Addendum NO. 2 (of 2) to the Manitoba COVID-19 Vaccine: Clinical Practice Guidelines – April 19, 2022

Please note there was an error corrected on page 58 of the Clinical Practice Guidelines, the change has been highlighted for ease of reference.

This information is intended for use by immunizers and health care providers and is a copy of a memo that was sent to health care providers on April 13, 2022 regarding COVID-19 Vaccine and Storage Updates.

This update contains information on the following:

1. **Novavax COVID-19 Vaccine Availability**
2. **12-17 years of age: COVID-19 Vaccine Booster Recommendation**
3. **18+ years of age: COVID-19 Vaccine Booster Recommendation**
4. **Pfizer and Moderna COVID-19 Vaccine Storage Requirements**

1. Novavax COVID-19 Vaccine Availability

- Novavax (Nuvaxovid™) COVID-19 Vaccine, has arrived in Manitoba and is available for health care providers to order through your regular COVID-19 vaccine ordering process.
- Distributed Channel Partners that bring in Novavax (Nuvaxovid™) COVID-19 Vaccine are required to update their inventory availability for the Vaccine Finder Map through https://forms.gov.mb.ca/update-covid-finder-map-info/.
- Novavax (Nuvaxovid™) is approved for use in those 18 years of age and older. Two doses are recommended as a primary seriese with at least 8 weeks between doses. It is to be stored in a temperature-monitored refrigerator at 2-8ºC and expires 6 hours after vial is punctured.
- Please see links below to resources, such as factsheets and product monographs, for more information about this product and its storage and handling requirements.
- The tariff for Novavax (Nuvaxovid™) COVID-19 Vaccine is 8291.

2. 12-17 years of age: COVID-19 Vaccine Booster Recommendation

- The National Advisory Committee on Immunization (NACI) has released an updated recommendation on first booster doses of COVID-19 vaccines for those 12-17 years of age. Manitoba is adopting the recommendations.
- A first booster dose of an mRNA COVID-19 vaccine **should** be offered at least 6 months after the completion of a primary series to adolescents 12 to 17 years of age who:
    - have an underlying medical condition that puts them at high risk of severe outcomes from COVID-19, including adolescents who are immunocompromised and have already received an additional vaccine dose;
    - are residents of congregate living settings;
    - belong to racialized and/or marginalized communities disproportionately affected by COVID-19.
        - In order to apply the NACI recommendation, providers are encouraged to respectfully ask about the patient/ family's racial, ethnic or Indigenous identity.
        - For patients/families that identify as a member of a racialized community (for example Black, Indigenous, South Asian, Filipino, etc.) the provider can explain that Manitoba's data has shown that members of diverse BIPOC communities are at higher risk for COVID-19 infection and severe outcomes at younger ages than other Manitobans.
        - Using this data as the foundation for the recommendation is important as it makes clear that there is a clinically important reason for asking about the patients' racial, ethnic or Indigenous identity.
- For all other adolescents 12 to 17 years of age:
    - A first booster dose of an mRNA COVID-19 vaccine **may** be offered at least 6 months after the completion of the primary series in the context of increased COVID-19 activity.

3. 18+ years of age: COVID-19 Vaccine Booster Recommendation

- NACI recommends that a first booster dose of an authorized COVID-19 vaccine should be offered ≥6 months after completion of a primary COVID-19 vaccine series to adults ≥18 years of age. An mRNA COVID-19 vaccine dose is preferred for the booster dose. (Strong NACI recommendation)

4. Pfizer and Moderna COVID-19 Vaccine Storage Requirements

- Most health care providers will receive their COVID-19 vaccine in the thawed state where they are to be stored in a temperature-monitored refrigerator at +2 to +8C.
- Once Pfizer (Comirnaty™) and Moderna (Spikevax™) COVID-19 vaccines are thawed and refrigerated they must be used within certain timelines, otherwise they need to be discarded. These timelines may be before the product's identified expiry date. The expiry date identified by the manufacturer on the packaging or online applies to product that has been stored at the frozen or ultra frozen state, according to the product monograph.
- Please review the product monographs for each product to confirm the storage and handling requirements and time lines for each product.
- All product that needs to be discarded should be removed from inventory and returned to the Provincial Distribution Warehouse for proper disposal.

Pfizer and Moderna Storage Requirements

	Pfizer Adult/Adolescent vaccine (purple cap)	**Pfizer Pediatric vaccine (orange cap)**	**Moderna vaccine**
Age Indication	12 years of age and over	5-11 years	6 years of age and over
Ultra Low Freezer Storage Time (-90C to -60C)‡	Until expiry date printed on vial (unless shelf life extensions are approved)	9 months after manufacturing date printed on vial (unless shelf life extensions are approved)	Do not store at this temperature
Freezer Storage Time (-25C to -15C)	2 weeks	Do not store at -25C to -15C	Until expiry date (unless shelf life extensions are approved)
Refrigerated Time (+2C to +8C)^	1 month	10 weeks	30 days
Room Temperature Storage Time Prior to Dilution (+8 to +25°C)	2 hours prior to dilution (including any thaw time)	12 hours prior to dilution	Up to 24 hours. No dilution required

Time After Dilution or First Puncture (+2C to +25C)	Discard after 6 hours	Discard after 12 hours	Discard after 24 hours
^ Length of time in refrigerator before discarding, unless the date of expiry occurs before that time. ‡ Expiry dates may be extended. Monitor for Health Canada announcements that may affect expiry dates.			

