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.