Memo

Priority groups for vaccination among 12- to 15-year-olds: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations on the use of the Pfizer vaccine

Date:	4 August 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
Cc:	Dr Ashley Bloomfield, Director-General of Health Maree Roberts, DDG, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on priority groups for Pfizer mRNA COVID-19 vaccination among 12- to 15-year-olds.

Context

2. In June, CV TAG advice was sought for the use of the Pfizer mRNA COVID-19 vaccine for children aged 12 to 15 years, following the provisional approval for use in this age group by Medsafe.
3. At that time, CV TAG recommended that the rollout continue to focus on the existing population groups aged 16 years and over, and that any decision to use the COVID-19 vaccine in the 12- to 15-year-old age group should reflect that priority.
4. Generally, children have a lower risk of poor health outcomes from COVID-19 than adults. Internationally, a number of peak bodies, such as the US CDC, recommend that everyone 12 years and over should be vaccinated to help protect against COVID-19, in the context of widespread community transmission in the US.[1]
5. In Australia, the TGA has approved the Pfizer COVID-19 vaccine for ages 12 to 15 years.[2] On 2 August 2021, the Australian Technical Advisory Group on Immunisation (ATAGI) provided recommendations for vaccinating adolescents and children aged 12 to 15 years. ATAGI recommended that 12- to 15-year olds with specified medical conditions that increase their risk of severe COVID-19 be prioritised for vaccination (these conditions included asthma, diabetes, obesity, cardiac and circulatory congenital anomalies, neuro-developmental disorders, epilepsy, immunocompromised individuals, and trisomy). Aboriginal and Torres Strait Islanders aged 12 to 15 years were also prioritised, as well as all adolescents and

children aged 12 to 15 years in remote communities. ATAGI deferred a decision on whether to vaccinate all 12 to 15 year olds, and they expect to make that decision in the coming months.

6. In late 2020, the UK's Joint Committee on Vaccination and Immunisation (JCVI) advised that only children at very high risk of exposure and serious outcomes, such as those with severe neuro-disabilities in residential care, should be offered vaccination.[2] On 19 July 2021, the JCVI issued an update to their advice, stating that "*At the current time, children 12 to 15 years of age with severe neuro-disabilities, Down's syndrome, underlying conditions resulting in immunosuppression, and those with profound and multiple learning disabilities (PMLD)…, severe learning disabilities or who are on the learning disability register are considered at increased risk for serious COVID-19 disease and should be offered COVID-19 vaccination*".[4]

7. Furthermore, JVCI recommended that vaccination be offered to children and young people who have immunocompromised people in their household: "*JCVI advises that children and young people aged 12 years and over who are household contacts of persons (adults or children) who are immunosuppressed should be offered COVID-19 vaccination on the understanding that the main benefits from vaccination are related to the potential for indirect protection of their household contact who is immunosuppressed*."[4] The recommendations from JVCI were made in the context of widespread community transmission.

8. Additionally, a North American study has found that 83% (40/48) of children in intensive care with COVID-19 had co-morbidities.[5] These were mostly "medically complex" (including long-term dependence on technological support, such as tracheostomy), immunosuppression/ malignancy, or obesity.

9. The Ministry's Policy team sought clinical and scientific advice from CV TAG on the use of the Pfizer COVID-19 vaccine for priority groups who are 12 to 15 years of age. This advice will be considered as part of the Decision to Use Framework and alongside policy considerations on the sequencing of the COVID-19 Immunisation Programme.

Recommendations

10. CV TAG met on 20 July, 27 July, and 3 August 2021 to discuss the use of the Pfizer COVID-19 vaccine in priority groups among 12- to 15-year-olds, within the COVID-19 Immunisation Programme.

11. **CV TAG noted that:**
    a. Aotearoa New Zealand's focus in the sequencing approach is on coverage of those most at risk of COVID-19 i.e., personal protection of individuals that may be more likely to be exposed to COVID-19 or experience severe health outcomes.

    b. The current recommendations are made in the context of the very low prevalence of COVID-19 in Aotearoa New Zealand. The recommendations may need to be reviewed in the event of new community transmission or outbreaks in Aotearoa New Zealand.

12. **CV TAG recommends that:**
    a. Children and young people aged 12 to 15 years should be vaccinated if they are at high risk of severe outcomes from COVID-19. Those at high risk include 12- to 15-year-olds with severe neuro-disabilities that require residential care, and those who

are about to undergo long-term immunosuppression, such as solid organ transplant candidates prior to transplant.

b. Children and young people aged 12 to 15 years who are household contacts of persons (adults or children) who are immunosuppressed should be offered vaccination noting that the main benefits from vaccination are related to the potential for indirect protection of their household contact who is immunosuppressed.

c. As part of outbreak management, vaccination should be offered to 12- to 15-year-olds in the affected area.

d. The COVID-19 vaccine should not be routinely administered to children and young people aged 12 to 15 years of age, at this time. Children and young people have a low risk of severe disease or death due to COVID-19 compared to adults, and, given the low prevalence of SARS-CoV-2 infection in Aotearoa New Zealand, there is currently a low risk of exposure.

e. CV TAG will make recommendations for use in all children in the 12 to 15 years age group at a later date, following a review of emerging information on several issues including:

    i. the safety and effectiveness of COVID-19 vaccines in adolescents as observed in overseas vaccination programmes;

    ii. the incidence, risk factors and outcomes of cases of myocarditis after receiving the Pfizer vaccine in this age group.

    iii. the updated advice from peak bodies internationally, including the updated advice from ATAGI on vaccinating children expected in the coming months.

f. Consideration should be given to equity and whānau-based approaches and ensuring that other childhood immunisation programmes are not compromised, e.g., measles and HPV vaccination.

13. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence and peak body recommendations become available.

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

References

1. COVID-19 Vaccines for Children and Teens. 23 July 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/adolescents.html#:~:text=CDC%20recommends%20everyone%2012%20years,did%20prior%20to%20the%20pandemic.
2. TGA approves Pfizer COVID-19 vaccine for 12 to 15-year-olds. 23 July 2021. https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/tga-approves-pfizer-covid-19-vaccine-for-12-to-15-year-olds
3. ATAGI statement regarding vaccination of adolescents aged 12–15 years: A statement from the Australian Technical Advisory Group on Immunisation (ATAGI) regarding vaccination of adolescents aged 12-15 years. 02 August 2021, https://www.health.gov.au/news/atagi-statement-regarding-vaccination-of-adolescents-aged-12-15-years
4. Joint Committee on Vaccination and Immunisation. Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination. 30 December 2020. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950113/jcvi-advice-on-priority-groups-for-covid-19-vaccination-30-dec-2020-revised.pdf
5. Public Health England. JCVI issues advice on COVID-19 vaccination of children and young people. 19 July 2021. https://www.gov.uk/government/publications/covid-19-vaccination-of-children-and-young-people-aged-12-to-17-years-jcvi-statement/jvci-statement-on-covid-19-vaccination-of-children-and-young-people-aged-12-to-17-years-15-july-2021
6. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. JAMA Pediatr 2020; 174(9): 868-73.

Memo

The use of COVID-19 vaccines during an outbreak: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations for prioritisation of first doses nationwide

Date:	20 August 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine and Immunisation Programme
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's recommendations on the use of COVID-19 vaccines during an outbreak, endorsing the prioritisation of vaccination capacity nationwide to allow the maximum number of people to receive at least a single dose of the Pfizer COVID-19 vaccine.

Context

2. On 19 May 2021, CV TAG provided advice on the use of the Pfizer/BioNTech (Comirnaty) COVID-19 vaccine in an outbreak. The recommendations were:

    - *The characteristics of the Pfizer/BioNTech (Comirnaty) COVID-19 vaccine mean that it cannot be used in the traditional sense of ring vaccination. However, targeted vaccination can be used to encourage 'community confidence' and increased uptake of the vaccine.*
    - *Any targeted vaccination should be implemented alongside other public health measures and not as a standalone measure. A protocol should be developed and ready for implementation if we have an outbreak.*
    - *There is no international data on using the COVID-19 vaccine for targeted vaccination to inform what the trigger point would be for deploying this strategy. The situation in New Zealand means that there may be an opportunity to gain some experience should it be necessary to deploy such a measure.*
    - *There will be communities with low vaccine coverage, and we will need a protocol to ensure increased coverage while maintaining equity in an outbreak setting. The process of progressively relaxing controls at the border may lead to potential outbreaks in some communities.*

3. Currently, New Zealand is at Alert Level 4, indicating COVID-19 is not contained, with a significant number of cases of community transmission in Auckland. Cases have also emerged in Wellington, linked to the Auckland cluster.

4. Demand for vaccinations is high, and there are concerns that at risk groups – such as essential workers – may not able to access vaccination in a timely manner.

5. There are also concerns that the ability to access vaccinations may be disproportionately difficult for some members of the population, and that this may worsen existing inequities in vaccine coverage, with consequences for the risk of transmission and infection in some communities.

6. The COVID-19 Vaccine and Immunisation Programme (CVIP) sought clinical and scientific advice from CV TAG on the use of the Pfizer COVID-19 vaccine in an outbreak.

Recommendations

7. CV TAG noted that:

    a. One dose of the Pfizer COVID-19 vaccine provides good protection against severe disease and hospitalisation.

    b. Two doses of the Pfizer COVID-19 vaccine are needed to fully protect against infection, and vaccine efficacy is lower in immunocompromised groups. Therefore it is important that immunocompromised groups and those in groups 1, 2 and 3 receive two doses.

    c. There is growing evidence that longer intervals between doses are not inferior, and may provide a better immune response, further supporting decisions to delay second doses.

8. CV-TAG endorses the following approach for the Pfizer COVID-19 vaccine:

    a. All capacity nationwide is used to prioritise:

        i. The two-dose course for Groups 1, 2 and 3 of the sequencing framework, including children 12 years of age and

        ii. A single dose for Group 4 including children 12 years of age and over.

    b. Māori and Pacific peoples should be urgently prioritised within all groups due to increased risk of infection, severe disease, and low current vaccination coverage.

9. This approach will apply for this current outbreak and will be kept under regular review or on request from CVIP.

Dr Ian Town

Chief Science Advisor

Chair, CV TAG

Memo

Coadministration of the COVID-19 vaccine with other vaccines, including the MMR and influenza vaccines: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	27 August 2021
To:	Joanne Gibbs, National Director Operations, COVID-19 Vaccine and Immunisation Programme Grant Pollard, Group Manager, Child & Community Health Kath Blair, Manager, Immunisation, Child & Community Health Jo Boyle, Senior Advisor, Immunisation, Child & Community Health
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 for coadministration of the Pfizer COVID-19 vaccine with the MMR, influenza, and other vaccines.

Context

2. On 02 March 2021, CV TAG considered the concomitant delivery of the Pfizer COVID-19 vaccine with other vaccines. Overall, CV TAG agreed with the following recommendations proposed by the Immunisation Advisory Centre (IMAC):[1]

    a. For the Influenza vaccine:

        i. The COVID-19 mRNA vaccine should take priority over influenza vaccine.

        ii. Ideally, the influenza vaccine can be administered two weeks before or after the COVID-19 vaccine.

        iii. Do not delay either vaccination if it is not practical to leave a space.

    b. For the MMR vaccine:

        i. It is advised to leave a four-week gap after a live vaccine (such as the MMR vaccine) before giving the COVID-19 vaccine.

        ii. Allow a two-week gap after COVID-19 vaccine and having another vaccine, including the MMR vaccine.

c. Note that there are no clinical safety concerns should the gap between vaccines be less than the recommendations above. Do not delay vaccination if such a gap is not possible.

d. The MMR and influenza vaccines can be given at the same time.

3. The current recommendations provided publicly on the Ministry of Health webpage (updated on 28 July 2021)[2] are summarized below:

a. Allow at least two weeks between the COVID-19 vaccine and the influenza vaccine, i.e., get the influenza vaccine from two weeks after the second dose of the COVID-19 vaccine, or get the first COVID-19 vaccination from two weeks after the influenza vaccine.

b. If you get the COVID-19 vaccine first, wait at least two weeks after the second dose before you get the MMR vaccine

c. If you get the MMR vaccine first, wait at least four weeks before you get the first dose of the COVID-19 vaccine.

4. There is limited clinical trial or observational evidence regarding the safety, immunogenicity, or efficacy of coadministration of live or non-live vaccines with COVID-19 vaccines. One trial has reported preliminary results evaluating the coadministration of the Novavax COVID-19 and an influenza vaccine; however, the results of this study are of limited relevance as the Pfizer COVID-19 vaccine uses mRNA technology, which is different to the protein-subunit technology used in the Novavax vaccine.[3]

5. Two trials are underway investigating coadministration of the Pfizer COVID-19 vaccine and influenza vaccines, but no data are available yet. There are no trials that we are aware of evaluating the coadministration of the Janssen and AstraZeneca COVID-19 vaccines with other vaccines.[4, 5]

6. Current recommendations and advice from peak bodies are based on immunological principles and knowledge of existing vaccines. These recommendations are outlined in the table below.

Organisation	**Recommendation for coadministration of a COVID-19 vaccine with MMR, influenza, or other vaccines**
United States Centers for Disease Control (US CDC)[6]	Coadministration of COVID-19 vaccine and other vaccines on the same day, as well as administration of other vaccines within 14 days. Recommendation includes live virus vaccines
The World Health Organization (WHO)[7]	Minimum interval of 14 days between vaccines

Australian Technical Advisory Group on Immunisation (ATAGI)[8]	Minimum interval of 7 days unless there is an increased risk of vaccine-preventable diseases
Public Health England (PHE)[9]	Administering other vaccines or COVID-19 vaccines should not be delayed in relation to each other with the exception of the live-attenuated zoster vaccine for shingles (Zostavax), where a 7-day interval should be implemented

7. One dose of live-attenuated zoster vaccine (Zostavax) is indicated for the prevention of shingles in New Zealand. Recommendations from IMAC for Zostavax include:[10, 11]
    a. One Zostavax is recommended for adults aged 65 years to under 81 years.
    b. Zostavax and influenza vaccine can be administered at the same visit.
    c. This vaccine contains a weakened form of the varicella-zoster virus, and as a live viral vaccine, is not suitable for some people with medical conditions or who are receiving treatments that affect their immune system.
8. Some DHBs have recently expressed their concerns to IMAC about the impact of the COVID-19 vaccine rollout on the MMR, HPV, and Boostrix (diphtheria, tetanus and pertussis) campaigns. Vaccine coverage is being impacted by the current recommendations on coadministration with the COVID-19 vaccine, because young people have had to defer their vaccination due to upcoming bookings for a COVID-19 vaccine or because they have recently received the COVID-19 vaccine.[12]
9. The Child and Community Health Group in the Ministry is seeking CV TAG advice on whether the current recommendations on the spacing of the COVID-19 vaccine with other vaccines can be updated to improve vaccine coverage.