You can also find Information about these products at:

- Pfizer: https://www.cvdvaccine.ca/
- Moderna: https://modernacovid19global.com/ca/

Please see links below to locate clinical and product information for the above updates:

- The Clinical Practice Guidelines: https://manitoba.ca/covid19/vaccine/healthcare-professionals.html
- COVID-19 Factsheets for download at: https://manitoba.ca/covid19/vaccine/resources.html#factsheets
- Product Monographs: https://www.gov.mb.ca/covid19/vaccine/resources.html.
- National Advisory Committee on Immunization: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html
- Canadian Immunization Guide – COVID-19 Chapter: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html
- Immunization and Biologics Tariff Listing: https://www.gov.mb.ca/health/publichealth/surveillance/immunization/docs/mims_tariff_codes.pdf

Addendum NO. 1 (of 2) to the Manitoba COVID-19 Vaccine: Clinical Practice Guidelines – April 8, 2022

This information is intended for use by immunizers and health care providers and is a summary of the National Advisory Committee on Immunization (NACI) statement, "Initial guidance on a second booster dose of COVID-19 vaccines in Canada" released April 5, 2022.[1] Please refer to the full NACI statement for more information. Manitoba-specific information is included in the textbox (page 2).

The National Advisory Committee on Immunization (NACI) continues to recommend a primary series with an mRNA vaccine in all authorized age groups. Immunization for those who are eligible for vaccination but have not yet received a primary vaccine series remains a top priority in Canada.

NACI recommends that in the context of protection against severe disease potentially decreasing over time following the first booster dose, and/or risk of immune evasion by highly transmissible variants of concern which can cause severe disease:

1. NACI recommends that jurisdictions prepare for the rapid deployment of a second COVID-19 vaccine booster dose program over the coming weeks prioritizing the following populations, as close surveillance and assessment suggest concerning trends in the COVID-19 pandemic:
    a. Adults 80 years of age and over living in the community *(strong NACI recommendation)*
    b. Residents of long-term care or other congregate living settings for seniors *(strong NACI recommendation)*
    c. While the greatest benefit is expected in adults 80 years of age and older, jurisdictions may also consider offering a second COVID-19 booster dose to adults 70-79 years of age living in the community *(discretionary NACI recommendation)*

NACI advises that a second booster dose among adults younger than 70 years of age in or from First Nations, Métis, or Inuit communities may be considered as these communities have a younger age distribution but increased risk for severe disease due to a variety of intersecting factors including underlying medical conditions and potential decreased access to health care.

Second booster doses are currently not authorized by Health Canada and therefore constitute off-label use.

Based on the above recommendations from NACI, Manitoba is making a second booster dose of COVID-19 vaccine available to the following individuals who provide informed consent following a review of the risks and benefits of vaccination:

- residents of personal care homes (PCHs), regardless of age;
- residents of elderly persons housing congregate living sites such as supportive housing and assisted living, regardless of age;
- individuals aged ≥ 70 years who live in the community; and
- First Nations, Inuit and Métis people aged ≥ 50 years, regardless of residence.

Manitoba is providing the following guidance with respect to the minimum interval and vaccine product:

- The second booster dose should be given 6 months after the first booster dose.
    - For immunocompetent people (in the groups indicated above – e.g., residents of PCHs): the second booster dose would be their fourth dose of vaccine.
    - For moderately to severely immunocompromised people (in the groups indicated above – e.g., residents of PCHs): the second booster dose would be their fifth dose (as immunocompromised people are recommended to receive three doses for the primary series).
    - NACI has suggested a 3-month interval between infection and COVID-19 booster dose or 6 months from the most recent vaccine dose, whichever is longer. Given high rates of Omicron infection in community and institutional settings between December 2021 and February 2022, a proportion of the population may have boosted their immune response following exposure to the Omicron variant.
- The second booster dose may be provided using either mRNA vaccine (Pfizer/Comirnaty™ (30 mcg) or Moderna/Spikevax™ (50mcg)), regardless of which COVID-19 vaccine was used for previous doses.
    - The use of Moderna/Spikevax™ (100mcg) may also be considered based on clinical discretion.
    - Novavax/Nuvaxovid™ may be offered to individuals who are unable or unwilling to receive an mRNA COVID-19 vaccine.

NACI provides the following considerations/summary of evidence:

- The Omicron variant, including the newly emerging Omicron sub-variant BA.2 is partially evasive to previous immunity conferred by COVID-19 vaccines or previous SARS-CoV-2 infection, thus impacting booster dose considerations.

The epidemiology of COVID-19 is continuing to change as public health measures are modified and as variants of concern (VOCs) emerge and circulate.

- Incidence of severe outcomes with BA.1 and BA.2 Omicron was highest among older adults ≥ 80 years of age, followed by older adults 70 to 79 years of age in Canada.
- Based on provincial and territorial roll out of first booster programs, individuals who were the first to receive a booster dose of COVID-19 vaccine may have reached or are approaching 6 months since their first booster dose.
- Some data on vaccine protection from a second booster dose against Omicron has become available. *In situations where a specific study is cited by NACI, the reference is included. Where other evidence is referenced, refer to the NACI statement for more information.*

  Vaccine effectiveness <u>over time following a first booster dose:</u>
  - Vaccine effectiveness against infection/symptomatic disease for Omicron from a first booster of mRNA vaccine is approximately 60% and decreases over time since vaccination in most studies.
  - Vaccine protection against severe disease and hospitalization due to COVID-19 has been more durable than protection against symptomatic disease or infection and is approximately 10 to 20% higher following a first booster compared to those who have only completed a primary series, reaching ~90% or more shortly following vaccination. Evidence regarding the duration of protection of a first booster against severe disease is limited, with a few studies suggesting some decrease over time. As an example, vaccine effectiveness against hospitalization was 78% (95% CI: 67 to 85%) at ≥ 4 months in one US study.[2]

  Vaccine effectiveness following <u>a second booster</u>:
  - Evidence on second booster vaccine effectiveness is limited and has mainly been assessed as a relative benefit compared to the first booster.
  - In a study[3] of a second booster among older adults ≥ 60 years of age who were vaccinated at least 4 months from their first booster, the rates of SARS-CoV-2 infection and COVID-19 severe illness were lower in those 12 or more days after the fourth dose (2.0-fold and 1.8-fold for infection and 4.3-fold and 4.0-fold for severe disease) compared to the two control groups, respectively (those eligible for the second booster dose but who did not receive it, and those who received the second booster dose but were within 3 to 7 days after receiving the second booster dose, which is before it is expected to take effect).

