Ontario

Ministry of Health

Q&A for Health Care Providers on Mixed COVID-19 mRNA Vaccine Schedules

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This document provides basic information only and is not intended to provide or take the place of medical advice, diagnosis or treatment, or legal advice.

Background

- Both mRNA COVID-19 vaccines authorized for use in Canada (Pfizer BioNTech and Moderna) have the same mechanism of action, have very similar side effect profiles and are highly effective against COVID-19 infection, hospitalization and death.

- It is crucial for all individuals to complete their vaccine series with a second dose of a COVID-19 vaccine to receive the optimal level of protection. Data from clinical trials and real-world studies clearly demonstrate that a complete two dose vaccine series provides enhanced protection against COVID-19.

- The increased circulation of the B.1.617.2 (Delta) variant of concern further emphasizes the importance of ensuring second doses are further accelerated for people living in Ontario.

- The National Advisory Committee on Immunization (NACI) recommendations on the use of a different mRNA COVID-19 vaccine product to complete a COVID-19 vaccine series started with an mRNA COVID-19 vaccine is being followed in Ontario:
    - NACI recommends that, if readily available*, the same mRNA COVID-19 vaccine product should be offered for the subsequent dose in a vaccine series started with an mRNA COVID-19 vaccine.

- However, when the same mRNA COVID-19 vaccine product is not readily available*, or is unknown, another mRNA COVID-19 vaccine product recommended for use in that age group can be considered and should be offered to complete the vaccine series.
- The previous dose should be counted, and the series need not be restarted.

*readily available = easily available at the time of vaccination without delay or vaccine wastage

- **Practically, this means that the next available mRNA vaccine should be provided when the patient is ready and eligible to receive their second dose.**
  - If both vaccines are simultaneously available, the same vaccine should be used for both the first and second doses. This is because there is established data from clinical trials showing very high vaccine efficacy (94-95%) when the first and second doses of vaccine are the same product.
  - If only an alternate mRNA vaccine product is available at the time of the second dose, a different mRNA vaccine can be used for the 2nd dose.

  Patients should understand which product they are receiving, have the opportunity to ask questions and understand the risk of delaying their second dose.

- Where a different product is used to complete the vaccine series, the earliest interval at which the vaccine can be given is the Health Canada product monograph authorized interval of the vaccine used for the first dose.

Vaccine for first dose	Vaccine for second dose	Earliest Interval per the product monographs
Pfizer	Pfizer	21 days*
Pfizer	Moderna	21 days*
Moderna	Moderna	28 days
Moderna	Pfizer	28 days

*Note: an interval of 28 days may be considered for operational feasibility

- More information on dose intervals for different population groups can be found on the Ministry's website in the COVID-19 Vaccine Series Second Dose Eligibility Quick Reference .

What do we know about a heterologous mRNA vaccine schedule?

This is not a new concept. Similar vaccines from different manufacturers are used when vaccine supply or public health programs change.

Foundational vaccine principles indicate that similar vaccines, from different manufacturers can be substituted when: they are authorized for the same purpose; for the same populations; have similar schedules; have similar or produce similar type(s) of antigens and are similar in terms of vaccine safety, immune responses and protection provided.

- The mechanism of action in both Pfizer and Moderna mRNA vaccines is the same. Both use the spike protein of the SARS-CoV-2 virus as the antigen. The spike protein encoded by either of the authorized mRNA vaccines is stabilized in the same manner, although other vaccine components like the lipid nanoparticle and the mRNA sequence may be different.
- Use of a heterologous vaccine schedule for COVID-19 vaccines is consistent with the current NACI guidance for vaccines that are used for the same indication and contain comparable antigens.

- In line with basic principles of vaccinology, it is expected that combining different COVID-19 vaccines that induce an immune response against the SARS-CoV-2 spike protein will lead to a robust immune response.
- During clinical trials, both mRNA vaccines (Pfizer-BioNTech, Moderna) demonstrated similar safety profiles and side effects (NACI). At this time, there is no reason to believe that completing an mRNA vaccine series with a different authorized mRNA vaccine product would result in any additional safety concerns (NACI).
- Both mRNA vaccines showed similar vaccine efficacy in clinical trials against symptomatic COVID-19 disease following the second dose, 95% and 94% respectively for Pfizer-BioNTech and Moderna (NACI).

What don't we know about a heterologous mRNA vaccine schedule?

Studies involving mixed schedules with vaccines using the same platforms (e.g. mRNA vaccine combinations) and different platforms (e.g. mRNA and viral vector vaccine combinations) are ongoing and real-world evidence will also be forthcoming.

- There is no published data on immunogenicity of a heterologous mRNA vaccine schedule available at this time.
- There is no reason to believe that mRNA vaccine series completed with a different authorized mRNA vaccine product would result in any additional safety issues or reduction in immune protection against COVID-19 at this time (NACI).

What do we know about the importance of getting the second dose when it is offered?

- It is essential to complete the vaccine series to boost the initial immune response and because it is anticipated to provide protection in the longer term.

- The risks associated with delaying the 2nd vaccine dose is increased with the emergence of the Delta variant virus in Ontario. Recent evidence examining the Pfizer-BioNTech vaccine and the AstraZeneca vaccine (Bernal et al., 2021) indicates there is lower vaccine effectiveness with one dose compared to two doses for both Pfizer-BioNTech and AstraZeneca vaccines against the Delta variant. Pfizer Bio-NTech vaccine effectiveness against symptomatic disease rose to an estimated 88% with two doses, from an estimated 36% with one dose (Bernal et al., 2021).
- A significant delay in receiving a second dose in order to match the mRNA product delays the improved protection available from a completed vaccine series

Additional Information

Bernal, J. L., Andrews, N., Gower, C., Gallagher, E., Simmons, R., Thelwall, S., Stowe, J., Tessier, E., Groves, N., Dabrera, G., Myers, R., Campbell, C., Amirthalingam, G., Edmunds, M., Zambon, M., Brown, K., Hopkins, S., Chand, M., & Ramsay, M. (2021). Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. *MedRxiv* [Preprint]. https://doi.org/10.1101/2021.05.22.21257658

National Advisory Committee on Immunization's (NACI) Recommendations on the use of COVID-19 vaccines - Canada.ca

National Advisory Committee on Immunization Rapid Response: Interchangeability of Authorized COVID-19 Vaccines

Public Health Agency of Canada: Interchangeability of Authorized COVID-19 vaccines

The Canadian MOSAIC Study (Mix and match of the second COVID-19 vaccine dose for SAfety and ImmunogeniCity)

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This document will be updated as important new information becomes available.