Recommendations

10. CV TAG met on 17 August 2021 to discuss and provide updated recommendations about the coadministration of the Pfizer COVID-19 vaccine and the MMR, influenza, and other vaccines.
11. **CV TAG noted that:**
    a. There are limited clinical trial, observational, or laboratory data on the safety and immunogenicity associated with the coadministration of the Pfizer COVID-19 vaccine and other vaccines.
    b. Based on first principles, there is the potential for a reduced immune response when two different types of vaccine are administered together or within several days of each other. However, there are no additional safety concerns associated with coadministration, over and above each vaccine's individual safety profile.

c. Older individuals that are administered the live-attenuated zoster vaccine (Zostavax) and the Pfizer COVID-19 vaccine at the same time could potentially have a reduced immune response to one or both of the vaccines.

d. Given that the catch-up campaigns for MMR, HPV, and Boostrix are largely among younger age groups, and that these individuals are likely to have a robust immune response, younger age groups are less likely to be adversely impacted by coadministration of vaccines.

e. Younger age groups have lower vaccination rates compared to others. Any obstacles to accessing and completing vaccinations should be removed and steps should be taken to encourage completion of the recommended vaccine schedules.

f. In general, the risk of reduced immune protection from coadministration of the Pfizer COVID-19 vaccine and other vaccines is low in younger age groups, while the public health benefit gained from higher vaccine coverage is substantial.

12. **CV TAG recommends that:**

a. 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.

b. The only exception to this advice is for the live-attenuated shingles vaccine (Zostavax) where a 7-day interval, before or after administering Pfizer COVID-19 vaccine, is advised.

13. CV TAG will continue to monitor the evidence and will update their recommendations as data become available.

Dr Ian Town

Chief Science Advisor

Chair, CV TAG

References

1. The Immunisation Advisory Centre (IMAC). *Spacing of vaccinations*. 10 August 2021]; Available from: https://covid.immune.org.nz/spacing-vaccinations.
2. Ministry of Health New Zealand. *COVID-19: Getting other vaccines*. 28 July 2021 10 August 2021]; Available from: https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-getting-vaccine/covid-19-getting-other-vaccines.
3. Toback, S., et al., *Safety, Immunogenicity, and Efficacy of a COVID-19 Vaccine (NVX-CoV2373) Co-administered With Seasonal Influenza Vaccines*. medRxiv, 2021: p. 2021.06.09.21258556.
4. *Combining influenza and COVID-19 vaccination (ComFluCOV) study*. 30 March 2021; Available from: https://doi.org/10.1186/ISRCTN14391248.
5. *Safety and Immunogenicity Study of 20vPnC When Coadministered With a Booster Dose of BNT162b2*. 2021; Available from: https://clinicaltrials.gov/ct2/show/NCT04887948?term=20vPnC&draw=2&rank=3.
6. Centers for Disease Control and Prevention (CDC). *Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States: Coadministration with other vaccines*. 16 July 2021 [cited 2021 27 July]; Available from: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Coadministration.
7. World Health Organisation. *Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing*. 15 June 2021 [cited 2021 27 July]; Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1.
8. Australian Technical Advisory Group on Immunisation (ATAGI). *Clinical guidance on use of COVID-19 vaccine in Australia in 2021 (v5.1)*. 17 June 2021 [cited 2021 27 July]; Available from: https://www.health.gov.au/sites/default/files/documents/2021/07/covid-19-vaccination-atagi-clinical-guidance-on-covid-19-vaccine-in-australia-in-2021.pdf.
9. Public Health England (PHE). *COVID-19 vaccination: information for healthcare practitioners Version 3.9*. Guidance for healthcare practitioners about the coronavirus (COVID-19) vaccination programme 6 July 2021 [cited 2021 27 July]; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/999527/COVID-19_vaccination_programme_guidance_for_healthcare_workers_6July2021_v3.9.pdf.
10. The Immunisation Advisory Centre (IMAC). *Zostavax*. February 2021 32 August 2021]; Available from: https://www.immune.org.nz/vaccines/available-vaccines/zostavax.
11. IMAC. *Zostavax resources for health professionals*. 2021 February 2021 [cited 2021 23 August 2021]; Available from: https://www.immune.org.nz/zostavax-health-professionals.
12. Auckland & Waitematā DHBs, *Communications between IMAC coordinators and DHBs*.

Memo

Guidance for the potential use of an extension/third dose in the context of a missed vaccination incident

Date:	6 September 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
Copy to:	Juliet Rumball-Smith, Chief Clinical Advisor, COVID-19 Immunisation, Testing and Supply
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To provide guidance for clinical decision-making around offering an extension/third dose in the context of a missed vaccination incident, including specific advice about those who are immunocompromised.

Background and context

2. A 'missed vaccination incident' is an incident whereby Dose 1 or Dose 2 of a two-dose regimen COVID-19 vaccine has been administered to a consumer, which has resulted in confirmed or suspected complete or partial underdosing of the COVID-19 vaccine.
3. An 'extension dose' is the term used to define an additional COVID-19 vaccination that occurs following a two-dose COVID-19 vaccination course, of which Dose 1 or Dose 2 is a missed vaccination incident.
4. A missed vaccination incident on 12 July 2021 at the Highbrook vaccination site has highlighted the challenges in decision making for an extension dose of the Comirnaty (Pfizer/BioNTech) COVID-19 vaccine. At Highbrook, 5 out of 732 consumers were possibly vaccinated with a low vaccine dose or saline, with the error being identified during vial reconciliation, late in the day.
5. Given the nature of the COVID-19 Vaccine Immunisation Programme, despite mitigating measures, similar incidents will still occur from time to time.
6. A Request for Advice (RFA) conducted by the Science & Technical Advisory team, finalised on 25 August 2021, outlines the current best evidence regarding a third dose.
7. Currently there is very limited information available on the safety profile of a third dose of the Pfizer vaccine.

8. The Pfizer vaccine has been provisionally approved in New Zealand on the basis that two doses, not three, would be administered to a consumer. Accordingly, a third dose can be prescribed with informed consent as it is a provisionally approved medicine for an unapproved indication.

9. The decision for an extension dose should be a fully informed process, including a risk and benefit discussion with the affected consumer, via the clinician(s) responsible, that considers an individual's clinical characteristics as well as the risk of their exposure to COVID-19. The management plan should be personalised to the individual consumer. It is recommended that informed consent to a third dose of the vaccine is given in writing by the affected consumer.

10. Where there are large numbers of consumers involved, it is helpful to offer guidance for clinicians to develop group-level management plans.

11. This guidance applies only to the two-dose Comirnaty (Pfizer/BioNTech) COVID-19 vaccine.

Clinical management considerations

12. Prior to Delta, vaccine effectiveness (VE) for a single dose of Pfizer was between 49% and 65% for all PCR-confirmed infection/symptomatic COVID-19, and 81-93% against severe disease (up to 90 days after the single dose - the limit of available data). For Delta, VE against PCR-confirmed infection/symptomatic COVID-19 ranges from 35.6-64.2% at least 14-21 days after the first dose, whereas VE against severe disease/hospitalisation is significantly higher at 78-94%, noting that the highest estimate is from the smallest study, and definitions of severe disease varied somewhat between studies.

13. In general, serological testing is not recommended to determine responses to vaccination. This is because there is as yet no threshold antibody level to determine if a consumer is protected or not and even if there was, this would only apply to one point in time (see FDA recommendation[1]).

14. However, serology may be helpful for individual consumers potentially affected by a Dose 1 incident, because almost all immunocompetent people develop anti-spike antibodies detectable by assays commercially available in New Zealand more than 14 days after Dose 1. In the majority of the country, it is unlikely that antibody presence would be due to prior COVID-19 infection, so detectable antibody post Dose 1 would be presumptive evidence that the consumer had received the vaccine.

15. The RFA (circulated prior) provides information on the use of additional doses of the Pfizer COVID-19 vaccine in the context of vaccine administration error. Key take-aways are on the need to balance of risk of the reactogenicity of an extension dose against the potential benefit. Public Health England summarises this in their 2021 Vaccine Incident Guidance:

    "*Given that revaccination is not without risk (both in terms of vaccine reactions and damage to public confidence in the immunisation programme and provider services), the decision to revaccinate should only be considered in situations where there is a high likelihood of a suboptimal response to the vaccine or where there is evidence of exceptionally poor practice overall that leads to great concern for the efficacy of vaccine(s) administered*."

16. In the international context, third or booster doses are generally only being given to those who finished their two-dose course some time ago (5 months or more), either in trials or in roll-out of third doses in some countries, or in specific clinical sub-groups.

17. The current evidence for clinical sub-groups is focused on those likely to be poorly protected by a single dose, who are moderate or severely immunocompromised (see extended list at CDC[2]).

Extension Dose Guidance

18. As indicated above, an individualised clinical management plan is best practice. However, if this is not possible due to the number of people potentially affected, the guidance below may be used as a tool. Our recommendation is that this should only be applied for groups larger than 40 people.

19. The scope of the guidance is limited to a few options given the lack of clinical data on third doses and it does not replace the clinical decision-making of a medical professional.

Steps	Categories	Approach	Extension Dose Action
Step 1	Incident at Dose 1*	Ensure all those whose incident occurred at Dose 1 vaccination continue to have their Dose 2 in accordance with current dose interval guidance	Go to step 2. If step 2 does not apply, go to step 3.
	Incident at Dose 2	Ensure all those whose incident occurred at Dose 2 vaccination are screened for severe AEFI**	If severe AEFI are observed after Dose 2, then the decision for an extension dose should be a fully informed process between the consumer and their clinician, and should include a risk/benefit analysis. If no severe AEFI observed, go to step 2. If step 2 does not apply, go to step 3.
Step 2	Immunocompromised	Moderate or severe immunocompromise***	Offer extension dose 6 weeks following Dose 2.
Step 3	All other consumers	Consider extent of any local and regional community transmission of COVID-19	If no/low community transmission: offer extension dose 20 weeks following Dose 2. If high community transmission: offer extension dose 6 weeks following Dose 2.

*Where it is not possible to identify the specific consumers who experienced a missed vaccination incident at Dose 1, serological testing (where practical) will give an indication of whether an individual is likely to be amongst those who did not receive the vaccine, as per point 14 above (noting that this assumes no history of previous COVID-19 infection). The serological test used

must measure anti-spike antibody and assays such as the Abbott or Roche product must be conducted a minimum of 14 days, but optimally at 21 days, after the presumed error to ensure accurate results.[3] If the test is positive, these consumers can then continue to have their Dose 2 in accordance with current dose interval guidance and do not require the offer of an extension dose. If the test is negative, then follow the step-by-step guidance above. Clinicians are advised to seek specialist support when considering serology in this situation.

**AEFI= Adverse events following immunisation. 'Dose 1' or 'Dose 2' in this guidance applies to the two-dose regimen of the Comirnaty (Pfizer/BioNTech) COVID-19 vaccine.

***Clinical judgement should be applied in determining if someone has moderate or severe immunocompromise; the CDC definition may be helpful.[2]

20. Informed consent from the affected consumer should be obtained for all interventions. An individual's risk factors, including their risk of a poor outcome if infected, the risk of suboptimal immune response and the risk of reactogenicity, should be considered with the consumer and clinical team.

21. Medsafe and Crown Law have been consulted in the development of this guidance, and the advice has been adjusted according to the feedback received.

22. In the absence of clinical data on missed vaccination incidents and third doses, further guidance has been sought from expert clinical immunologists.

Recommendations

23. CV TAG met on 31 August 2021 to consider the draft guidance on extending doses for missed vaccination incidents. This guidance was endorsed.

24. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

Dr Ian Town

Chief Science Advisor and Chair of the COVID-19 Vaccine Technical Advisory Group

References

1. FDA. *Antibody Testing Is Not Currently Recommended to Assess Immunity After COVID-19 Vaccination: FDA Safety Communication*. May 19, 2021; Available from: https://www.fda.gov/medical-devices/safety-communications/antibody-testing-not-currently-recommended-assess-immunity-after-covid-19-vaccination-fda-safety.
2. CDC. *COVID-19 Vaccines for Moderately to Severely Immunocompromised People*. August 27, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html.
3. Eyre, D.W., et al., *Quantitative SARS-CoV-2 anti-spike responses to Pfizer-BioNTech and Oxford-AstraZeneca vaccines by previous infection status.* medRxiv, 2021: p. 2021.03.21.21254061.

Memo

Date:	6 September 2021
To:	Maree Roberts, Deputy Director General, System Strategy and Policy
Copy:	Alison Cossar, Manager, Public Health Policy, Systems Strategy and Policy Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme Niki Stefanogiannis, Deputy Director Public Health, Population Health and Prevention
From:	Dr Ian Town, Chief Science Advisor
Subject:	COVID-19 vaccines recognised for work at the Aotearoa New Zealand Border
For your:	Consideration

Purpose

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on COVID-19 vaccines that Aotearoa New Zealand recognises for those working at the international border ('the Border'), including advice on the criteria for deciding which vaccines should be recognised at the Border, and how to approach incomplete vaccination with recognised COVID-19 vaccines and vaccination with non-recognised COVID-19 vaccines among 'Border Workers'.

Context

2. The COVID-19 Public Health Response (Vaccinations) Order 2021 (the Vaccinations Order) requires certain work only be undertaken by vaccinated workers. This is due to the high risk of exposure to SARS-CoV-2 (the virus causing COVID-19) that these workers may experience in the course of their work and the risk of the workers becoming infected and transmitting SARS-CoV-2 to others. The current approach to COVID-19 vaccinations required for work at the Border does not accommodate New Zealanders who return from working overseas having received a COVID-19 vaccine other than 'Comirnaty', the Pfizer-BioNTech mRNA COVID-19 vaccine (the Pfizer vaccine).
3. The New Zealand Defence Force (NZDF) report having more than 250 personnel who have been vaccinated overseas with the Moderna, AstraZeneca, or Janssen vaccines. These personnel cannot be reassigned to work at managed quarantine and isolation facilities (MIQFs) because they do not meet the vaccination requirements in the Vaccinations Order. The NZDF has signalled that the inability to reassign personnel to work at the Border has created a workforce capacity issue that is becoming more acute over time.
4. In the longer-term, the Ministry of Health (the Ministry) is developing advice about which COVID-19 vaccines Aotearoa New Zealand will recognise to be considered for reduced testing or MIQF requirements for inbound travellers as part of the Reconnecting New Zealanders work. Any decisions made in the short-term about approved COVID-19 vaccines for work at the Border will

likely inform future decisions, however these fall outside of the scope of this memo and recommendations, which is restricted to discussing requirements for work at the Border.