- In a separate study[4] of healthcare workers who received a second booster dose given at least 4 months after the first booster dose, there was a relative adjusted vaccine effectiveness after a second booster compared to a first booster against symptomatic disease of 43% (95% CI: 7% to 65%) in the Pfizer group and 31% (95% CI: -18% to 60%) in the Moderna group.

Immunogenicity in older adults and long-term care (LTC) residents:

- Evidence on immune responses in older adults and LTC residents suggests that after a first booster of mRNA COVID-19 vaccine, humoral immune responses, including neutralizing antibody responses against Omicron, increase to levels that are similar to or greater than those observed shortly after the second dose of the primary series. After a second booster in LTC residents in Ontario and in a separate study in healthcare workers ≥ 18 years of age in Israel,[5,6] a similar trend was observed where the second booster resulted in similar titres to that achieved after the first booster dose.
- Emerging evidence suggests that humoral immune responses after a first booster in older adults and LTC residents wane over a period of approximately 15 weeks; longitudinal data on immune responses after a second booster are not available.
- It is currently unclear if the rate at which post first or second booster dose immune responses wane is different than the rate at which immune responses waned after previous doses, and it is not known if and for how long immune responses will remain above a threshold correlated with protection from infection or other clinical outcomes (e.g., severe disease). Immunological correlates of protection have not yet been defined for COVID-19. The impact of repeated vaccine doses is also yet to be determined.

Safety:

- Preliminary data indicate that the safety of a second booster of an mRNA COVID-19 vaccine is comparable to previous doses. Overall, from both Canadian and international safety surveillance data, a second booster of mRNA COVID-19 vaccine was well tolerated and no new safety signal was identified. However, this second booster was generally administered in specific populations (e.g., LTC residents, older adults) or in small groups. Evidence monitoring is ongoing.

[1] https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/naci-guidance-second-booster-dose-covid-19-vaccines.pdf

[2] Ferdinands JM, Rao S, Dixon BE, Mitchell PK, DeSilva MB, Irving SA, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance - VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep. 2022 Feb 18;71(7):255,263. doi: 10.15585/mmwr.mm7107e2.

[3] Bar-On Y, Goldberg Y, Mandel M, Bodenheimer O, Amir O, Freedman L, et al. Protection by 4th dose of BNT162b2 against Omicron in Israel. medRxiv. 2022 Feb 1. https://doi.org/10.1101/2022.02.01.22270232

[4] Regev-Yochay G, Gonen T, Gilboa M, Mandelboim M, Indenbaum V, Amit S, et al. 4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC. medRxiv. 2022 Feb 15. https://doi.org/10.1101/2022.02.15.22270948

[5] Regev-Yochay G, Gonen T, Gilboa M, Mandelboim M, Indenbaum V, Amit S, et al. Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron. N Engl J Med. 2022 Mar 16. doi: 10.1056/NEJMc2202542

[6] Regev-Yochay G, Gonen T, Gilboa M, Mandelboim M, Indenbaum V, Amit S, et al. 4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC. medRxiv. 2022 Feb 15. https://doi.org/10.1101/2022.02.15.22270948

Manitoba COVID-19 Vaccine: Clinical Practice Guidelines for Immunizers and Health Care Providers

This Clinical Practice Guideline (Version 28) is current as of April 7, 2022 and is intended for use by immunizers and health care providers.

Please note: As of April 8, 2022, this document will no longer be updated. Any updates to the guidance contained herein will be captured in an addendum at the frontend of this document.

Manitoba

Table of Contents

Summary of Notable Changes

May 3, 2022

- Corrected dated operational information on page 55 (note: change highlighted for ease of reference).

April 14, 2022

- Corrected error on page 63 (note: change highlighted for ease of reference).

April 8, 2022

- Health Canada approved the Moderna vaccine in the 6 to 11 year old population, updated "guidance for use of the mRNA vaccine in the pediatric population".
- Updated "guidance for use in special populations". Added information on immunizing children 5 to 11 years of age.
- Updated "guidance for use of the viral vector vaccines" to take into account the introduction of the protein subunit vaccine.
- Addition of the section titled, "guidance for use of the protein subunit vaccine in the primary series and booster dose for the adult population."
- Updates to the following clinical practice questions & answers: 5, 6, 10, 20 & 22; the following questions & answers have been removed: 1.
- Updated Appendix D – Management of Inadvertent Vaccine Errors (note: changes are highlighted for ease of reference).

March 3, 2022

- Updated "guidance for use of the mRNA vaccines in the primary series for the adolescent/adult population aged ≥ 12 years." Specifically, updated guidance on interchangeability.
- Updated "guidance on booster doses of mRNA vaccines for adolescents and adults." Specifically, updated guidance on interchangeability as well as guidance for individuals aged ≥ 12 years who received non-Health Canada approved COVID-19 vaccines.

February 9, 2022

- Updated "guidance on booster doses of mRNA vaccines for adolescents and adults."
- Updated information in the section titled, "guidance for use of the mRNA vaccine in the pediatric population."
- Updated the following clinical practice questions and answers: 25. (This question/answer has been referenced in the "recommended interval" section for the mRNA vaccines for pediatrics, adolescents and adults).

