safety profile of the second booster appears similar to the safety profile of the first booster, providing no indication that there would be a different response, albeit based on relatively limited data to date.

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d. In consideration of risk-benefit of the second booster, and limited safety data, there is insufficient evidence for a broad recommendation of a second booster to:

   i. Young people (particularly those aged under 30 years) without comorbidities and

   ii. Healthy, pregnant women

e. Data on increased benefits from healthcare workers receiving a second booster remains marginal. There is no evidence within the available New Zealand data to suggest healthcare workers (particularly if young and without comorbidities), have a higher risk of acquiring and transmitting infection at their place of work.

f. In consideration of the updated ATAGI advice and limited international evidence, CVTAG defers any specific recommendation related to healthcare workers who do not otherwise meet the recommendations made here.

g. When compared to other COVID-19 vaccines, the Comirnaty (Pfizer) vaccines are better studied, especially in relation to safety, and effectiveness of second boosters.

h. Given the limited safety and effectiveness data, particularly for younger populations, CV TAG would not support any further mandates with regards to second boosters.

24. CV TAG recommended:

a. Maximising efforts to ensure that at-risk populations receive their first booster dose, as this remains the priority, as advised on 1 April 2022.

b. In accordance with ATAGI recommendations, and previously issued advice, a second booster dose be offered to:

   - People aged 65 years and over
   - Māori and Pacific peoples aged 50 years and over
   - Residents of aged care and disability care facilities
   - Severely immunocompromised people (people aged 12 years and older) who were eligible for and received a three-dose primary course, with the first booster as a fourth dose (noting this is a fifth dose for this group).

- That additional groups recommended to receive a second booster include people aged 16 years or older, who have:
  - A medical condition that increases the risk of severe breakthrough COVID-19 illness (see **Table 1** in appendix for expanded groups)
  - Disabled people with significant or complex health needs, or multiple comorbidities which increases the risk of poor outcomes from COVID-19.

c. A second booster dose is not recommended for healthy pregnant women (unless meeting criteria above).

d. The recommendations outlined above apply to all COVID-19 vaccines currently approved in New Zealand and in use within the National COVID-19 Vaccine and Immunisation Programme i.e. Comirnaty (Pfizer), Nuvaxovid (Novavax) and Vaxzevria (AstraZeneca). CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

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Dr Dan Bernal (Manager, Science and Technical Advisory, Deputy Chair CV TAG)

acting on behalf of

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

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References

1. Swets, M.C., et al., *SARS-CoV-2 co-infection with influenza viruses, respiratory syncytial virus, or adenoviruses.* The Lancet, 2022.
2. Steyn, N., Binny, R. N., Hannah, K., Hendy, S. C., James, A., Lustig, A., Ridings, K., Plank, M. J., Sporle, A., *Māori and Pacific people in New Zealand have a higher risk of hospitalisation for COVID-19.* New Zealand Medical Journal, 2021. **134**(1538).
3. Steyn, N., et al., *Estimated inequities in COVID-19 infection fatality rates by ethnicity for Aotearoa New Zealand.* New Zealand Medical Journal, 2020. **133**(1521): p. 28-39.
4. McLeod, M., et al., *COVID-19: we must not forget about Indigenous health and equity.* Australian and New Zealand Journal of Public Health, 2020. **44**(4): p. 253-256.
5. Johnson, A., P. Howden-Chapman, and S. Eaqub, *A stocktake of New Zealand's housing: February 2018*. 2018: Ministry of Business, Innovation and Employment (New Zealand).
6. Ferdinands, J.M., et al., *Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022.* MMWR. Morbidity and Mortality Weekly Report, 2022. **71**(7): p. 255-263.
7. UK Health Security Agency. *COVID-19 vaccine surveillance report, Week 7*. 17 February 2022; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1055620/Vaccine_surveillance_report_-_week_7.pdf.
8. Collier, D.A., et al., *Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2.* Nature, 2021.
9. Kontopoulou, K., et al., *Immunogenicity after the first dose of the BNT162b2 mRNA Covid-19 vaccine: real-world evidence from Greek healthcare workers.* Journal of Medical Microbiology, 2021. **70**(8).
10. Meyer, M., et al., *Humoral immune response after COVID-19 infection or BNT162b2 vaccine among older adults: evolution over time and protective thresholds*. 2021, Cold Spring Harbor Laboratory.
11. Tober-Lau, P., et al., *Long-term immunogenicity of BNT162b2 vaccination in the elderly and in younger health care workers*. 2021, Cold Spring Harbor Laboratory.
12. Benotmane, I., et al., *Weak anti-SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients.* Kidney Int, 2021.
13. Monin-Aldama, L., et al. *Interim results of the safety and immune-efficacy of 1 versus 2 doses of COVID-19 vaccine BNT162b2 for cancer patients in the context of the UK vaccine priority guidelines*. 17 March 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.03.17.21253131v1.
14. Goupil, R., et al. *Short-term antibody response and tolerability of one dose of BNT162b2 vaccine in patients receiving hemodialysis*. 1 April 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.03.30.21254652v1.
15. Kennedy, N.A., et al., *Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab.* Gut, 2021. **70**(5): p. 865-875.
16. Deepak, P., et al., *Glucocorticoids and B Cell Depleting Agents Substantially Impair Immunogenicity of mRNA Vaccines to SARS-CoV-2.* medRxiv, 2021.
17. Palich, R., et al., *Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients.* Ann Oncol, 2021.
18. Jerome, B., et al., *Impaired immunogenicity of BNT162b2 anti SARS-CoV-2 vaccine in patients treated for solid tumors.* Ann Oncol, 2021.