5. The Ministry's Public Health Policy team sought advice from CV TAG on the short and longer-term options for COVID-19 vaccines recognised in New Zealand. On 22 June 2021 CV TAG met to consider the issue and recommended that individuals with a complete course of a vaccine approved by regulators in countries with similar regulatory systems to New Zealand could be eligible to work at the Border. However, CV TAG signalled that further discussion on the issue was required to clearly understand what the vaccines approved or provisionally approved by these agencies were. It was agreed that a list of COVID-19 vaccines with approval, provisional approval, or emergency use provisions from a Medsafe recognised authority would be brought to a future CV TAG meeting for discussion.

6. Medsafe considers that the authorities listed below have robust approval processes and conduct thorough assessments of applications for new medicines. They follow similar international standards and guidelines in their assessments to Medsafe. This allows Medsafe to rely on their assessments and approval to facilitate abridged evaluations of new medicine applications in New Zealand submitted via the abbreviated application pathway. The Medsafe recognised authorities are:[1]

    a) The Australian Therapeutic Goods Administration (TGA)

    b) The United States Food and Drug Administration (FDA)

    c) Health Products and Food Branch of Health Canada

    d) Medicines and Healthcare products Regulatory Agency (MHRA), in the United Kingdom

    e) European Medicines Agency (EMA) (centralised procedure only)

    f) EU member states (decentralised or mutual recognition procedure only)

7. The COVID-19 vaccines currently provisionally approved by Medsafe for use in New Zealand are **Pfizer, Janssen, and AstraZeneca**. An application for the **Novavax COVID-19 vaccine** has been received, however further data has been requested from the sponsor.[2]

8. As of 31 August 2021, COVID-19 vaccines that do not have Medsafe approval or provisional approval, but that do have approval, provisional approval, or emergency use provisions from Medsafe-recognised authorities are: **Moderna mRNA vaccine** (Spikevax) approved by the TGA, FDA, Health Canada, MHRA, and EMA; and **the AstraZeneca vaccine manufactured by the Serum Institute of India (Covishield)** has received separate approval from Health Canada.[3-7] Vaccines that are currently under rolling review by the EMA but have not yet been approved include CureVac, Gamalaya (Sputnik V), Sinovac (Coronavac) and Vidprevtyn from Sanofi-GSK. These are not currently recognised as part of these recommendations.

9. The vaccines provisionally approved by Medsafe and other regulatory bodies provide protection against COVID-19 and have good safety profiles, however, efficacy/effectiveness varies between the vaccines (see Table 1). A high level of protection against COVID-19 is needed for Border workers, not only for the direct individual benefits of protection against symptomatic infection and moderate-severe disease, but there is also a broader public health benefit through reducing viral infection and onward transmission.

Table 1: Vaccine efficacy/effectiveness of provisionally approved and recognised vaccines

	Pfizer	**AstraZeneca**	**Janssen**	**Moderna**
Against symptomati	*Efficacy*:	*Efficacy*:	*Efficacy*:	*Efficacy*:

c COVID-19 infection	95% (95%CI: 90.3-97.6) >7 days post 2nd dose.[8] *Effectiveness*: 94% (95%CI: 87-98.0) against symptomatic infection.[9] 85–95.3% >7 days post 2nd dose in Israel, UK and Italy.[9-13] UK: 70% (95%CI: 62-77) reduction in transmission post 2nd dose.[13] Israel: ~77% reduction among elderly post 2nd dose.[14]	63.1% (95%CI: 51.8-71.1) >14 days post 2nd dose.[15] US trial: 76% (95%CI: 68.0-82.0) from 15 days post 2nd dose when given four weeks apart.[16] 54.1% (95%CI: 44.7-61.9) >14 days post 2nd doses.[15] *Effectiveness*: Scotland: 88% (95%CI: 75-94) against hospitalisation 28-34 days post 1st dose.[17] UK: 80.4% (95%CI: 36.4-94.5) against hospitalisation post 1st dose in the elderly.[18]	74% (95%CI: 46.8-88.4) >28 days post vaccination.[19] *Effectiveness:* US: 76.7% (95%CI: 30.3-95.3) >14 days post vaccination.[20]	94.1% (95% CI:89.3–96.8) against infection including severe disease >14 days post 2nd dose.[21] *Effectiveness:* 98.2% (95%CI: 97.5-98.6) >7 days post 2nd dose.[22] 91.3% (95%CI: 79.3-96.3) against symptomatic infection and 68.3% (95%CI: 27.9-85.7) against asymptomatic infection >14 days post 2nd dose.[23]
Delta	*Effectiveness against symptomatic infection:* 88% (95%CI: 85.3-90.1) against symptomatic Delta infection.[24] 96% (95%CI: 86-99) against hospitalisation with Delta infection.[25] Scotland: 79% (95%CI 75-82) against infection[26] *Effectiveness against asymptomatic infection*: No data	*Effectiveness against symptomatic infection:* UK: 67% (95%CI: 61.3-71.8) against symptomatic Delta infection.[24] UK:92% (95%CI: 75-97) against hospitalisation with Delta infection.[25] *Effectiveness against asymptomatic infection:* No data	No data	*Effectiveness against symptomatic infection:* US: 66% (95%CI: 22-84) (pooled data with Pfizer).[27] US: 76% (95%CI: 58-87) >14 days post 2nd dose.[28] *Effectiveness against asymptomatic infection:* No data

10. There is some evidence that a single dose of the Janssen vaccine may not be as effective against infection and may pose a greater risk for work at the Border. A US study from General

Massachusetts Hospital compared immune responses in ambulatory adults vaccinated with Pfizer, Moderna or Janssen vaccines and found lower antibody concentrations and neutralisation titres for the Janssen vaccine. However, administering a second dose of either Pfizer or Moderna vaccines boosted the immune response.[29] Trials are underway to assess the efficacy after a second 'booster' dose and are showing promising preliminary results with a nine-fold increase in spike-binding antibodies (noting that this data has yet to be formally released, published in a journal, or evaluated by regulatory authorities).[30]

11. Recommendations are also needed for the following groups: individuals with incomplete vaccination with recommended vaccines; individuals with complete or incomplete vaccination with COVID-19 vaccines that are not recommended for use at the Border.

Recommendations

12. CV TAG met on 17 and 31 August 2021 to consider recommendations regarding which COVID-19 vaccines can be recognised for Border work, and how to approach incomplete and complete vaccination with non-recognised COVID-19 vaccines.

13. **CV TAG noted that:**

    a) Data are still emerging on the efficacy of heterologous vaccine schedules from approved and recognised vaccines in New Zealand's portfolio, however initial results show that mixing vaccine doses is associated with a low incidence of adverse effects and could provide an improved immune response through increased anti-spike antibody titres and neutralising antibodies.[31-33]

    b) Protection against symptomatic infection is of enhanced importance for work at the Border. Extensive data has emerged showing high efficacy and effectiveness against symptomatic infection after two doses of the Pfizer, AstraZeneca, or Moderna vaccines in Phase 3 clinical trials and large post-marketing studies. There is strong evidence that the Janssen vaccine (the single-dose, adenovirus vector vaccine) provides a high degree of protection against moderate and severe disease from COVID-19, however there are less data on the efficacy or effectiveness against symptomatic infection, especially in the context of the Delta variant of SARS-CoV-2, and the immune response appears to be lower.

14. **CV TAG recommends that:**

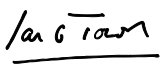
    a) A full course of vaccination with a COVID-19 vaccine recognised by Medsafe (or a Medsafe recognised authority) provides sufficient protection from COVID-19 for work at the Border, with the exception of the Janssen vaccine as a single dose schedule.

    b) A 'booster' dose of the Pfizer vaccine should be administered for Border Workers who have only received a single dose of the Janssen vaccine, due to the higher risk of SARS-CoV-2 infection for Border work, and the need for enhanced protection against infection among Border Workers.

    c) If a worker is in New Zealand and has an incomplete vaccination with a vaccine recognised by Medsafe (or a Medsafe recognised authority) they should complete their vaccination by receiving one dose of the Pfizer vaccine. This should occur at least 21 days after the first dose of the non-Pfizer vaccine, or at least 28 days after the first dose if this was AstraZeneca or Moderna. There is no upper time limit on time for when that dose can be administered.

    d) Workers who have received a partial or complete course of vaccine with a non-recognised COVID-19 vaccine, should also receive one dose of the Pfizer vaccine.

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



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Chair, CV TAG

References

1. Medsafe, *New Zealand Regulatory Guidelines for Medicines*, in *Part A: When is an application for approval of a new or changed medicine required?*, Medsafe, Editor. 2014, Medsafe: Medsafe. p. 132.
2. Medsafe. *Approval status of COVID vaccines applications received by Medsafe*. 2021 [cited 2021 27 August]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.
3. The Australian Therapeutics Goods Administration. *COVID-19 vaccine: Provisional registrations*. 2021; Available from: https://www.tga.gov.au/covid-19-vaccine-provisional-registrations.
4. European Medicines Agency. *COVID-19 vaccines: authorised*. 2021 [cited 2021 27 August]; Available from: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#authorised-covid-19-vaccines-section.
5. Government of Canada. *Drug and vaccine authorizations for COVID-19: List of applications received*. 2021; Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/applications.html.
6. National Health Service. *Coronavirus (COVID-19) vaccines*. 2021 [cited 2021 27 August]; Available from: https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/coronavirus-vaccine/.
7. US Food and Drug Administration. *COVID-19 Vaccines*. 2021 [cited 2021 27 August]; Available from: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
8. Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.* New England Journal of Medicine, 2020. **383**(27): p. 2603-2615.
9. Dagan, N., et al., *BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting.* New England Journal of Medicine, 2021.
10. Hall, V.J., et al., *COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study.* The Lancet, 2021. **397**(10286): p. 1725-1735.
11. Haas, E.J., et al., *Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data.* The Lancet.
12. Fabiani, M., et al., *Effectiveness of the Comirnaty (BNT162b2, BioNTech/Pfizer) vaccine in preventing SARS-CoV-2 infection among healthcare workers, Treviso province, Veneto region, Italy, 27 December 2020 to 24 March 2021.* Eurosurveillance, 2021. **26**(17): p. 2100420.
13. Pritchard, E., et al., *Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom.* Nature Medicine, 2021.
14. Rossman, H., et al., *COVID-19 dynamics after a national immunization program in Israel.* Nature Medicine, 2021. **27**(6): p. 1055-1061.
15. Voysey, M., et al., *Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials.* The Lancet, 2021. **397**(10277): p. 881-891.
16. AstraZenenca. *AZD1222 US Phase III primary analysis confirms safety and efficacy*. 2021; Available from: https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/azd1222-us-phase-iii-primary-analysis-confirms-safety-and-efficacy.html.
17. Vasileiou, E., et al., *Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study.* The Lancet, 2021. **397**(10285): p. 1646-1657.
18. Hyams, C., et al., *Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study.* The Lancet Infectious Diseases, 2021.

19. Food and Drug Administration (FDA). *Vaccines and Related Biological Products Advisory Committee Meeting February 26, 2021, FDA Briefing Document, Janssen Ad26.COV2.S Vaccine for the Prevention of COVID-19*. 2021; Available from: https://www.fda.gov/media/146217/download.
20. Corchado-Garcia, J., et al., *Real-world effectiveness of Ad26.COV2.S adenoviral vector vaccine for COVID-19.* medRxiv, 2021: p. 2021.04.27.21256193.
21. Baden, L.R., et al., *Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.* New England Journal of Medicine, 2020. **384**(5): p. 403-416.
22. Butt, A.A., et al., *SARS-CoV-2 Vaccine Effectiveness in a High-Risk National Population in a Real-World Setting.* Annals of Internal Medicine, 2021.
23. Andrejko, K.L., et al., *Prevention of COVID-19 by mRNA-based vaccines within the general population of California.* Clinical Infectious Diseases, 2021.
24. Lopez Bernal, J., et al., *Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant.* New England Journal of Medicine, 2021.
25. Stowe, J., et al. *Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant*. 2021; Available from: https://khub.net/documents/135939561/479607266/Effectiveness+of+COVID-19+vaccines+against+hospital+admission+with+the+Delta+%28B.1.617.2%29+variant.pdf/1c213463-3997-ed16-2a6f-14e5deb0b997?t=1623689315431.
26. Sheikh, A., et al., *SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness.* Lancet, 2021. **397**(10293): p. 2461-2462.
27. Fowlkes, A., et al., *Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance - Eight U.S. Locations, December 2020–August 2021.* MMWR Morb Mortal Wkly Rep, 2021. **70**: p. 1167-1169.
28. Puranik, A., et al., *Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence.* medRxiv, 2021: p. 2021.08.06.21261707.
29. Naranbhai, V., et al., *Immunogenicity of mRNA-1273, BNT162b2 and Ad26.COV2.S COVID-19 vaccines.* medRxiv, 2021: p. 2021.07.18.21260732.
30. Johnson and Johnson. *Johnson & Johnson Announces Data to Support Boosting its Single-Shot COVID-19 Vaccine*. 2021 [cited 2021 27 August]; Available from: https://www.jnj.com/johnson-johnson-announces-data-to-support-boosting-its-single-shot-covid-19-vaccine.
31. Gross, R., et al., *Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity.* medRxiv, 2021: p. 2021.05.30.21257971.
32. Borobia, A.M., et al., *Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomised, Adaptive, Phase 2 Trial (CombiVacS).* SSRN, 2021.
33. Liu, X., et al., *Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial.* The Lancet, 2021.

Memo

Additional Pfizer mRNA COVID-19 vaccine dose in the immunocompromised: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	21 September 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
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 an additional Pfizer mRNA COVID-19 vaccine dose in those who are immunocompromised.

Background and context

2. Some immunocompromised people do not mount an immune response following vaccination that is sufficient to provide protection from COVID-19.[1] Immunocompromised individuals are also at higher risk of severe outcomes from COVID-19 compared to the general population. Several underlying medical conditions, including diabetes, asplenia, and chronic lung and kidney disease, are also associated with increased risk of severe outcomes from COVID-19.[2, 3]

3. Immunocompromised individuals tend to have prolonged infection and viral shedding, are at higher risk of developing a new variant during infection, and are more likely to transmit the virus to household contacts than non-immunocompromised groups.[4] They are also more likely to have a breakthrough infection after being vaccinated, with studies in the US and Israel having estimated that 40-44% of hospitalised breakthrough cases are immunocompromised.[5, 6] Consequently, an additional vaccine dose may deliver better protection in immunocompromised individuals.