January 20, 2022

- Updated guidance for use in special populations.
- Updated "guidance for use of the mRNA vaccines in the primary series for the adolescent/adult population" aged ≥ 12 years.
- Updated "guidance on booster doses of mRNA vaccines."
- Clarified the recommended interval for the primary series for the pediatric population, in the section titled, "guidance for use of the mRNA vaccine in the pediatric population."
- Updated the following clinical practice questions and answers: 10, 18, 20, 25 & 29.

- Updated Appendix D – Guidance document on management of inadvertent vaccine errors.

December 20, 2021

- Updated “guidance for use in special populations for all authorized COVID-19 vaccines used in Manitoba” by removing the requirement of immunizers/health care providers to have additional discussions about the benefits/risks with clients/patients who are pregnant and/or breastfeeding, in light of evolving evidence and recommendations.
- Updated “guidance for use of the viral vector vaccine” to include two additional rare risks (immune thrombocytopenia and venous thromboembolism) following immunization.
- Updated “guidance for use of the mRNA vaccines in the primary series for the adolescent/adult population” aged ≥ 12 years, specifically with respect to the sections on interchangeability and recommended interval, with clarifications to the sections on dosage and guidance for immunocompromised populations. Guidance on timing of vaccine administration following monoclonal antibody treatment has been added.
- Updated “guidance for use of the mRNA vaccine in the pediatric population,” specifically with respect to the recommended interval for the primary series and guidance for children who are immunocompromised.
- Updated the following clinical practice questions and answers: 4, 5, 6, 10, 19 and 25; removed questions 8 and 9.
- Clarified that Appendix C – guidance/precautions as it pertains to vaccination of allergic patients – that applies to persons aged ≥ five years.
- Added Appendix F – definition of moderately to severely immunocompromised individualised aged ≥ five years.
- The summary table for clinicians to guide decision-making around recommended and minimum intervals for the primary series was Appendix F and is now Appendix G.

November 23, 2021

- Health Canada approved the Pfizer vaccine in the five to 11 year old population; added a section titled, “guidance on the use of the mRNA vaccine in the Pediatric Population.”
- Third/booster doses of both mRNA vaccines are now approved by Health Canada at least six months since the last dose for use in individuals aged ≥ 18 years; updated the, “Guidance on Additional/Third/Booster Doses of mRNA Vaccines” to reflect the approval.
- A link to public-facing information on the viral vector vaccines has been added to the top of the section titled, “guidance on use of the viral vector vaccines” section.

November 10, 2021

- Updated “guidance on use of an Additional/Third/Booster Doses of mRNA Vaccines.”
- Updates to the following clinical practice questions & answers: 9.

November 4, 2021

- Updated “guidance on use of the viral vector vaccines.”
- Updated “guidance for use of the mRNA vaccines.”
- Updated “guidance on use of an Additional/Third/Booster Doses of mRNA Vaccines.”
- Updates to the following clinical practice questions & answers: 1, 5, 6, 12 & 19.
- Updated Appendix C – National Advisory Committee on Immunization precautions as it pertains to vaccination of allergic persons.

- Updated Appendix F – Guidance table on recommended and minimum intervals.

October 19, 2021

- Added reference to the Public Health Agency of Canada (PHAC)'s online guidance document for health care providers, in the section titled "Purpose of the Clinical Practice Guideline" and relevant appendices.
- Updated guidance on subsequent doses, most notably added information to the subsection on general guidance for booster doses, including guidance for First Nation people living on-reserve.

October 6, 2021

- Addition of the section titled, "COVID-19 Vaccine Medical Exemption Program."
- Updated guidance on subsequent doses, most notably added clarifying guidance for travel purposes and added a subsection on general guidance for booster doses.
- Updates to the following clinical practice questions & answers: 5, 6 & 27.

September 15, 2021

- Updated the section on "Vaccination Risks and Benefits for Clients/Patients who are Immunosuppressed &/or have an Autoimmune Condition" to direct clinicians looking for guidance on additional doses after 1- or 2-dose primary series for immunocompromised populations, to the section titled, "Guidance on Subsequent Doses".
- Updated guidance on who requires further consultation before immunization.
- Updated guidance on subsequent doses.
- Updated guidance on the use of mRNA vaccines as it pertains to additional doses after 1- or 2-dose primary series and myocarditis/pericarditis.
- Updates to the following clinical practice questions & answers: 6 & 9.
- Updated Appendix F - Guidance table on recommended and minimum intervals between COVID-19 vaccine doses, to note the minimum interval for additional doses after 1- or 2-dose primary series.

September 2, 2021

- Updated guidance on the use of mRNA vaccines, including the Health Canada authorization for Moderna among adolescents aged 12 years and older as well as updated guidance on myocarditis and pericarditis.
- Updates to the following clinical practice questions & answers: 8, 9, 10, 16, 21 & 23; the following question is new and has been added: 29.
- Updated the section on "Guidance on Second Doses" to be more broad, and renamed this section "Guidance on Subsequent Doses." Removed historical information from this section to Appendix E and added a new sub-section titled, "Additional Doses of COVID-19 Vaccine."
- Updated Appendix D – Management of Inadvertent Vaccine Errors (note: changes are highlighted for ease of reference).
- Addition of Appendix E - MB's plan for launching second doses of COVID-19 vaccine (with this addition, the original Appendix E was shifted to Appendix F - Guidance table on recommended and minimum intervals between COVID-19 vaccine doses). The Guidance table (Appendix F) was updated (note: changes are highlighted for ease of reference).

July 19, 2021

- Allergy referral section updated with Pediatric Allergy Department fax number.