PROACTIVELY RELEASED

19. Weigert, A., et al., *Longitudinal analysis of antibody responses to the Pfizer BNT162b2 vaccine in Patients Undergoing Maintenance Hemodialysis*. 2021, Cold Spring Harbor Laboratory.
20. Tzarfati, K.H., et al., *BNT162b2 COVID-19 Vaccine is significantly less effective in patients with hematologic malignancies.* Am J Hematol doi: 10.1002/ajh.26284, 2021.
21. Prendecki, M., et al., *Comparison of humoral and cellular responses in kidney transplant recipients receiving BNT162b2 and ChAdOx1 SARS-CoV-2 vaccines*. 14th July 2021, Cold Spring Harbor Laboratory.
22. Clarke, C.L., et al., *Comparison of immunogenicity between BNT162b2 and ChAdOx1 SARS-CoV-2 vaccines in a large haemodialysis population*. 14th July 2021, Cold Spring Harbor Laboratory.
23. Whitaker, H., et al. *Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups* 9th July 2021; Available from: https://khub.net/documents/135939561/430986542/RCGP+VE+riskgroups+paper.pdf/a6b54cd9-419d-9b63-e2bf-5dc796f5a91f.
24. Espi, M., et al., *The ROMANOV study found impaired humoral and cellular immune responses to SARSCov-2 mRNA vaccine in virus unexposed patients receiving maintenance hemodialysis.* Kidney International, 2021.
25. Hadjadj, J., et al., *Immunogenicity of BNT162b2 vaccine Against the Alpha and Delta Variants in Immunocompromised Patients*. 9th August 2021, Cold Spring Harbor Laboratory.
26. Del Bello, A., et al., *Efficiency of a boost with a third dose of anti–SARS-CoV-2 messenger RNA–based vaccines in solid organ transplant recipients.* American Journal of Transplantation, 2021.
27. Labriola, L., et al., *Immunogenicity of BNT162b2 SARS-CoV-2 Vaccine in a Multicenter Cohort of Nursing Home Residents Receiving Maintenance Hemodialysis.* American Journal of Kidney Diseases, 2021.
28. Cotugno, N., et al., *HUMORAL AND CELLULAR IMMUNOGENICITY and SAFETY UP TO 4 MONTHS AFTER VACCINATION WITH BNT162B2 mRNA COVID-19 VACCINE IN HEART AND LUNG TRANSPLANTED YOUNG ADULTS*. 2021, Cold Spring Harbor Laboratory.
29. Wei, J., et al., *Antibody responses to SARS-CoV-2 vaccines in 45,965 adults from the general population of the United Kingdom.* Nature Microbiology, 2021.
30. Regev-Yochay, G., et al. *4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC*. medRxiv 2022; 2022.02.15.22270948]. Available from: http://medrxiv.org/content/early/2022/02/15/2022.02.15.22270948.abstract.
31. Yechezkel, M., et al., *Safety of the fourth COVID-19 BNT162b2 mRNA (second booster) vaccine.* medRxiv, 2022: p. 2022.06.07.22276117.
32. Munro, A.P.S., et al., *Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (COV-BOOST): a multicentre, blinded, phase 2, randomised trial.* Lancet Infect Dis, 2022.
33. Medicines and Healthcare products Regulatory Agency. *Coronavirus Vaccines Summary of Yellow Card reporting*. 01 June 2022; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1080316/Coronavirus_vaccine_-_summary_of_Yellow_Card_reporting_DLP_25.05.2022.pdf.
34. Nicola Klein and Tom Shimabukuro. *Safety update of 1st booster mRNA COVID-19 vaccination*. 20 April 2022; Available from:

PROACTIVELY RELEASED

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-04-20/03-COVID-Klein-Shimabukuro-508.pdf.
35. Bar-On, Y.M., et al. *Protection by 4th dose of BNT162b2 against Omicron in Israel*. medRxiv 2022; 2022.02.01.22270232]. Available from: http://medrxiv.org/content/early/2022/02/01/2022.02.01.22270232.abstract.
36. Su, J.R. *Myopericarditis following COVID-19 vaccination: Updates from the Vaccine Adverse Event Reporting System (VAERS)*. August 30, 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/03-COVID-Su-508.pdf.
37. Mevorach, D., et al., *Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel.* New England Journal of Medicine, 2021.
38. Bar-On, Y.M., et al., *Protection by a Fourth Dose of BNT162b2 against Omicron in Israel.* N Engl J Med, 2022. **386**(18): p. 1712-1720.
39. Magen, O., et al., *Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting.* N Engl J Med, 2022. **386**(17): p. 1603-1614.
40. Gazit, S., et al., *Relative Effectiveness of Four Doses Compared to Three Dose of the BNT162b2 Vaccine in Israel.* medRxiv, 2022: p. 2022.03.24.22272835.
41. Grewal, R., et al. *Effectiveness of a Fourth Dose of COVID-19 Vaccine among Long-Term Care Residents in Ontario, Canada: Test-Negative Design Study*. 1 June 2022; Available from: https://www.medrxiv.org/content/10.1101/2022.04.15.22273846v2.full.pdf.
42. Brosh-Nissimov, T., et al. *Hospitalized patients with severe COVID-19 during the Omicron wave in Israel - benefits of a fourth vaccine dose*. medRxiv 2022; 2022.04.24.22274237]. Available from: http://medrxiv.org/content/early/2022/04/27/2022.04.24.22274237.abstract.
43. Gazit, S., et al., *Short term, relative effectiveness of four doses versus three doses of BNT162b2 vaccine in people aged 60 years and older in Israel: retrospective, test negative, case-control study.* BMJ, 2022. **377**: p. e071113.
44. Mallapaty, S. *Fourth dose of COVID vaccine offers only slight boost against Omicron infection*. Nature 2022 23 February [cited 2022 25 February]; Available from: https://www.nature.com/articles/d41586-022-00486-9.
45. Statistics NZ. *Growth in life expectancy slows*. 2021 21/06/2022]; Available from: https://www.stats.govt.nz/news/growth-in-life-expectancy-slows.
46. Gurney, J., J. Stanley, and D. Sarfati *The inequity of morbidity: Disparities in the prevalence of morbidity between ethnic groups in New Zealand*. Journal of Comorbidity, 2020. **10**, 2235042X20971168 DOI: 10.1177/2235042x20971168.

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Appendix

Table 1: ATAGI - Additional groups recommended for a winter booster dose as of 25 May 2022

People in these groups are likely to have an ongoing increased risk of severe COVID-19 even after primary vaccination. These examples are not exhaustive, and providers may include individuals with conditions similar to those listed below, based on clinical judgment

Category	**Examples**
Immunocompromising conditions	
Cancer	Non-haematological cancer including those diagnosed within the past 5 years or on chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy (active treatment or recently completed) or with advanced disease regardless of treatment. Survivors of childhood cancer.
Chronic inflammatory conditions requiring medical treatment with disease modifying anti-rheumatic drugs (DMARDs) or immune-suppressive or immunomodulatory therapies.	Systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, ulcerative colitis, and similar who are being treated.
Chronic lung disease	Chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and severe asthma (defined as requiring frequent hospital visits or the use of multiple medications).
Chronic liver disease	Cirrhosis, autoimmune hepatitis, non-alcoholic fatty liver disease, alcoholic liver disease.
Severe chronic kidney disease (stage 4 or 5)	
Chronic neurological disease	Stroke, neurodegenerative disease (e.g dementia, motor neurone disease, Parkinson's disease), myasthenia gravis, multiple sclerosis, cerebral palsy, myopathies, paralytic syndromes, epilepsy.
Diabetes mellitus requiring medication	
Chronic cardiac disease	Ischaemic heart disease, valvular heart disease, congestive cardiac failure, cardiomyopathies, poorly controlled hypertension, pulmonary hypertension, complex congenital heart disease.
People with disability with significant or complex health needs or multiple comorbidities which increase risk of poor outcome from COVID-19	Particularly those with trisomy 21 (Down Syndrome) or complex multi-system disorders.
Severe obesity with BMI ≥ 40 kg/m^2	
Severe underweight with BMI < 16.5 kg/m^2	

PROACTIVELY RELEASED