4. Emerging evidence suggests that a third dose of the Pfizer COVID-19 vaccine may increase the antibody titres in immunocompromised individuals who developed low antibody titres to the original two-dose regimen and result in the detection of antibodies in some of the non-responders.[4] Among those who had no detectable antibody response to an initial 2-dose mRNA vaccine series, about 33-50% developed an antibody response to a third dose. So far, reactions reported after the third dose in small studies were similar to those after two doses, with fatigue and pain at injection site being the most commonly reported side effects, and overall, most side effects reported were mild to moderate.[7]

5. One study evaluated the humoral response to a third dose of the Pfizer vaccine in 101 solid organ transplant patients.[8] Patients were given two doses of Pfizer one month apart, followed by a third dose of Pfizer two months later. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive one month after the third dose.

6. Another study found that among 82 hemodialysis patients, only a small proportion (15.9%) failed to seroconvert after two doses.[9] Of these, 12 patients were given a third dose one month later and five (41.6%) developed an immune response following the third dose.

7. The level of individual protection that a third dose confers on an immunocompromised person is unknown. However, based on the emerging data for the COVID vaccines, and principles of vaccinology and immunology, an additional dose in the immunocompromised is unlikely to be associated with any significant risks, and may offer benefits to some individuals.

8. The Pfizer vaccine has been provisionally approved in Aotearoa New Zealand on the basis that two doses, not three, would be administered to a consumer. However, an unapproved indication, such as an additional dose for immunocompromised individuals, can be prescribed with informed consent.

9. On 12 August 2021, the US Food and Drug Administration (FDA) approved the use of an additional dose of the Pfizer COVID-19 vaccine at least 28 days following the original two-dose regimen in those who are immunocompromised.[10] The US Centers for Disease Control (CDC) have recommended that *"…moderately to severely immunocompromised people receive an additional dose. This includes people who have:*

- *Been receiving active cancer treatment for tumours or cancers of the blood*
- *Received an organ transplant and are taking medicine to suppress the immune system*
- *Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system*
- *Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)*
- *Advanced or untreated HIV infection*
- *Active treatment with high-dose corticosteroids or other drugs that may suppress their immune response*

People should talk to their healthcare provider about their medical condition, and whether getting an additional dose is appropriate for them."[7]

10. On 01 September 2021, the UK's Joint Committee on Vaccination and Immunisation (JCVI) issued guidance for COVID-19 vaccinations for individuals aged 12 years and over with severe immunosuppression.[11-13] JCVI recommended that a third dose should be offered to people aged 12 and over who were severely immunosuppressed at the time of their first or second dose, including those with leukaemia, advanced HIV, and recent organ transplants.

11. JCVI noted that the guidance for third doses for severely immunocompromised groups was separate to any potential booster programme for the general population: "*A third primary dose is an extra 'top-up' dose for those who may not have generated a full immune*

response to the first 2 doses. In contrast, a booster dose is a later dose to extend the duration of protection from the primary course of vaccinations."[11]

Recommendations

12. CV TAG met on 31 August and 07 September 2021 to discuss recommendations for the use of an additional dose in the immunocompromised.

13. CV TAG noted that:

    a. An additional dose of the Pfizer COVID-19 vaccine is likely to be beneficial and well-tolerated in the severely immunocompromised.

    b. An additional dose would offer extra protection to severely immunocompromised people and may help to reduce transmission from immunocompromised individuals who become infected.

    c. People with functional or anatomical asplenia and those with chronic liver or kidney disease not taking immunosuppressants (including those receiving hemodialysis) may also have immunocompromise. In addition, those with diabetes are at higher risk of severe infection. Thus, emerging information for these groups will be monitored and considered for any potential recommendations as data become available.

    d. 'Ring-fencing' of immunocompromised people through vaccination of household contacts can provide indirect protection to people with immunocompromise.

    e. People with immunocompromise may have a suboptimal immune response to vaccination and should be counselled to continue other protective measures against COVID-19 even after vaccination, such as physical distancing, wearing a face mask, practicing hand hygiene, and isolation or quarantine as advised by public health authorities.

14. CV TAG recommend that:

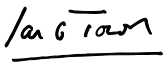
    a. Those with severe immunocompromise be offered an additional dose of the Pfizer vaccine. The list of eligible individuals is taken from the one developed by JCVI and is provided in Appendix 1.

    b. The additional dose should be administered more than 8 weeks after the second dose, with special attention paid to current or planned immunosuppressive therapies. Where possible, the third primary dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent. If not possible, consideration should be given to vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.

    c. The administration of an additional dose is covered by s25 of The Medicines Act 1981, and as such, should only be offered by an authorised prescriber with informed consent from the consumer.

    d. The standard two-dose course of vaccine should be offered to any eligible unvaccinated household contacts aged 12 and over, of immunocompromised individuals.

15. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.



Dr Ian Town

Chief Science Advisor and Chair of the COVID-19 Vaccine Technical Advisory Group

Appendix 1

JCVI list of eligible individuals[12]

1. Individuals with primary or acquired immunodeficiency states at the time of vaccination due to conditions including:
    a. acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who were under treatment or within 12 months of achieving cure.
    b. individuals under follow up for chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (note: this list is not exhaustive).
    c. immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/µl for adults or children 12 years of age and over.
    d. primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ul) or with a functional lymphocyte disorder.
    e. those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months.
    f. those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD).
    g. persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease/therapy.
2. Individuals on immunosuppressive or immunomodulating therapy at the time of vaccination including:
    a. those who were receiving or had received immunosuppressive therapy for a solid organ transplant in the previous 6 months.
    b. those who were receiving or had received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but in this case the recipient would be considered immunosuppressed for a 6-month period), T-cell co-stimulation modulators, monoclonal tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (note: this list is not exhaustive).
    c. those who were receiving or had received in the previous 6 months immunosuppressive chemotherapy or immunosuppressive radiotherapy for any indication.
3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination including:
    a. high-dose corticosteroids (equivalent to ≥ 20mg prednisolone per day) for more than 10 days in the previous month.
    b. long-term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day for more than 4 weeks) in the previous 3 months.
    c. non-biological oral immune modulating drugs, such as methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day, 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day in the previous 3 months.

   d. certain combination therapies at individual doses lower than above, including those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months.

4. Individuals who had received high-dose steroids (equivalent to >40mg prednisolone per day for more than a week) for any reason in the month before vaccination. Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (for example, asthma / chronic obstructive pulmonary disease / COVID-19) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed sufficient to have prevented response to the primary vaccination.

References

1. Centers for Disease Control and Prevention (CDC). *Science Brief: COVID-19 Vaccines and Vaccination*. July 27, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html.
2. Centers for Disease Control and Prevention (CDC). *People with Certain Medical Conditions*. 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.
3. UK Government. *Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination*. 30 December 2020; Available from: https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-30-december-2020/joint-committee-on-vaccination-and-immunisation-advice-on-priority-groups-for-covid-19-vaccination-30-december-2020.
4. Oliver, S. *Data and clinical considerations for additional doses in immunocompromised people*. July 22, 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/07-COVID-Oliver-508.pdf.
5. Tenforde, M.W., et al., *Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States.* medRxiv, 2021: p. 2021.07.08.21259776.
6. Brosh-Nissimov, T., et al., *BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully-vaccinated hospitalized COVID-19 patients in Israel.* Clinical Microbiology and Infection, 2021.
7. Centers for Disease Control and Prevention (CDC). *COVID-19 Vaccines for Moderately to Severely Immunocompromised People*. August 27, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html.
8. Kamar, N., et al., *Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients.* The New England journal of medicine, 2021. **385**(7): p. 661-662.
9. Longlune, N., et al., *High immunogenicity of a messenger RNA-based vaccine against SARS-CoV-2 in chronic dialysis patients.* Nephrology Dialysis Transplantation, 2021.
10. US Food and Drug Administration. *FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals*. August 12, 2021; Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised.
11. PHE. *JCVI issues advice on third dose vaccination for severely immunosuppressed*. Press release: vaccinations for coronavirus 2021 01 September 2021 [cited 2021 10 September 2021]; Available from: https://www.gov.uk/government/news/jcvi-issues-advice-on-third-dose-vaccination-for-severely-immunosuppressed.
12. JCVI. *Updated JCVI guidance for vaccinating immunosuppressed individuals with a third primary dose*. 2021 02 September 2021 [cited 2021 12 September]; Available from: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/09/C1399-Updated-JCVI-guidance-for-vaccinating-immunosuppressed-individuals-with-third-primary-dose.pdf.
13. JCVI. *Independent report: Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination*. Independent report 2021 01 September [cited 2021 12 September]; Available from: https://www.gov.uk/government/publications/third-primary-covid-19-vaccine-dose-for-people-who-are-immunosuppressed-jcvi-advice/joint-committee-on-vaccination-and-immunisation-jcvi-advice-on-third-primary-dose-vaccination#advice.

Memo

COVID-19 vaccines for arrivals to Aotearoa New Zealand: COVID-19 Vaccine Technical Advisory Group (CV TAG) Recommendations

Date:	29 September 2021
To:	Maree Roberts, Deputy Director General, System Strategy and Policy
Copy to:	Alison Cossar, Manager, Public Health Policy, Systems Strategy and Policy Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme Niki Stefanogiannis, Deputy Director Public Health, Population Health and Prevention
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. This memo summarises the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on COVID-19 vaccination requirements for people arriving to the country and entering managed isolation and quarantine (MIQ) for 14 days. These recommendations are made as a part of a first step in the phased introduction of vaccination requirements at the border.

Background and context

2. CV TAG has previously provided advice on COVID-19 vaccination requirements for Border Workers, recognising that enhanced protection against infection was needed due to their individual occupational risk profile but also the broader public health benefit through reducing viral infection and onward transmission. Details of recommendation are provided in Appendix 1.
3. Other jurisdictions have implemented COVID-19 vaccination requirements at the border. For example, Canada requires those entering to have received the full series of a vaccine or a combination of vaccines accepted by the Government of Canada (Pfizer, Moderna, AstraZeneca, Janssen) and to have received the last dose at least 14 days before arrival. The EU states that if member states accept proof of vaccination to waive travel restrictions, they should in principle lift restrictions on non-essential travel for travellers who have received the last recommended dose of a vaccine approved by the European Medicines Agency (EMA), at least 14 days before arrival.
4. As part of the continual improvement approach to reduce the risk of COVID-19 entering the community, the Government has signalled it wants to look at vaccination requirements for arrivals to New Zealand.

5. In the short term, imposing a vaccination requirement on inbound travellers (in addition to testing and managed isolation and quarantine (MIQ) for 14 days) has been proposed as a first step in the phased introduction of vaccination requirements at the border. A Cabinet paper is being prepared on this proposal, which will need to include a recommendation on the vaccination requirements to enter MIQ (and therefore Aotearoa New Zealand).

6. There are currently 22 COVID-19 vaccines worldwide approved for use by at least one government or other authority (Appendix 2).

7. The COVID-19 vaccines currently provisionally approved by Medsafe for use in New Zealand are Pfizer, Janssen, and AstraZeneca. However, not every country has at least one of these vaccines approved and available for use. As of 17th September 2021, 26 of 193 countries had no approval for Pfizer, Janssen, or an AstraZeneca formulation. These 26 countries include, for example, China, Russia and Syria (Appendix 2).

8. Medsafe considers that the authorities listed below have robust approval processes and conduct thorough assessments of applications for new medicines. They follow similar international standards and guidelines in their assessments to Medsafe. This allows Medsafe to rely on their assessments and approval to facilitate abridged evaluations of new medicine applications in New Zealand submitted via the abbreviated application pathway. The Medsafe recognised authorities are:[1]

    a. The Australian Therapeutic Goods Administration (TGA)

    b. The United States Food and Drug Administration (FDA)

    c. Health Products and Food Branch of Health Canada

    d. Medicines and Healthcare products Regulatory Agency (MHRA), in the United Kingdom

    e. European Medicines Agency (EMA) (centralised procedure only)

    f. EU member states (decentralised or mutual recognition procedure only)

9. Medsafe recognised authorities have approved a number of COVID-19 Vaccines for Emergency Use. These are Pfizer, Janssen, AstraZeneca, and Moderna. The countries where these vaccines are approved are shown in Appendix 2.

10. The COVID-19 Policy team have consequently sought CV TAG advice on COVID-19 vaccination requirements for people arriving to the country and entering managed isolation and quarantine (MIQ) for 14 days.

Recommendations

11. CV TAG met on 7, 14 and 21 September 2021 to consider recommendations regarding COVID-19 vaccines for people arriving to Aotearoa New Zealand.

12. CV TAG noted that:

    a. officials are preparing a proposal for the Minister for COVID-19 Response to take to Cabinet that would impose a pre-entry requirement from 1 November 2021, that all (non-New Zealand citizen) arrivals by air are fully vaccinated.

    b. under this proposal all arrivals would still undergo testing and 14 days MIQ, which will continue to be the key line of defence.

c. this is being proposed as an additional precautionary measure to further reduce the risk of COVID-19 entering the New Zealand community (and until New Zealand achieves high vaccination coverage).

d. there are significant ethical and equity issues given that most people have no choice about which vaccine they receive, and many countries still have poor access to vaccines and low vaccination rates.

e. while the effectiveness varies across the different vaccine products, any vaccine is better than no vaccine.

f. new recommendations will be needed if requirements around MIQ on entry to Aotearoa New Zealand change. This is due to different considerations around requirements of vaccines without MIQ as the key line of defence.

g. updated recommendations will likely be needed if there are changes to the approved COVID-19 vaccination schedules in New Zealand.

13. CV TAG recommends that:

a. a full primary course of vaccination with any of the 22 COVID-19 vaccines approved by at least one government or authority (or an approved combination of those vaccines in their origin country) with the last dose at least 14 days before arrival would be acceptable for entering MIQ for 14 days, given that testing and MIQ would provide the key line of defence. Vaccination should be documented in the manner that the origin country provides.

b. an exemption process should be put in place for those who require an exemption on humanitarian grounds, because they are below the approved age for COVID-19 vaccination in their origin country, or for other similar reasons.

c. those aged 12 years or over who enter the country with a full primary course of vaccination, but with a vaccine that is NOT one of those approved by a Medsafe-recognised authority should be offered an additional dose of Pfizer vaccine as soon as possible after entry to New Zealand (and at the latest as they leave MIQ). This should occur at least 28 days after the last dose, with no upper limit on time since the last dose.

d. those who enter the country, are aged 12 years or over, and have received no doses of any of the 22 COVID-19 vaccines, should be offered a full course of Pfizer vaccine as soon as possible after entry to New Zealand (and at the latest receiving the first dose as they leave MIQ).

e. those who enter the country, are aged 12 years or over and have received an incomplete primary course of any of the 22 COVID-19 vaccines (whether approved by a Medsafe-recognised authority or not), should be offered an additional dose of Pfizer vaccine as soon as possible after entry to New Zealand.

    i. This should occur at least 28 days after the most recent dose of COVID-19 vaccine, with no upper limit on time since the last dose.

    ii. If the interval since the most recent dose allows, vaccination with Pfizer should be offered to people while in MIQ or at the latest as they leave MIQ.

iii. If the interval since most recent dose does not allow vaccination on or before leaving MIQ, a future vaccination booking should be offered as they leave MIQ at the latest.