July 6, 2021

- Updated guidance on people who should not routinely be immunized.
- Guidance on the recommendations for use of the viral vector vaccine have been updated.
- Updated information and guidance on the use of mRNA vaccines (new section; previously titled, “Emerging Evidence – Information on Myocarditis and Pericarditis”).

July 2, 2021

- Guidance on the recommendations for use of the viral vector vaccine have been updated.
- Updated information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), specifically updated excerpt from the AstraZeneca product monograph.
- Updated information in the Emerging Evidence - Information on Myocarditis and Pericarditis.

June 25, 2021

- Amendment to Appendix E – guidance table on recommended and minimum intervals between COVID-19 vaccine doses.

June 21, 2021

- Removed the option to securely fax signed and completed COVID-19 vaccine consent forms to Manitoba Health and Seniors Care for upload into the Public Health Information Management System (PHIMS).
- Updated “Guidance for the use of the Viral Vector Vaccine,” including updated eligibility criteria, with the addition of a section that lists the locations that have stock of the AstraZeneca vaccine.
- Updated information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT).
- Updated guidance on second doses, including the addition of evidence on interchangeability for mRNA and viral vector vaccines.
- Updated information related to pericarditis/myocarditis in the section titled, “Emerging Evidence.”
- Updates to the following clinical practice questions & answers: 1, 4, 6, 9, 10, 16, 19, 23 & 27; the following questions & answers have been removed: 7 & 11.
- Addition of Appendix E – guidance table on recommended and minimum intervals between COVID-19 vaccine doses.

June 1, 2021

- Updated information contained in the “Vaccination Risks and Benefits for Pregnant &/or Breastfeeding Clients/Patients.”
- Updated information contained in the “Vaccination Risks and Benefits for Clients/Patients who are Immunosuppressed &/or have an Autoimmune Condition.”
- Updated “Guidance for the use of the Viral Vector Vaccine,” including updated eligibility criteria.

- Updated information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), including an updated rate of VITT in Canada.
- Updated guidance on second doses, including interchangeability recommendations for mRNA and viral vector vaccines.
- Addition of a new section titled, “Emerging Evidence,” which is intended to provide an overview of new evidence and data this being explored provincially and/or (inter)nationally.
- Updates to the following clinical practice questions & answers: 1, 6, 19 and 23; the following clinical practice questions & answers are new and have been added at the end: 25, 26, 27 and 28.
- Addition of Appendix D - Guidance Document on the Management of Inadvertent Vaccine Errors.

May 21, 2021

- Updated decision-tree for diagnosing and ruling out VITT (page 21) and a list of resources has been added for diagnosing and managing VITT.
- Updates to the following clinical practice questions & answers: 1, 8, 12, 19 and 20.

May 12, 2021

- Addition of “Guidance on the Prioritization of Second Doses.”

May 7, 2021

- Updates to the information contained in the “Vaccination Risks and Benefits for Pregnant &/or Breastfeeding Individuals”.
- Updates to the information about people who should routinely not be immunized, under the section, “People who Require Further Consultation before Immunization.”
- Updated “Guidance for the use of the Viral Vector Vaccine”, to include the Janssen vaccine.
- Updated information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT).
- Updates to the following clinical practice questions & answers: 1, 6, 8, 10, 19, 20 and 23.

April 30

- Updates to the guidance on the use of the viral vector vaccine, including:
    - Addition of a note preceding the section.
    - Clarification to the guidance for individuals who require a compressed immunization schedule who already received a dose of AstraZeneca.
    - Updates to the eligibility criteria for the AstraZeneca and Janssen vaccine.

April 26, 2021

- Addition of Canada’s COVID-19 immunization response goal (page 4).
- Updates to the guidance for the use of the viral vector vaccine, including recommendations for use (pages 13 and 16).
- Updates to the information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) *(previously referred to as* Vaccine-Induced Pro-thrombotic Immune Thrombocytopenia (VIPIT)).
- Updates to the following clinical practice questions and answers: 6 and 10.

- Addition of Appendix C that provides precautionary information on national guidance related to allergic responses to vaccination.

April 21, 2021

- Updates to the guidance for the use of the viral vector vaccine, including eligibility criteria for AstraZeneca.
- Updates to the following clinical practice questions and answers: 8, 12 and 19.
- Addition of Appendix B that provides a historical reference for priority health conditions for AstraZeneca prioritization.

April 16, 2021

- Updates to the information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT).
- Updates to the following clinical practice questions and answers: 1, 6, 10, 12, 16 and 20.
- Clarification that low-to-moderate dose prednisone is not a contraindication/precaution to vaccination.

April 6, 2021

- Updates to the eligibility criteria for AstraZeneca.
- Clarification that low-dose methotrexate is not a contraindication/precaution to vaccination.

Purpose of this Clinical Practice Guideline

The goal of Canada's pandemic response is to minimize serious illness and death while minimizing societal disruption as a result of the COVID-19 pandemic. The goal of Canada's COVID-19 immunization response is to enable as many Canadians as possible to be immunized against COVID-19 as quickly as possible, while ensuring that high-risk populations are prioritized.

Manitoba's Vaccine Implementation Task Force, compromised of vaccine experts from Manitoba Health and Seniors Care makes COVID-19 vaccine recommendations by critically conducting a review of:

- provincial epidemiology, to guide determination of priority populations.
- clinical trial data on safety and effectiveness.
- post-marketing studies, including reports of adverse events following immunization.
- plans and practices of other jurisdictions in Canada and around the globe.
- summary statements and recommendations from national and international expert committees, including NACI.

Consultation with experts form the medical community across the province is also undertaken in various stage of the review and development process.

The COVID-19 landscape is constantly changing as we learn more about the disease and the vaccines that protect against it. Vaccine recommendations are subject to change as the evidence continues to evolve.