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

Dr Ian Town
Chief Science Advisor and Chair of the COVID-19 Vaccine Technical Advisory Group

References

1. Medsafe, *New Zealand Regulatory Guidelines for Medicines*, in *Part A: When is an application for approval of a new or changed medicine required?*, Medsafe, Editor. 2014, Medsafe: Medsafe. p. 132.
2. Gross, R., et al., *Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity.* medRxiv, 2021: p. 2021.05.30.21257971.
3. Borobia, A.M., et al., *Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomised, Adaptive, Phase 2 Trial (CombiVacS).* SSRN, 2021.
4. Liu, X., et al., *Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial.* The Lancet, 2021.

Appendix 1: Previous CV TAG recommendations for Border Workers

CV TAG has previously provided advice on COVID-19 vaccination requirements for Border Workers, recognising that enhanced protection against infection was needed due to their individual occupational risk profile but also the broader public health benefit through reducing viral infection and onward transmission. CV TAG noted that:

a. Data are still emerging on the efficacy of heterologous vaccine schedules from approved and recognised vaccines in New Zealand's portfolio, however initial results show that mixing vaccine doses is associated with a low incidence of adverse effects and could provide an improved immune response through increased anti-spike antibody titres and neutralising antibodies.[2-4]

b. Protection against symptomatic infection is of enhanced importance for work at the Border. Extensive data has emerged showing high efficacy and effectiveness against symptomatic infection after two doses of the Pfizer, AstraZeneca, or Moderna vaccines in Phase 3 clinical trials and large post-marketing studies. There is strong evidence that the Janssen vaccine (the single-dose, adenovirus vector vaccine) provides a high degree of protection against moderate and severe disease from COVID-19, however there are fewer data on the efficacy or effectiveness against symptomatic infection, especially in the context of the Delta variant of SARS-CoV-2, and the immune response appears to be lower.

On this basis, CV TAG recommended for Border Workers that:

c. A full course of vaccination with a COVID-19 vaccine recognised by Medsafe or a Medsafe recognised authority provides sufficient protection from COVID-19 for work at the Border, with the exception of the Janssen vaccine as a single dose schedule.

d. A 'booster' dose of the Pfizer vaccine should be administered for Border workers who have only received a single dose of the Janssen vaccine, due to the higher risk of SARS-CoV-2 infection for Border work, and the need for enhanced protection against infection among Border Workers

e. If a worker is in New Zealand and has an incomplete vaccination with a vaccine recognised by Medsafe or a Medsafe recognised authority, they should complete their vaccination by receiving one dose of the Pfizer vaccine. This should occur at least 21 days after the first dose of the Pfizer vaccine, or at least 28 days after the first dose of AstraZeneca or Moderna. There is no upper time limit on time for when that dose can be administered.

f. Border workers who have received a partial or complete course of vaccine with a COVID-19 vaccine not approved by Medsafe or a Medsafe recognised authority, should also receive one dose of the Pfizer vaccine.

Appendix 2: Vaccines authorised/approved in each country

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
"Approved" by Medsafe recognised authority					yes	yes	yes	yes	yes																		
Afghanistan	1	1					x																				
Australia	4	1			x	x		x	x																		
Austria	4	1			x	x		x	x																		
Barbados	1	1					x																				
Belgium	4	1			x	x		x	x																		
Bermuda	2	1			x	x																					
Bhutan	2	1					x		x																		
Bosnia and Herzegovina	2	1			x	x																					
Botswana	4	1			x	x	x		x																		
Bulgaria	4	1			x	x		x	x																		
Burkina Faso	1	1				x																					
Cabo Verde	2	1			x		x																				
Canada	5	1			x	x	x	x	x																		
Central African Republic	1	1				x																					
Costa Rica	2	1			x	x																					
Côte d'Ivoire	2	1				x	x																				
Croatia	4	1			x	x		x	x																		

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Cyprus	4	1			x	x		x	x																		
Czechia	4	1			x	x		x	x																		
Democratic Republic of the Congo	1	1				x																					
Denmark	3	1			x			x	x																		
Dominica	1	1					x																				
Estonia	4	1			x	x		x	x																		
Eswatini	1	1				x																					
Ethiopia	1	1					x																				
Faroe Islands	3	1			x			x	x																		
Fiji	2	1				x			x																		
Finland	4	1			x	x		x	x																		
France	4	1			x	x		x	x																		
Germany	4	1			x	x		x	x																		
Greece	4	1			x	x		x	x																		
Greenland	2	1			x				x																		
Grenada	2	1				x	x																				
Guinea-Bissau	1	1				x																					
Haiti	2	1				x			x																		
Iceland	4	1			x	x		x	x																		
Ireland	4	1			x	x		x	x																		
Israel	2	1			x				x																		
Italy	4	1			x	x		x	x																		

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Jamaica	2	1				x	x																				
Kosovo	1	1				x																					
Kuwait	4	1			x	x		x	x																		
Latvia	4	1			x	x		x	x																		
Lesotho	1	1				x																					
Liberia	1	1				x																					
Liechtenstein	4	1			x	x		x	x																		
Lithuania	4	1			x	x		x	x																		
Luxembourg	4	1			x	x		x	x																		
Madagascar	1	1					x																				
Malawi	1	1				x																					
Malta	4	1			x	x		x	x																		
Monaco	1	1			x																						
Nauru	1	1				x																					
Netherlands	4	1			x	x		x	x																		
New Zealand	3	1			x	x		x																			
Norway	3	1			x			x	x																		
Papua New Guinea	2	1				x		x																			
Poland	4	1			x	x		x	x																		
Portugal	4	1			x	x		x	x																		
Qatar	2	1			x				x																		
Republic of Korea	4	1			x	x		x	x																		
Romania	4	1			x	x		x	x																		

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Rwanda	3	1			x	x			x																		
Saint Kitts and Nevis	1	1					x																				
Saint Lucia	1	1					x																				
Sao Tome and Principe	1	1				x																					
Saudi Arabia	3	1			x	x			x																		
Singapore	2	1			x				x																		
Slovakia	4	1			x	x		x	x																		
Slovenia	4	1			x	x		x	x																		
South Sudan	1	1				x																					
Spain	4	1			x	x		x	x																		
Sudan	1	1				x																					
Suriname	1	1					x																				
Sweden	4	1			x	x		x	x																		
Switzerland	3	1			x			x	x																		
The Bahamas	1	1					x																				
Tonga	1	1					x																				
Uganda	1	1				x																					
United Kingdom of Great Britain and Northern Ireland	4	1			x	x		x	x																		
United States of America	3	1			x			x	x																		

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Vatican	1	1			x																						
Yemen	1	1				x																					
Zambia	2	1				x		x																			
Albania	4		1		x	x				x				x													
Angola	4		1			x					x			x	x												
Antigua and Barbuda	2		1				x							x													
Argentina	7		1		x	x	x			x	x			x			x										
Armenia	3		1			x				x				x													
Azerbaijan	4		1		x	x				x				x													
Bahrain	6		1		x		x	x			x			x	x												
Bangladesh	7		1		x		x	x	x	x	x			x													
Belize	2		1			x					x																
Benin	2		1			x				x																	
Bolivia (Plurinational State of)	3		1				x				x			x													
Brazil	7		1		x	x	x	x		x	x			x													
Brunei Darussalam	4		1		x	x			x		x																
Cambodia	3		1			x				x	x																
Chile	6		1		x	x		x		x				x			x										
Colombia	5		1		x	x		x	x	x																	
Dominican Republic	3		1		x	x				x																	
Ecuador	5		1		x	x				x				x			x										

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Egypt	6		1			x	x	x		x	x			x													
El Salvador	3		1		x	x				x																	
Gambia	2		1			x					x																
Georgia	4		1		x	x				x	x																
Ghana	4		1			x	x	x						x													
Guatemala	3		1			x			x					x													
Guyana	4		1			x					x			x				x									
Honduras	3		1				x		x					x													
Hong Kong	2		1		x					x																	
Hungary	8		1		x	x	x	x	x		x			x			x										
India	7		1			x	x	x	x					x				x	x								
Indonesia	7		1		x	x		x	x	x	x						x										
Iran (Islamic Republic of)	5		1			x					x			x				x				x					
Iraq	4		1		x	x					x			x													
Japan	3		1		x	x							x														
Jordan	4		1		x	x					x			x													
Kenya	4		1			x			x		x			x													
Lebanon	4		1		x		x				x			x													
Libya	5		1		x	x		x	x					x													
Malaysia	7		1		x	x		x	x	x	x						x										
Maldives	6		1		x		x	x	x		x			x													
Mali	2		1			x								x													
Mauritius	5		1			x					x			x	x			x									

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Mexico	9		1		x	x		x	x	x	x			x			x	x									
Mongolia	6		1		x	x			x		x			x	x												
Morocco	4		1			x	x				x			x													
Myanmar	2		1				x							x													
Namibia	3		1				x				x			x													
Nepal	5		1				x			x	x			x				x									
Nicaragua	3		1				x							x	x												
Niger	2		1			x					x																
Nigeria	7		1		x	x	x	x	x		x			x													
North Macedonia	4		1		x	x					x			x													
Oman	4		1		x	x				x				x													
Pakistan	7		1		x	x			x	x	x			x			x										
Panama	4		1		x	x				x				x													
Paraguay	6		1		x	x				x	x			x				x									
Peru	3		1		x	x					x																
Philippines	10		1		x	x		x	x	x	x			x	x	x		x									
Republic of Moldova	3		1		x	x								x													
Saint Vincent and the Grenadines	5		1		x		x	x	x					x													
Senegal	2		1			x					x																
Serbia	4		1		x	x					x			x													
Seychelles	4		1				x		x		x			x													
Sierra Leone	2		1			x					x																

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Solomon Islands	2		1				x				x																
Somalia	2		1				x				x																
South Africa	4		1		x		x	x		x																	
Sri Lanka	5		1		x		x			x	x			x													
Taiwan	3		1			x			x																	x	
Tajikistan	2		1			x				x																	
Thailand	6		1		x	x		x	x	x	x																
Timor-Leste	2		1			x				x																	
Togo	3		1			x	x			x																	
Trinidad and Tobago	3		1		x		x				x																
Tunisia	6		1		x	x		x		x	x			x													
Turkey	3		1		x					x				x													
Ukraine	4		1		x		x	x		x																	
United Arab Emirates	5		1		x	x			x		x			x													
Uruguay	3		1		x	x				x																	
Uzbekistan	3		1			x								x						x							
Vanuatu	2		1			x					x																
Viet Nam	6		1		x	x		x	x		x			x													
West Bank	4		1		x				x					x	x												
Zimbabwe	5		1					x		x	x			x				x									
Algeria	1			1										x													
Belarus	3			1							x			x	x												

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Cameroon	2			1							x			x													
Chad	1			1							x																
China	6			1						x	x					x	x			x	x						
Comoros	1			1							x																
Congo	1			1											x												
Cuba	2			1							x																x
Djibouti	1			1										x													
Equatorial Guinea	1			1							x																
Gabon	2			1							x			x													
Guinea	1			1										x													
Kazakhstan	4			1						x				x	x										x		
Kyrgyzstan	4			1							x			x	x										x		
Lao People's Democratic Republic	3			1						x	x			x													
Mauritania	1			1							x																
Montenegro	2			1							x			x													
Mozambique	1			1							x																
Puerto Rico	0			1																							
Republic of the Congo	2			1							x			x													
Russian Federation	4			1										x	x								x	x			
San-Marino	1			1										x													

Country	n vaccines	Only Medsafe recognised	Medsafe recognised plus others	No Medsafe recognised	Pfizer	AZ	AZ SII	Janssen	moderna	Sinovac	Sinopharm (beijing)	Novavax*	moderna (takeda)	Gamaleya (sputnik)	Gamaleya (sputnik light)	Sinopharm	Cansino	Bharat biotech	Zydus cadila	anhui zhifei	minhai	shifa	FBRI	chumakov	khazakstan ribsp	medigen	CIGB
Syrian Arab Republic	1			1										x													
Turkmenistan	2			1										x									x				
United Republic of Tanzania	1			1						x																	
Venezuela (Bolivarian Republic of)	3			1							x			x	x												

Source: https://covid19.trackvaccines.org/trials-vaccines-by-country 17 September 2021

* Novavax included in table although not approved/authorised in any country

Memo

COVID-19 vaccines for arrivals to Aotearoa New Zealand: COVID-19 Vaccine Technical Advisory Group (CV TAG) Recommendations

Date:	1 October 2021
To:	Laupepa Va'a, Workstream Lead, Polynesian Pandemic Preparedness, Pacific Health Corridors, Global Health
Copy to:	Alison Cossar, Manager, Public Health Policy, Systems Strategy and Policy Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme Maree Roberts, Deputy Director General, System Strategy and Policy Niki Stefanogiannis, Deputy Director Public Health, Population Health and Prevention
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. This memo summarises the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on COVID-19 vaccination requirements for people arriving to the country under the Recognised Seasonal Employer (RSE) scheme. These recommendations are made as a part of the next step in the phased introduction of vaccination requirements at the border.

Background and context

2. CV TAG has previously provided recommendations on COVID-19 vaccination requirements for Border Workers, recognising that enhanced protection against infection was needed due to their individual occupational risk profile but also the broader public health benefit through reducing viral infection and onward transmission. Details of recommendation are provided in Appendix 1.

3. Recommendations have also been provided on vaccination requirements for entering managed isolation and quarantine (MIQ). These recommendations specify that a full primary course of vaccination with any COVID-19 vaccine would be acceptable for entering MIQ. For those who have had a full primary course of a vaccine NOT approved, provisionally approved, or authorised for emergency use by a Medsafe-recognised authority, they should be offered an additional dose of Pfizer vaccine. Further details of recommendation are provided in Appendix 2.

4. COVID-19 vaccines currently provisionally approved by Medsafe for use in New Zealand are Pfizer, Janssen, and AstraZeneca. An application for the Novavax COVID-19 vaccine has been received, but the timeframe for completion depends on further data from the sponsor.[1]

5. Medsafe considers that the following authorities follow similar international standards and guidelines to Medsafe. This allows Medsafe to facilitate abridged evaluations of new medicine applications in New Zealand via the abbreviated application pathway. The Medsafe recognised authorities are: The Australian Therapeutic Goods Administration (TGA), The United States Food and Drug Administration (FDA), Health Products and Food Branch of Health Canada, Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom, the European Medicines Agency (EMA) (centralised procedure only) and EU member states (decentralised or mutual recognition procedure only).[2]

6. COVID-19 vaccines that do not have Medsafe approval or provisional approval, but comply with requirements of Medsafe-recognised authorities are: Moderna mRNA vaccine (Spikevax) - TGA, FDA, Health Canada, MHRA, and EMA; and the AstraZeneca vaccine manufactured by the Serum Institute of India (Covishield) - Health Canada.[3-7] Vaccines that are currently under rolling review by the EMA but not yet approved include CureVac, Gamalaya (Sputnik V), Sinovac (Coronavac) and Vidprevtyn from Sanofi-GSK.

7. As part of the continual improvement approach to reduce the risk of COVID-19 entering the community, the Government has signalled it wants to look at vaccination requirements for arrivals to New Zealand. In the short term, imposing a vaccination requirement on inbound RSE workers has been proposed as a next step in the phased introduction of vaccination requirements at the border.

8. The Government have announced that a one-way quarantine-free travel scheme will be open for RSE workers from Samoa, Tonga and Vanuatu. This begins from 4 October for RSE workers from Vanuatu, and 12 October for RSE workers from Samoa and Tonga. This scheme will allow up to 14,400 workers from those Pacific nations to enter without 14 days in MIQ.

9. Current requirements as part of this scheme specify that RSE workers must have had at least one dose of vaccination pre-departure, undertake Day 0 and Day 5 tests, and complete a 7-day self-isolation period in employer-arranged accommodation. They will be released to work after a negative Day 5 result.

10. RSE workers are expected to arrive having received either the AstraZeneca vaccine (Samoa, Tonga and Vanuatu) or the Sinopharm vaccine (Vanuatu). The Government has been informed that most RSE workers will be fully vaccinated, however some may arrive having only had one dose. The issue of people arriving with 1 dose will be time-restricted in that by late 2021 all incoming RSE workers should be fully vaccinated.

11. The Ministry of Health's Global Health Polynesian Health Corridors team and Polynesian Pandemic Preparedness Workstream has requested advice about the vaccination requirements for RSE workers:

    a. who have received a full primary course of vaccination with the AstraZeneca vaccine;

    b. who have received a full primary course of vaccination with the Sinopharm vaccine;

    c. who have received an incomplete primary course of one dose of the AstraZeneca vaccine;

    d. who have received an incomplete primary course of one dose of the Sinopharm vaccine.

Recommendations

12. CV TAG met on 21 September 2021 to consider recommendations regarding COVID-19 vaccines for arrivals to Aotearoa New Zealand.

13. CV TAG noted that:

    a. There have been no cases of COVID-19 in Samoa, Tonga, and Vanuatu in the last 6 months. Therefore, the purpose of these entry requirements for RSE workers is to ensure they are protected from COVID-19 while in New Zealand with a similar level of protection as others in New Zealand.

    b. Data are still emerging on the efficacy of heterologous vaccine schedules from approved and recognised vaccines in New Zealand's portfolio. Initial results show that mixing doses of mRNA and adenovirus-vectored vaccines is associated with an acceptable reactogenicity profile and generates levels of anti-spike neutralising antibody titres shown to provide high levels of protection in primary efficacy trials.[8-10]

    c. Because receiving vaccines for COVID-19 are free to all within New Zealand, no cost will be associated with administration of any additional doses to RSE workers.

14. CV TAG recommends that:

For RSE workers who have received	**Recommendation**
a. 2 doses of the AstraZeneca vaccine	This is a full primary course of vaccination approved by Medsafe. Considered 'fully vaccinated'.
b. 2 doses of the Sinopharm vaccine	This vaccine is NOT approved by Medsafe and/or Medsafe recognised authorities. These RSE workers should receive one dose of the Pfizer vaccine.
c. 1 dose of the AstraZeneca vaccine	These RSE workers should receive one dose of the Pfizer vaccine.
d. 1 dose of the Sinopharm vaccine	

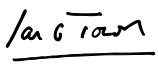
    e. Regarding timing, administration of any additional doses should occur:

        i. At least 28 days after the most recent dose of COVID-19 vaccine, with no upper limit on time since the last dose.

        ii. If the interval since the most recent dose allows, the Pfizer dose should be offered to people on entry, while in self-isolation or at the latest as they leave self-isolation.

iii. If the interval since the most recent dose does not allow vaccination before leaving self-isolation, a vaccination booking at the earliest available opportunity will be made before leaving self-isolation.

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



Dr Ian Town
Chief Science Advisor and Chair of the COVID-19 Vaccine Technical Advisory Group

References

1. Medsafe. *Approval status of COVID vaccines applications received by Medsafe*. 2021 [cited 2021 27 August]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.
2. Medsafe, *New Zealand Regulatory Guidelines for Medicines*, in *Part A: When is an application for approval of a new or changed medicine required?*, Medsafe, Editor. 2014, Medsafe: Medsafe. p. 132.
3. The Australian Therapeutics Goods Administration. *COVID-19 vaccine: Provisional registrations*. 2021; Available from: https://www.tga.gov.au/covid-19-vaccine-provisional-registrations.
4. European Medicines Agency. *COVID-19 vaccines: authorised*. 2021 [cited 2021 27 August]; Available from: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#authorised-covid-19-vaccines-section.
5. Government of Canada. *Drug and vaccine authorizations for COVID-19: List of applications received*. 2021; Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/applications.html.
6. National Health Service. *Coronavirus (COVID-19) vaccines*. 2021 [cited 2021 27 August]; Available from: https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/coronavirus-vaccine/.
7. US Food and Drug Administration. *COVID-19 Vaccines*. 2021 [cited 2021 27 August]; Available from: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
8. Gross, R., et al., *Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity.* medRxiv, 2021: p. 2021.05.30.21257971.
9. Borobia, A.M., et al., *Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomised, Adaptive, Phase 2 Trial (CombiVacS).* SSRN, 2021.
10. Liu, X., et al., *Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial.* The Lancet, 2021.

Appendix 1: Previous CV TAG recommendations for Border Workers

CV TAG has previously provided advice on COVID-19 vaccination requirements for Border Workers, recognising that enhanced protection against infection was needed due to their individual occupational risk profile but also the broader public health benefit through reducing viral infection and onward transmission. CV TAG noted that:

a. Data are still emerging on the efficacy of heterologous vaccine schedules from approved and recognised vaccines in New Zealand's portfolio, however initial results show that mixing vaccine doses is associated with a low incidence of adverse effects and could provide an improved immune response through increased anti-spike antibody titres and neutralising antibodies.[8-10]

b. Protection against symptomatic infection is of enhanced importance for work at the Border. Extensive data has emerged showing high efficacy and effectiveness against symptomatic infection after two doses of the Pfizer, AstraZeneca, or Moderna vaccines in Phase 3 clinical trials and large post-marketing studies. There is strong evidence that the Janssen vaccine (the single-dose, adenovirus vector vaccine) provides a high degree of protection against moderate and severe disease from COVID-19, however there are fewer data on the efficacy or effectiveness against symptomatic infection, especially in the context of the Delta variant of SARS-CoV-2, and the immune response appears to be lower.

On this basis, CV TAG recommended for Border Workers that:

c. A full course of vaccination with a COVID-19 vaccine recognised by Medsafe or a Medsafe recognised authority provides sufficient protection from COVID-19 for work at the Border, with the exception of the Janssen vaccine as a single dose schedule.

d. A 'booster' dose of the Pfizer vaccine should be administered for Border workers who have only received a single dose of the Janssen vaccine, due to the higher risk of SARS-CoV-2 infection for Border work, and the need for enhanced protection against infection among Border Workers

e. If a worker is in New Zealand and has an incomplete vaccination with a vaccine recognised by Medsafe or a Medsafe recognised authority, they should complete their vaccination by receiving one dose of the Pfizer vaccine. This should occur at least 21 days after the first dose of the Pfizer vaccine, or at least 28 days after the first dose of AstraZeneca or Moderna. There is no upper time limit on time for when that dose can be administered.

f. Border workers who have received a partial or complete course of vaccine with a COVID-19 vaccine not approved by Medsafe or a Medsafe recognised authority, should also receive one dose of the Pfizer vaccine.

Appendix 2: Previous CV TAG recommendations for entry to MIQ

CV TAG have previously provided advice on COVID-19 vaccination requirements for entering MIQ. CV TAG noted that:

a. officials are preparing a proposal for the Minister for COVID-19 Response to take to Cabinet that would impose a pre-entry requirement from 1 November 2021, that all (non-New Zealand citizen) arrivals by air are fully vaccinated.

b. under this proposal all arrivals would still undergo testing and 14 days MIQ, which will continue to be the key line of defence.

c. this is being proposed as an additional precautionary measure to further reduce the risk of COVID-19 entering the New Zealand community (and until New Zealand achieves high vaccination coverage).

d. are significant ethical and equity issues given that most people have no choice about which vaccine they receive, and many countries still have poor access to vaccines and low vaccination rates.

e. while the effectiveness varies across the different vaccine products, any vaccine is better than no vaccine.

f. new recommendations will be needed if requirements around MIQ on entry to Aotearoa New Zealand change. This is due to different considerations around requirements of vaccines without MIQ as the key line of defence.

g. updated recommendations will likely be needed if there are changes to the approved COVID-19 vaccination schedules in New Zealand.

On this basis, CV TAG recommended for arrivals to MIQ:

a. a full primary course of vaccination with any of the 22 COVID-19 vaccines approved by at least one government or authority (or an approved combination of those vaccines in their origin country) with the last dose at least 14 days before arrival would be acceptable for entering MIQ for 14 days, given that testing and MIQ would provide the key line of defence. Vaccination should be documented in the manner that the origin country provides.

b. an exemption process should be put in place for those who require an exemption on humanitarian grounds, because they are below the approved age for COVID-19 vaccination in their origin country, or for other similar reasons.

c. those aged 12 years or over who enter the country with a full primary course of vaccination, but with a vaccine that is NOT one of those approved by a Medsafe-recognised authority should be offered an additional dose of Pfizer vaccine as soon as possible after entry to New Zealand (and at the latest as they leave MIQ). This should occur at least 28 days after the last dose, with no upper limit on time since the last dose.

d. those who enter the country, are aged 12 years or over, and have received no doses of any of the 22 COVID-19 vaccines, should be offered a full course of Pfizer vaccine as soon as possible after entry to New Zealand (and at the latest receiving the first dose as they leave MIQ).

e. those who enter the country, are aged 12 years or over and have received an incomplete primary course of any of the 22 COVID-19 vaccines (whether approved by a Medsafe-recognised authority or not), should be offered an additional dose of Pfizer vaccine as soon as possible after entry to New Zealand.

   ii. this should occur at least 28 days after the most recent dose of COVID-19 vaccine, with no upper limit on time since the last dose.

   iii. if the interval since the most recent dose allows, vaccination with Pfizer should be offered to people while in MIQ or at the latest as they leave MIQ.

   iv. if the interval since most recent dose does not allow vaccination on or before leaving MIQ, a future vaccination booking should be offered as they leave MIQ at the latest.

Memo

Decision to use the AstraZeneca COVID-19 vaccine: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	27th October 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
Cc:	Dr Ashley Bloomfield, Director-General of Health Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the decision to use the AstraZeneca COVID-19 vaccine ('the AstraZeneca vaccine').

Context

2. In February 2021, CV TAG advice was sought for use of the Pfizer COVID-19 vaccine for people who were 16 years and over, following Medsafe provisional approval. Cabinet agreed that the COVID-19 Vaccine Immunisation Programme proceed with the rollout of the Pfizer vaccine. It was noted that further advice would be provided to Cabinet on each vaccine candidate as they became available for use (following Medsafe approval), without knowing if a future vaccine was going to be more suitable or effective. In order to make decisions given the uncertainty, a Decision to Use framework was developed.
3. In July 2021, CV TAG advice was sought on the use of the Janssen COVID-19 vaccine for people aged 16 years and over, following Medsafe provisional approval. CV TAG advised that there was no current indication for wide use of the Janssen vaccine, however that it could be considered at an individual level where the Pfizer vaccine was not suitable e.g., anaphylaxis or other rare side effects following the first dose of the Pfizer vaccine. Cabinet considered the recommendations for the Decision to Use the Janssen vaccine and agreed to proceed with taking receipt of up to 500,000 doses in October 2021 for those individuals unable to receive the Pfizer vaccine (e.g., anaphylaxis), or for people who are hesitant to receive a messenger RNA (mRNA) vaccine.
4. At the time Cabinet made this decision, it was expected that Janssen's vaccine would be available in New Zealand in Q4 2021. However, as a result of subsequent regulatory issues relating to the manufacture of Janssen's vaccine, it is unlikely that Janssen will be able to provide supply any earlier than January 2022. Given the uncertainty around accessing

Janssen's vaccine in 2021, the Ministry's Policy team are looking to secure supply of the AstraZeneca vaccine in the coming weeks.

5. The Ministry's Policy team sought clinical and scientific advice from CV TAG on the use of the AstraZeneca vaccine in New Zealand.

6. The AstraZeneca vaccine was granted provisional approval by Medsafe for use in people aged 18 and over in New Zealand on 22 July 2021, under section 23 of the Medicines Act, with conditions.[1]

7. It is a two-dose non-replicating viral vector vaccine, and the second dose is administered between 4 and 12 weeks after the first dose. It can be stored at 2-8°C for up to 6 months. Multiple doses may be pre-drawn from one vial and used within one hour if stored at room temperature, or within six hours if stored at 2-8°C.[2]

8. The overall safety and efficacy of the AstraZeneca vaccine is based on analysis of pooled data from four phase III clinical trials (COV001, COV002, COV003, and COV005) conducted in the United Kingdom (UK), Brazil, and South Africa. At the time of analysis, 24,244 participants aged 18 and over had been randomised and received either the AstraZeneca vaccine or control. Additional safety of the AstraZeneca vaccine was established in a randomised phase III clinical trial conducted in the United States, Peru, and Chile.[3, 4]

9. The AstraZeneca vaccine provides efficacy against COVID-19 infection and severe disease. Vaccine efficacy against symptomatic, lab-confirmed, COVID-19 at least 14 days after two standard doses, with 4-to-12-week intervals, was 63.1% (95%CI: 51.8-71.1) in pooled data from the trials conducted in the UK, Brazil and South Africa.[3] In the US, Chile, and Peru trial, efficacy was 74% (95%CI: 65.3-80.5) from 15 days after the second dose when given four weeks apart.[4] Efficacy against severe disease or hospitalisation was found to be 100% (95% CI 72.2-100%) from >21 days after the second dose across clinical trials.[3, 4]

10. Intervals between doses varied in clinical trials, and post hoc analysis indicated that longer intervals were associated with a stronger immune response. When the dose interval was stratified in the initial phase III trial, an interval of <6 weeks was associated with 55.1% (95%CI 33.0-69·9%) efficacy, at 6-8 weeks it was 59·9% (95%CI 32.0–6.4%), at 8-11 weeks it was 63.7% (95%CI 28.0-81.7%) and ≥12 weeks it was 81.3% (95%CI 60.3 – 91.2%).[5]

11. Estimates for effectiveness against viral infection ranged from 73% to 94.9% pre-Delta,[6-9] and against severe disease were 72.8% (95%CI: 71.8-73.8).[10] Real world effectiveness has seen a modest decline, however it is unclear if this is due to Delta or waning efficacy of the vaccine. Results from a UK study demonstrated high vaccine effectiveness against hospitalisation, however it declined from 93.9% (95% CI: 91.3%-95.7%) at 1 week after the second dose to 77% (95% CI: 70.3%-82.3%) at 20+ weeks. Effectiveness against symptomatic COVID-19 also declined from 62.7% (95% CI: 61.7%-63.8%) at 1 week after the second dose to 47.3% (95% CI: 45%-49.6%) at 20+ weeks.[11] Effectiveness against death was 94.1% (95%CI: 91.8-95.8) at 2-9 weeks after the second dose and then fell to 78.7% (95%CI: 52.7-90.4) by 20+ weeks.[11]

12. Data about effects on transmission remain limited. Unvaccinated members of a household, in which the primary infection is someone vaccinated with one dose of AstraZeneca, were (for respectively AstraZeneca, and AstraZeneca and Pfizer together) around 40-50%,[12] and 30%,[13] less likely to become a secondary infection compared to those in unvaccinated healthcare worker households.