This Clinical Practice Guidance for Immunizers and Health Care Providers in Manitoba is intended to accompany the National Advisory Committee on Immunization (NACI) recommendations and statements, which can be accessed at: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html; Manitoba-specific recommendations and policies are contained herein. In October 2021, the Public Health Agency of Canada (PHAC) released an online guidance document for health care providers that provides a summary of recommendations on the use of COVID-19 vaccines (mainly based on NACI recommendations), as well as direction on handling vaccine administration errors. The document provides guidance only; clinical judgement in certain situations may result in management decisions that differ from those outlined the document. PHAC also notes that it will update the document based on new information or guidance. This **Quick Reference Guide on use of COVID-19 Vaccines** is available at: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/quick-reference-guide-covid-19-vaccines.html.

Resources for health care providers including the most up-to-date version of these Clinical Practice Guidelines as well as questions & answers and provincial memos can be found online at: https://www.gov.mb.ca/covid19/vaccine/healthcare-professionals.html. Information and resources specifically for pharmacists and physicians can be found here: https://www.gov.mb.ca/covid19/vaccine/partners/index.html.

Product monographs, factsheets for general public use and the **COVID-19 Vaccine Consent Form** can be found here: https://www.gov.mb.ca/covid19/vaccine/resources.html.

Guidance for use in Special Populations: Vaccination Risks and Benefits for Pregnant &/or Breastfeeding Clients

Most people who become infected with SARS-CoV-2 during pregnancy will have mild to moderate symptoms and many can be asymptomatic. Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of invasive ventilation with an equivalent mortality to age-matched peers, as well as premature birth, caesarean delivery and newborn admission to the neonatal intensive care unit (NICU). The risk of severe morbidity from COVID-19 in pregnancy appears to be associated with risk factors including:

- an age of 35 or older
- obesity
- pre-existing or gestational diabetes
- pre-existing hypertension
- heart disease
- severe and/or uncontrolled asthma

The National Advisory Committee on Immunization (NACI) cites emerging research that suggests that COVID-19 mRNA vaccination during pregnancy results in comparable antibody titres to those generated in non-pregnant women. Maternal IgG humoral response to mRNA COVID-19 vaccines transfers across the placenta to the fetus, leading to a significant and potentially protective, antibody titre in the neonatal bloodstream.

NACI notes observational studies consistently show that both anti-spike IgG and IgA are present in breastmilk for least for weeks after maternal vaccination with mRNA vaccines. NACI also notes that in one small cohort study, mRNA from COVID-19 vaccines was undetectable in breastmilk four to 48 hours post-vaccination. Because COVID-19 vaccines are not live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.

Vaccine recipients and health care providers are encouraged to enroll patients who have received a COVID-19 vaccine during pregnancy in COVID-19 vaccine pregnancy registries.

Manitoba public health officials, NACI and the Society of Obstetricians and Gynecologists of Canada (SOGC) recommend that a complete vaccine series with a COVID-19 vaccine should be offered to pregnant and/or breastfeeding individuals if informed consent includes discussion about the evidence on the use of COVID-19 vaccines in this population. Pregnant and/or breastfeeding individuals will likely seek counsel from their prenatal care provider to assist in weighing the risks and benefits, so that they might arrive at an informed and autonomous decision that is right for them as an individual. Such a discussion should prioritize patient autonomy and may include the following:

- Currently, there is evolving evidence that pregnancy is a risk factor for severe COVID-19, particularly when complicated by advanced maternal age, obesity, severe and/or uncontrolled asthma, pre-existing or gestational diabetes, pre-pregnancy high blood pressure or heart disease.
- Evolving data suggests that SARS-CoV-2 infection in pregnancy may increase the risk of complications requiring hospitalization and intensive care, premature birth and caesarean delivery.

- Some individuals who are pregnant, breastfeeding or of reproductive age may be at increased risk of exposure to SARS-CoV-2 (e.g., healthcare or essential workers) and/or at increased risk of severe COVID-19 disease (e.g., due to a pre-existing medical condition or a body mass index of 35 kg/m2 or more).
- Evidence to date has not shown safety issues following vaccination with an mRNA COVID-19 vaccine among pregnant persons or the fetus. This safety data suggests mRNA vaccine administration within 30 days of conception is safe. Those who are trying to become pregnant do not need to avoid pregnancy after vaccination with an mRNA vaccine.
- There is evidence that suggests that the mRNA vaccine itself does NOT cross the placenta but that antibodies DO cross the placenta, but the level of protection that this provides to the fetus is unknown.
- There is emerging data that shows antibodies are present in breastmilk following vaccination. No safety signals have been detected with mRNA vaccination during breastfeeding. Individuals should continue to breastfeed after vaccination.
- Relevant epidemiology and risk of community acquisition of COVID-19.
- Workplace situation and risk of work-related acquisition of COVID-19.
- Individual risk for COVID-related morbidity including consideration for comorbidities including advanced maternal age, immunosuppressive conditions, pre-existing or gestational diabetes, pre-existing hypertension, obesity or chronic respiratory conditions.

COVID-19 Vaccine Product Recommendations

Consistent with NACI, Manitoba public health officials preferentially recommend an mRNA COVID-19 vaccine product for pregnant and/or breastfeeding individuals for the primary series and booster dose. (Refer to the appropriate section for guidance on the use of mRNA COVID-19 vaccines, noting specific product recommendations for certain ages).

- An authorized recombinant protein subunit COVID-19 vaccine may be offered to individuals who are not able or willing to receive an mRNA COVID-19 vaccine, taking into consideration that the safety and efficacy of a recombinant protein subunit COVID-19 vaccine (Novavax/Nuvaxovid™) has not been established in pregnant and/or breastfeeding people. Therefore, informed consent should include discussion that there is currently limited evidence on the use of Novavax/Nuvaxovid™ in these populations, while there is evidence on the safety profile and effectiveness of mRNA COVID-19 vaccines in these populations based on real world use with large numbers of individuals. (Refer to the appropriate section for guidance on the use of recombinant protein subunit COVID-19 vaccines).
- A viral vector COVID-19 vaccine (AstraZeneca or Janssen) may be offered when all other authorized COVID-19 vaccines are contraindicated. Refer to the section titled, “Guidance on the use of viral vector vaccines” for information about the risks of vaccination for the purposes of obtaining informed consent.

Guidance for use in Special Populations: Vaccination Risks and Benefits for Clients who are Immunosuppressed &/or have an Autoimmune Condition

The National Advisory Committee on Immunization (NACI) recommends COVID-19 vaccination should be offered to individuals who are immunosuppressed and/or to those who have an autoimmune condition if informed consent includes discussion about the evidence on the use of COVID-19 vaccine in this population. The vaccine series should be completed at least two weeks before the initiation of immunosuppressive therapies, where possible.

Immunosuppressed people or those with autoimmune conditions will likely seek counsel from a health care provider to assist in weighing the risks and benefits, so they can make informed and autonomous decisions that are right for them as individuals. Such a discussion should prioritize patient autonomy and may include the following information:

- Although there is limited evidence to indicate that immunosuppression or having an autoimmune condition is an independent risk factor for severe COVID-19, these conditions have been identified as independent risk factors for prolonged infection and severe outcomes from SARS-COV-2 infection.
- Recent Canadian surveillance data indicates that compared to the general population, a higher proportion of the immunocompromised population or those with malignancy are hospitalized or admitted to the ICU due to COVID-19.
- Immunocompromising conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the progression of disease and use of medications that suppress immune function.
- No safety signals of concern have been noted to date in non-immunosuppressed individuals with an immunocompromising condition (e.g., stable HIV infection) including in clinical trials. People living with HIV that are considered immunocompetent may be vaccinated.
- Emerging real-world data suggests that COVID-19 mRNA vaccines are as safe in individuals with autoimmune conditions compared to individuals without an autoimmune condition. NACI notes that observational studies indicate that the frequency and severity of adverse events in this population is comparable to that of individuals without autoimmune conditions and what was reported in clinical trials. The onset of new autoimmune disease or disease exacerbation following vaccination with mRNA COVID-19 vaccines was rare or comparable to the background incidence of these events in the general population.
- Emerging real-world data suggests that COVID-19 mRNA vaccines are as safe in individuals who are immunosuppressed due to disease or treatment, compared to those who are not immunosuppressed. There is growing data demonstrating a higher risk of breakthrough infections for individuals who are severely immunocompromised.
- Autoimmune conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the severity and progression of disease and use of medications that impact immune function.

- There is limited data on COVID-19 vaccinations in people who are immunosuppressed, or who have an autoimmune condition, or both. Furthermore, there is evidence to demonstrate that people who are immunosuppressed due to disease or treatment or who have an autoimmune condition will benefit from vaccination (although the degree of benefit will vary by individual, and the duration of benefit is unknown).
- People who are immunosuppressed or those with autoimmune conditions are known to benefit from other vaccinations, such as the annual seasonal influenza vaccine.
- There is no evidence to suggest that people who are immunosuppressed have increased adverse events associated with COVID-19 mRNA vaccines (unlike with live vaccines).
- Fever is a possible side effect of vaccination and this could make symptoms of an autoimmune condition temporarily worse.

Recommended schedule

See the appropriate section for guidance on the three-dose primary series for the pediatric and adolescent/adult populations as well as a fourth (booster) dose for the adult/adolescent population for individuals who are moderately to severely immunocompromised (see appendix F for a definition of moderately to severely immunocompromised). It will be necessary to ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving a third dose and fourth (booster) dose (where fourth (booster) dose is recommended).

The recommended immunization schedule for immunocompromised individuals is as follows:

	Interval between dose 1 and dose 2		Interval between dose 2 and dose 3		Interval between dose 3 and booster (4th) dose	
	Min.	**Recommended**	**Min.**	**Recommended**	**Min.**	**Recommended**
Ages 5 to ≤ 11 years	21 days (Pfizer specific)	8 weeks	≥ 28 days	As per clinical discretion [a]	Not authorized and/or recommended at this time; may be updated in future based on emerging evidence.	
Ages 6 to ≤ 11 years	28 days (Moderna specific)	8 weeks	≥ 28 days	As per clinical discretion [a]	Not authorized and/or recommended at this time; may be updated in future based on emerging evidence.	
Ages 12 years and older	21 or 28 days (product specific)	8 weeks	≥ 28 days	As per clinical discretion [a]	≥ 28 days	6 months

NOTES:
[a] There is limited data to determine the optimal interval for the third dose. It is recommended to consider the risk factors for exposure and severe disease when deciding on the time interval. At this time, the minimum interval of the third dose from the preceding dose is 28 days. In general, NACI recommends that immunocompromised individuals be immunized at the time when maximum immune response can be anticipated:

- Immunize prior to any planned immunosuppression such that optimal immunogenicity is achieved, if possible.
- Delay immunization if the immunodeficiency is transient (if this can be done safely because exposure is unlikely in the individual's setting and circumstance).
- Stop or reduce immunosuppression to permit better vaccine response, if appropriate. Consult the Canadian Immunization Guide for more detail on the timing of vaccination in relation to immunosuppressive therapy: www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25.

Individuals who are living with an autoimmune condition who are not immunocompromised would follow the same immunization schedule for the general population, where immunization is offered/indicated.