13. Continued safety monitoring is essential to understand the long-term safety profile of this platform.

    a. Severe occurrences of various systemic reactions after the first dose were reported in <10% 18-55 year olds in the phase I/II trial, which were reduced with the use of prophylactic paracetamol.[14] The most frequent solicited adverse events (reported in more than 1 in 10 people) were injection-site tenderness and pain, feeling feverish (pyrexia), chills, myalgia, headache, malaise, arthralgia, and nausea.[14, 15] Systemic adverse events of all severities were less common in those over 55 years compared to younger adults, and also less common after a second dose.[16] Overall, reactogenicity rates appear higher among ≤ 50 than > 50 year-olds, women and those with prior symptomatic/confirmed COVID-19.[17]

14. *Thrombosis with thrombocytopaenia syndrome (TTS):* A very rare and serious syndrome called thrombosis with thrombocytopaenia syndrome (TTS) has been observed following vaccination with the AstraZeneca vaccine during post-marketing use. This includes cases presenting as venous thrombosis, including unusual sites such as cerebral venous sinus thrombosis (CVST), splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia.[18]

    a. The European Medicines Agency (EMA) concluded on 8 April 2021 that there was a strong relationship between TTS coagulation disorders and administration of the vaccine, such as disseminated intravascular coagulation, CVST, as well as arterial thromboembolic and haemorrhagic stroke. According to the EMA, a total of 1,503 cases had been reported worldwide as of 31 July 2021, while around 592 million doses of the AstraZeneca vaccine had been administered by 25 July 2021. The majority of the events occurred within the first 21 days following vaccination but have also been reported after this period.[19-21]
    b. Whilst specific risk factors for thromboembolism in combination with thrombocytopenia have not been identified, cases have occurred in patients with a previous history of thrombosis, as well as in patients with autoimmune disorders, including immune thrombocytopenia.[18]
    c. Up to 6 October 2021, there were 424 cases of TTS reported to the UK's MHRA following vaccination with AstraZeneca, of which 46 were following the second dose. Of the 424 reports, 213 occurred in women, and 207 occurred in men aged from 18 to 93 years. The overall case fatality rate was 17% with 72 deaths, six of which occurred after the second dose. This equates to 15.2 cases reported per million first doses.[22]
    d. In Australia, the risk of developing TTS after a first dose of AstraZeneca was estimated to be 20 in a million.[23] As of 17 October, there have been 156 cases of TTS assessed as related to the AstraZeneca vaccine in Australia from approximately 12.6 million vaccine doses. These cases most often occurred about 2-3 weeks after vaccination. The risk of TTS after a second dose appears to be much lower than after the first dose. The risk of dying from TTS after vaccination is reported to be approximately 1 in a million (for people receiving a first dose), and somewhat less than this when both doses are taken into consideration.[24]
    e. The incidence rate is higher in the younger adult age groups following the first dose compared to older age groups. According to data from the UK's MHRA, the incidence

rate is 20.9 per million doses in those aged 18-49 years, compared to 10.9 per million doses in those aged 50 years and over.[22] According to data from Australia's COVID-19 vaccine weekly safety report up to 21 October 2021, the reporting rate of TTS remains higher in people aged under 60 years (2.5 per 100,000 doses) compared to those aged 60 and over (1.8 per 100,000 doses). Women in younger age groups seem to be slightly more likely to develop clots in unusual locations, such as the brain or abdomen, which have more serious outcomes. Eight people have died as a result of TTS, and of those six were women.[24]

15. *Guillian-Barré syndrome (GBS).* GBS has been reported very rarely following vaccination with the AstraZeneca vaccine.[18] At the EMA Pharmacovigilance Risk Assessment Committee (PRAC) meeting from 05-08 July 2021, it was recommended that a warning for GBS following vaccination be added to the data sheet. They did not ascribe causality but concluded that it is possible that GBS is a side effect of the vaccine.[25] On 08 September, the EMA added GBS following vaccination as a very rare side effect to the AstraZeneca product information sheet.[26]
16. *Capillary leak syndrome (CLS).* Very rare cases of CLS have been reported in the first days after vaccination with the AstraZeneca vaccine. A history of CLS was apparent in some of these cases. Fatal outcome has been reported.[18] Both the UK's MHRA and the EMA's PRAC recommend that people with a history of CLS should not receive the vaccine.[27, 28] On 10 June 2021, PRAC recommended that CLS be added as an adverse reaction for the AstraZeneca vaccine.
17. Several countries have restricted the use of the AstraZeneca vaccine in different age groups, including Australia, Canada, Germany and the UK.[29-32]
    a. In Australia, the Australian Technical Advisory Group on Immunisation (ATAGI) has provided guidance about the risk-benefit for the AstraZeneca vaccine by age group. In a large outbreak, ATAGI advises that the benefits of the AstraZeneca vaccine are greater than the risk of rare side effects for all age groups. Where background risk of COVID-19 exposure and disease is low, AstraZeneca vaccine is recommended only for people aged 60 and over. However, anyone aged 18 to 59 years can choose to receive the AstraZeneca vaccine either following discussion with a qualified health professional, or if they provide verbal or written consent. Most people have their second dose 12 weeks after their first, but ATAGI recommends 4 to 8 weeks between the first and second doses in an outbreak so maximal protection against COVID-19 can be achieved earlier.[23]
    b. In Canada, the National Advisory Committee on Immunisation recommends the AstraZeneca vaccine for individuals 30 years of age and older who do not wish to wait for an mRNA vaccine, expanded from its previous guidance of a higher age limit of 55 years because of concerns over TTS.[31]
    c. In the UK, MHRA recommend adults aged 18-39 years with no underlying health conditions are offered an alternative to the Oxford-AstraZeneca vaccine, if this does not cause delays in having the vaccine.
18. This advice should be considered as part of the Decision to Use Framework and alongside policy considerations on the sequencing of the COVID-19 Vaccine and Immunisation Programme.

Recommendations

19. CV TAG met on 19 October to discuss use of the AstraZeneca COVID-19 vaccine, noting the information provided in the Pfizer vaccine Data Sheet.

20. **CV TAG noted that**:

    a. The contraindications for the AstraZeneca vaccine are:[18]

        i. Hypersensitivity to the active substance or to any of the excipients.
        ii. Patients who have experienced major venous and/or arterial thrombosis with thrombocytopenia following vaccination with any COVID-19 vaccine.
        iii. Individuals who have previously experienced episodes of capillary leak syndrome.

    b. COVID-19 disease is associated with many complications including the development of blood clots. Administration of the AstraZeneca vaccine is rarely associated with thrombosis and thrombosis with thrombocytopaenia syndrome (TTS). TTS has a higher incidence among younger populations which is important to be aware of, however the risk is much less common than thrombotic complications from the COVID-19 disease itself.
    c. In general, the Pfizer vaccine offers a higher level of protection than the AstraZeneca vaccine. The efficacy of the AstraZeneca vaccine against symptomatic, laboratory confirmed COVID-19 at least 14 days after two standard doses, with 4-to-12-week intervals, was 63.1% (95%CI: 51.8-71.1)[3], compared to 95% (95%CI: 90.3-97.6) for the Pfizer vaccine.[33] However the AstraZeneca vaccine still provides high protection and efficacy against infection, disease, and death.
    d. Data are still emerging on the safety and efficacy of heterologous ("mixed dose") vaccine schedules from approved vaccines in New Zealand. Initial results show that mixed schedules of the Pfizer vaccine with the AstraZeneca vaccine (for example, one dose of AstraZeneca followed some weeks later by one dose of Pfizer) is associated with an acceptable reactogenicity profile and generates levels of anti-spike neutralising antibody equivalent or greater than those associated with high levels of protection in primary efficacy trials.[34-36] In the UK COM-COV study, participants were randomised to a first dose of Pfizer with a second dose of AstraZeneca 4-weeks later. Antibody responses were inferior to two doses of Pfizer/BioNTech (homologous).[36] The relevance of this to clinical effectiveness is unknown, though the vaccine schedule was still considered to provide protection.
    e. Data on safety and efficacy of the AstraZeneca vaccine in people aged less than 18 years and old and in pregnant women, or women who became pregnant after receiving the vaccine, are limited. Medsafe consider available data insufficient to assess risk-benefit in people aged less than 18 years old or pregnant women.[18]
    f. The AstraZeneca vaccine is included as part of the ComFluCOV study looking at the safety and immunogenicity of concomitant administration of AstraZeneca or Pfizer COVID-19 vaccines with three different seasonal influenza vaccines in adults. Most reactions were mild to moderate, with local and unsolicited systemic reactions similar between randomised groups. No significant difference was observed regardless of whether the shots were given on the same day or 3-4 weeks apart.[37]

21. **CV TAG recommends that:**

a. The COVID-19 Vaccine Immunisation Programme use the AstraZeneca vaccine as a second-line vaccine, with Pfizer remaining the first-line and preferred vaccine.

b. Use of the AstraZeneca vaccine be restricted to people who have a contraindication to the Pfizer vaccine, or people who would prefer to get the AstraZeneca vaccine and are currently under a Vaccination Order, or who are unvaccinated or incompletely vaccinated and hesitant about getting the Pfizer vaccine.

c. Within the groups outlined in 21)b, the AstraZeneca vaccine be made available to the following eligible groups:

   i. People aged 60 years and over without contraindications.

   ii. People aged 18 to 59 without contraindications and who prefer to receive the AstraZeneca vaccine after discussion with a qualified health professional.

d. There is currently insufficient data on the AstraZeneca COVID-19 vaccine to recommended it during pregnancy. Use in pregnancy should be based on an assessment of benefits and risks by the consumer and their healthcare professional.

e. With regard to timing:

   i. two doses of the AstraZeneca vaccine, given 4 to 12 weeks apart, are necessary to be considered fully vaccinated.

   ii. a shorter interval of more than 4 to less than 8 weeks between the first and second doses is recommended in an outbreak to provide earlier protection.

   iii. administration of the AstraZeneca vaccine as a second dose should occur at least 28 days after the most recent dose of another COVID-19 vaccine.

   iv. there be no upper limit on time since the last dose.

   v. the AstraZeneca vaccine may be administered before, after, or at the same time as the influenza, MMR, HPV, diphtheria/tetanus/pertussis combination vaccine (Boostrix), and other vaccines. The only exception to this advice is for the live-attenuated shingles vaccine (Zostavax) where a 7-day interval, before or after administering the AstraZeneca vaccine is advised.

22. CV TAG will continue to monitor the evidence and will update their recommendations as data become available.

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

References

1. Medsafe. *Approval status of COVID vaccines applications received by Medsafe*. 2021 25 August 2021 [cited 2021 18 October]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.
2. NSW Government. *COVID-19 Vaccination Program Procedures*. 2021; Available from: https://www.health.nsw.gov.au/Infectious/covid-19/vaccine/Documents/az-refrigerator-to-administration.pdf.
3. Voysey, M., et al., *Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials*. The Lancet, 2021. **397**(10277): p. 881-891.
4. Falsey, A.R., et al., *Phase 3 Safety and Efficacy of AZD1222 (ChAdOx1 nCoV-19) Covid-19 Vaccine*. New England Journal of Medicine, 2021.
5. Voysey, M., et al., *Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials*. Lancet, 2021. **397**(10277): p. 881-891.
6. Pritchard, E., et al., *Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom*. Nature Medicine, 2021.
7. S, G., et al., *COVISHIELD (AZD1222) VaccINe effectiveness among healthcare and frontline Workers of INdian Armed Forces: Interim results of VIN-WIN cohort study*. Medical journal, Armed Forces India, 2021. **77**.
8. Sheikh, A., et al., *SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness*. The Lancet, 2021. **397**(10293): p. 2461-2462.
9. Issac, A., J. J Kochuparambil, and L. Elizabeth, *SARS-CoV-2 Breakthrough Infections among the Healthcare Workers Post-Vaccination with ChAdOx1 nCoV-19 Vaccine in the South Indian State of Kerala*. medRxiv, 2021.
10. Villela, D.A.M., et al., *Effectiveness of Mass Vaccination in Brazil against Severe COVID-19 Cases*. medRxiv, 2021: p. 2021.09.10.21263084.
11. Andrews, N., et al., *Vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK*. medRxiv, 2021: p. 2021.09.15.21263583.
12. Harris, R.J., et al., *Impact of vaccination on household transmission of SARS-COV-2 in England*. 2021.
13. V Shah, A.S., et al., *Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households*. 2021, Cold Spring Harbor Laboratory.
14. Folegatti, P.M., et al., *Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial*. Lancet, 2020. **396**(10249): p. 467-478.
15. Adam, M., et al., *Evaluation of Post-Vaccination Symptoms of Two Common COVID-19 Vaccines Used in Abha, Aseer Region, Kingdom of Saudi Arabia*. Patient Preference and Adherence, 2021. **Volume 15**: p. 1963-1970.
16. Ramasamy, M.N., et al., *Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial*. The Lancet, 2020. **396**(10267): p. 1979-1993.
17. Powell, A.A., et al., *Real-world data shows increased reactogenicity in adults after heterologous compared to homologous prime-boost COVID-19 vaccination, March-June 2021, England*. Euro Surveill, 2021. **26**(28).
18. Medsafe. *COVID-19 Vaccine AstraZeneca, Solution for injection, 5 x 1010 VP/0.5mL (TT50-10877)*. Approval status of COVID vaccines applications received by Medsafe 2021 04 June 2021 [cited 2021 09 June 2021]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.

19. (PRAC), P.R.A.C., *Signal assessment report on embolic and thrombotic events (SMQ) with COVID-19 Vaccine (ChAdOx1-S [recombinant]) – Vaxzevria (previously COVID-19 Vaccine AstraZeneca) (Other viral vaccines)*, in *PRAC Recommendation*, E.M. Agency, Editor. 2021, EMA: ema.europa.eu. p. 117.
20. European Medicines Agency (EMA). *Summary of product characteristics - AstraZeneca*. 2021 [cited 2021 23 August]; Available from: https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf.
21. **EMA**. *COVID-19 vaccine safety update VAXZEVRIA AstraZeneca AB*. 8 September 2021; Available from: https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-8-september-2021_en.pdf.
22. GOV UK. *Coronavirus vaccine - weekly summary of Yellow Card reporting*. 2021; Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting.
23. Department of Health. *Vaxzevria (AstraZeneca)*. 2021 [cited 2021 18 October]; Available from: https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines/approved-vaccines/astrazeneca.
24. Therapeutic Goods Administration. *COVID-19 vaccine weekly safety report - 21-10-2021*. COVID-19 vaccine weekly safety report 2021; Available from: https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-21-10-2021.
25. EMA. *Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5-8 July 2021*. Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) [Website] 2021 09 July 2021 [cited 2021 17 July 2021]; Available from: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-july-2021.
26. **EMA**. *COVID-19 vaccine safety update VAXZEVRIA AstraZeneca AB*. 8 September 2021; Available from: https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-8-september-2021_en.pdf.
27. MHRA, *Coronavirus Vaccine - summary of Yellow Card reporting*, in *Yellow card reporting*, M.a.H.p.R. Agency, Editor. 2021, MHRA: assets.publishing.service.gov.uk. p. 20.
28. EMA. *Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 7-10 June 2021*. News 2021 11 June 2021 [cited 2021 20 June 2021]; Available from: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-7-10-june-2021.
29. @Reuters. *Australia limits use of AstraZeneca COVID-19 vaccine to people over 60*. 2021 2021-06-17; Available from: https://www.reuters.com/business/healthcare-pharmaceuticals/australia-panel-recommend-astrazeneca-vaccines-only-above-60s-media-2021-06-17/.
30. The Independent. *Germany makes AstraZeneca vaccine available to all adults*. 2021; Available from: https://www.independent.co.uk/news/germany-makes-astrazeneca-vaccine-available-to-all-adults-astrazeneca-jens-spahn-germany-berlin-europe-b1843349.html.
31. CTVNews. *Canadians aged 30 and older can be offered AstraZeneca vaccine, national vaccine panel says | CTV News*. 2021 2021-04-23; Available from: https://www.ctvnews.ca/health/coronavirus/canadians-aged-30-and-older-can-be-offered-astrazeneca-vaccine-national-vaccine-panel-says-1.5399901.
32. BBC. *Under 40s to be offered alternative to AZ vaccine*. 2021 7 May 2021 [cited 2021 15 October]; Available from: https://www.bbc.com/news/health-57021738.

33. Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*. New England Journal of Medicine, 2020. **383**(27): p. 2603-2615.
34. Gross, R., et al., *Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity*. medRxiv, 2021: p. 2021.05.30.21257971.
35. Borobia, A.M., et al., *Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomised, Adaptive, Phase 2 Trial (CombiVacS)*. SSRN, 2021.
36. Liu, X., et al., *Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial*. The Lancet, 2021.
37. Lazarus, R., et al., *The Safety and Immunogenicity of Concomitant Administration of COVID-19 Vaccines (ChAdOx1 or BNT162b2) with Seasonal Influenza Vaccines in Adults: A Phase IV, Multicentre Randomised Controlled Trial with Blinding (ComFluCOV)*. 30th September 2021.

Memo

Temporary Medical Exemptions for the COVID-19 Vaccine: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	3 November 2021
To:	Dr Juliet Rumball-Smith, General Manager Clinical Quality & Safety, COVID-19 Vaccine Immunisation Programme (CVIP) Joanne Gibbs, Director of National Operations, CVIP
From:	Dr Ian Town, Chief Science Advisor, Ministry of Health
For your:	Consideration

Purpose of report

1. To outline the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the clinical criteria for medical exemptions to the first or second dose of the Pfizer COVID-19 vaccine.

Background and context

2. COVID-19 Vaccine Certificates (CVCs) are an important potential tool to help support the broader public health response to COVID-19, being particularly important in settings where there is greater risk of community transmission. In this context, CVCs, either in paper form or the digital equivalent, will allow people to demonstrate that they have been fully vaccinated or are medically exempt from vaccination for a defined period.

3. Evidence of medical exemption for vaccination is also important for people who are mandated to be vaccinated in certain roles due to their employment, such as border workers, teachers, healthcare workers, and employees of businesses where CVCs are mandatory.

4. To date, the Pfizer COVID-19 vaccine has shown an excellent safety and efficacy profile[1] and is recommended for all New Zealanders 12 years of age and over.[2]

5. The only contraindication to the Pfizer vaccine is hypersensitivity to the active substance or to any of the excipients, for example anaphylaxis to a vaccine component, such as polyethylene glycol (PEG).[3] Such reactions are rare and, even people with this history can usually receive the Pfizer vaccine after specialist assessment under supervision.[3]

6. Well-defined clinical criteria for a temporary medical exemption from full vaccination are needed for both the health professionals who will be asked to provide the exemption and for the people applying for an exemption, especially where CVCs are mandatory.

Medical Exemptions

7. Overall, the number of people in New Zealand estimated to be eligible for a medical exemption is expected to be small, and includes those who may be waiting for an alternative vaccine for their second dose, for example due to an adverse reaction following the first dose of the Pfizer vaccine.

8. The Australian Technical Advisory Group on Immunisation (ATAGI) have released guidance on medical exemptions.[4] ATAGI states that "*Vaccinations may reasonably be temporarily deferred for individuals with some acute major medical conditions (e.g. undergoing major surgery or hospital admission for a serious illness). Typically, these are time-limited conditions (or the medical treatment for them is time limited) and therefore temporary exemptions are considered appropriate. These exemptions are only to be given where a suitable alternative COVID-19 vaccine is not readily available for the individual*." Furthermore, the ATAGI guidance recommends a maximum duration of 6 months, with review as the individual recovers from their acute major medical illness.

First dose

9. The Pfizer data sheet provided to Medsafe documents the following contraindications only: *'Hypersensitivity to the active substance or to any of the excipients'*.[5] PEG is an excipient in the vaccine that is potentially associated with hypersensitivity reactions, but these are rare.[3, 6] It is possible for the Pfizer vaccine to be successfully administered despite a history of PEG allergy.[7]

10. It is difficult to estimate the number of people affected by these contraindications, due in part to the rarity of the events. However, the incidence of anaphylaxis following administration of the Pfizer vaccine is estimated at 8 cases per million doses administered in the US.[3] The current reporting rate for anaphylaxis (reports meeting levels 1-3 of the Brighton Collaboration case definition) in New Zealand is approximately 11 per million doses administered.[8]

11. Fewer people should request a medical exemption to the first dose of the Pfizer vaccine when a second class of vaccine becomes available, such as a vector-based vaccine (Janssen or AstraZeneca) for the population aged 18 and over.

Second dose

12. Myocarditis and/or pericarditis is a known rare side effect of the Pfizer vaccine and such events occurring after the first Pfizer dose may provide the basis for an exemption to the second dose.

13. Other adverse events that have been reported to the Centre for Adverse Reactions Monitoring (CARM), the Immunisation Advisory Centre (IMAC), or have been observed internationally[9] include: shingles, appendicitis, lymphadenopathy with or without fever, exacerbation of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), regional pain syndrome, and neurological events with localised arm pain. These events may or may not be related to the vaccine and it is generally advised to defer the second dose until the symptoms have fully resolved.

14. The number of people with medical exemptions to the second dose of the Pfizer vaccine should also decrease in size when a second class of vaccine becomes available, such as a vector-based vaccine (Janssen or AstraZeneca) for the population aged 18 and over.

Proposed principles of medical exemption

15. There are very few situations where a vaccine is contraindicated and, as such, a medical exemption is expected to be rarely required.

16. Vaccinations may reasonably be temporarily deferred for individuals with some acute major medical conditions, such undergoing major surgery or hospital admission for a serious illness. Typically, these conditions are considered time-limited, and therefore a temporary exemption is considered appropriate.

17. Exemptions are only to be given where a suitable alternative COVID-19 vaccine is not readily available for the individual.

18. Exemptions should be for a specified time, reflecting, for example, recovery from clinical conditions or the availability of alternate vaccines.

19. It is likely that most people who are not medically exempt can be safely vaccinated with extra precautions.

Recommendations

20. CV TAG recommends that the clinical criteria given in Table 1 below be used as the basis for temporary exemptions:

Table 1 Criteria for temporary COVID-19 vaccine exemption

	Type of vaccine	**Criteria for temporary exemption**
1.	Pfizer	1. Anaphylaxis to the first dose of the vaccine or known severe allergy to the excipients of the vaccine as per the datasheet provided to Medsafe.[a, b] 2. Myocarditis/pericarditis following the first dose of the vaccine.
2.	mRNA COVID-19 vaccine e.g. Pfizer, Moderna	1. Inflammatory cardiac illness within the past 6 months including: myocarditis, pericarditis, endocarditis, acute rheumatic fever or acute rheumatic heart disease (i.e., with active myocardial inflammation). 2. Acute decompensated heart failure. Although myocarditis and/or pericarditis is very rare following vaccination, if such an event were to occur, then it may exacerbate a patient's pre-existing heart failure.
3.	All COVID-19 vaccines	1. PCR-confirmed SARS-CoV-2 infection until complete recovery from the acute illness. Chronic symptoms following COVID-19 ("Long COVID") is

		not a contraindication to COVID-19 vaccine but does warrant a clinical discussion with the patient regarding the benefits and risks. 2. Serious adverse event[c] attributed to a previous dose of the same COVID-19 vaccine with no other cause identified. 3. Unable to tolerate vaccine administration with resulting risk to themselves or others (e.g., due to severe neurodevelopmental condition such as autistic spectrum disorder). This may warrant a temporary exemption while additional resources and support to facilitate a safe administration of a second dose are arranged.

Notes for table above:

a. This criterion will be removed as an exemption when there is an alternative vaccine available in New Zealand.

b. Many of these individuals will be able to be safely vaccinated in a controlled environment, and we recommend clinical immunologist/specialist assessment.

c. An adverse event is considered serious for the purposes of these criteria[1] if it:
i) requires in-patient hospitalisation or prolongation of existing hospitalisation OR results in persistent or significant disability/ incapacity.

AND
ii) has been reported to CARM.

AND

iii) has been determined following review by, and/or on the opinion of, a relevant medical specialist to be associated with a risk of recurrence of the serious adverse event if another dose of the same vaccine is given.

Note that if a serious adverse event to a previous dose of a COVID-19 vaccine is used as a reason for the exemption, then this may require discussion with a suitably qualified health professional, such as a Medical Doctor or Nurse Practitioner, who is registered with the relevant responsible authority, and holds a current Annual Practising Certificate (APC) issued by that authority.

21. The CV TAG also recommends:

a. Those who are confirmed as having a non-placebo vaccine in any COVID-19 vaccine trial in New Zealand (for example, the Valneva COVID-19 vaccine trial NCT04956224) should be offered a temporary exemption. Note that this exemption does not equate

[1] Examples of serious AEFIs may include but are not limited to: a medically significant illness (e.g., immune thrombocytopenia purpura (ITP), myocarditis, potentially life-threatening events (e.g., anaphylaxis), severe ME/CFS, or persistent or significant disability (e.g., Guillain-Barré Syndrome). These reactions do not include common expected local or systemic reactions known to occur within the first few days after vaccination.

to determining them to be adequately vaccinated for the purposes of a CVC or fulfilment of the Vaccination Order.

b. A maximum duration of 6 months for the exemption, with the ability to apply for a new exemption if required. This time limitation will allow individuals who can safely be vaccinated, with either the same vaccine or an alternative vaccine, as appropriate, to be protected against COVID-19 in a timely way.

c. Those who are not medically exempt include the following:

   i. People who had an otherwise negative experience that is not mentioned above, with other vaccines in the past.

   ii. People with disabilities, once adequate resources are available to support safe delivery. People with disabilities are generally at higher risk from COVID-19, and therefore are a priority for vaccination.

   iii. Pregnant people. Pregnancy is not a valid reason for exemption in the absence of any of the criteria listed in the above table. Pregnancy is associated with higher risk from COVID-19 compared to the general population and therefore this group are a priority for vaccination.

22. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

Dr Ian Town

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References

1. Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*. New England Journal of Medicine, 2020. **383**(27): p. 2603-2615.
2. Medsafe. *Approval status of COVID vaccines applications received by Medsafe*. 2021 25 August 2021 [cited 2021 18 October]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.
3. Greenhawt, M., et al., *The Risk of Allergic Reaction to SARS-CoV-2 Vaccines and Recommended Evaluation and Management: A Systematic Review, Meta-Analysis, GRADE Assessment, and International Consensus Approach*. The Journal of Allergy and Clinical Immunology: In Practice, 2021. **9**(10): p. 3546-3567.
4. ATAGI. *ATAGI expanded guidance on acute major medical conditions that warrant a temporary medical exemption relevant for COVID-19 vaccines*. 2021; Available from: https://www.health.gov.au/sites/default/files/documents/2021/10/atagi-expanded-guidance-on-temporary-medical-exemptions-for-covid-19-vaccines.pdf.
5. Medsafe - New Zealand Medicines and Medical Devices Safety Authority. *New Zealand Data Sheet, Comirnaty Covid-19 Vaccine*. 2021; Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/comirnatyinj.pdf.
6. Sellaturay, P., et al., *Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine*. Clinical & Experimental Allergy, 2021. **51**(6): p. 861-863.
7. Krantz, M.S., et al., *Safety Evaluation of the Second Dose of Messenger RNA COVID-19 Vaccines in Patients With Immediate Reactions to the First Dose*. JAMA Internal Medicine, 2021.
8. Medsafe. *Adverse events following immunisation with COVID-19 vaccines: Safety Report #31 – 2 October 2021*. Available from: https://medsafe.govt.nz/COVID-19/safety-report-31.asp.
9. Barda, N., et al., *Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting*. New England Journal of Medicine, 2021. **385**(12): p. 1078-1090.