COVID-19 Vaccine Product Recommendations

Consistent with NACI, Manitoba public health officials preferentially recommend an mRNA COVID-19 vaccine product for individuals who are immunosuppressed due to disease or treatment and/or who have an autoimmune condition for the primary series and booster dose. (Refer to the appropriate section for guidance on the use of mRNA COVID-19 vaccines, noting specific product recommendations for certain ages).

- An authorized recombinant protein subunit COVID-19 vaccine may be offered to individuals aged ≥ 18 years who are not able or willing to receive an mRNA COVID-19 vaccine, taking into consideration that the safety and efficacy of a recombinant protein subunit COVID-19 vaccine (Novavax/Nuvaxovid™) has not been established in individuals who are immunosuppressed due to disease or treatment and/or who have an autoimmune condition. Therefore, informed consent should include discussion that there is currently limited evidence on the use of Novavax/Nuvaxovid™ in these populations, while there is evidence on the safety profile and effectiveness of mRNA COVID-19 vaccines in these populations based on real world use with large numbers of individuals. (Refer to the appropriate section for guidance on the use of recombinant protein subunit COVID-19 vaccines).
- A viral vector COVID-19 vaccine (AstraZeneca or Janssen) may be offered to adults aged ≥ 18 years when all other authorized COVID-19 vaccines are contraindicated. Refer to the section titled, "Guidance on the use of viral vector vaccines" for information about the risks of vaccination for the purposes of obtaining informed consent.

Operational Considerations

Clients/patients who are immunosuppressed due to disease or treatment and/or have an autoimmune condition will indicate so by answering yes to questions 9 and/or 10 of section B on the **COVID-19 Vaccine Consent Form.** This is the signal to the immunizer that they must ensure the client reviews the "COVID-19 Vaccine Information for Individuals who are Immunosuppressed &/or have an Autoimmune Condition" factsheet (available online at: www.manitoba.ca/covid19/vaccine/resources.html). The immunizer or health care provider must also reference to the client/patient, the pertinent information contained in these guidelines. After the client/patient independently reviews the factsheets and listens to the information provided by

the immunizer or health care provider, the immunizer or health care provider should address any remaining questions the client/patient has about the risks and benefits of vaccination, and sign and date the appropriate section of the **COVID-19 Vaccine Consent Form**.

There are limited situations (as written in the section titled, “People who Require Further Consultation before Immunization”) where a client/patient in one or more special populations is unlikely to mount an acceptable immune response to the COVID-19 vaccine and therefore, require further consultation with a relevant specialist before proceeding with immunization.

Clients/patients that sign section D of the **COVID-19 Vaccine Consent Form** are acknowledging that they have read and understood the information in the factsheets. They are also acknowledging that their immunizer or health care provider has satisfactorily answered their questions through an information exchange aided by these guidelines.

Resources for Special Populations

- the National Advisory Committee on Immunization (NACI) Statement on the Recommendations on the use of the COVID-19 vaccines at: www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html#a7
- the Canadian Rheumatology Association Position Statement on COVID-19 Vaccination at: https://rheum.ca/wp-content/uploads/2020/12/CRA-Position-Statement-on-COVID-19-Vaccination-v2-FINAL.pdf
- National Transplant Consensus Guidance on COVID-19 Vaccine at: www.cst-transplant.ca/_Library/Reference_Documents/National_Transplant_Guidance_on_COVID_vaccine_-_Dec_18_2020_Final_1_.pdf
- the Society of Obstetricians and Gynecologists of Canada Statement on COVID-19 Vaccination in Pregnancy at: www.sogc.org/en/-COVID-19/COVID-19/en/content/COVID-19/COVID-19.aspx?hkey=dd7d7494-49fa-4966-ab4d-4dca362a9655
- the Multiple Sclerosis Society of Canada COVID-19 Vaccine Guidance for People Living with MS at: https://mssociety.ca/resources/news/article/covid-19-vaccine-guidance-for-people-living-with-ms
- the Canadian Stem Cell Transplant and Cellular Therapy Director Consensus Statement at: https://www.cttcanada.org/page/covid19
- the International Society of Heart & Lung Transplantation Recommendations from the COVID-19 Task Force (released March 15, 2021) at: https://ishlt.org/ishlt/media/Documents/COVID19_Vaccine-Recommendations_3-15-2021.pdf

People who Require Further Consultation before Immunization

People who fall into one or more of the below categories are unlikely to mount an acceptable immune response to the COVID-19 vaccine at this time and therefore, require further consultation with a relevant specialist before immunizing. (Note that this section, while related, is not referring to medical exemptions for vaccines; refer to page 17 for information on the COVID-19 Vaccine Medical Exemption Program):

- People receiving CAR-T therapy within the last three months.[1]
- People receiving an allogenic or autologous stem cell transplant within the last three months.[5]
- Solid organ transplant recipients: pre-transplant within two weeks of transplant and post-transplant within the last month regardless of induction therapy.[5]
- People receiving active chemotherapy including cyclical chemotherapy:[2] administer vaccine after consultation with prescribing physician. In some cases, it may be possible to administer vaccine one week before the next cycle. If this is not possible, administer vaccine when neutrophil recovery has occurred. For more detailed clinical guidance on the timing of vaccination, please see Appendix A.
- People who are taking, or have taken, one or more of the following medications[4] within the last six months:[5,6]
    - Alemtuzumab
    - Anti-Thymocyte Globulin (ATG) / Thymoglobulin
    - Basiliximab
    - Blinatumomab
    - Cyclophosphamide
    - Obinatuzumab
    - Ocrelizumab
    - Ofatumumab
    - Rituximab
- People with an immediate allergic reaction of any severity to:
    - Polyethylene glycol (PEG) which may be found in a multitude of products including bowel preparation products for colonoscopies, laxatives, cough syrup, cosmetics, contact lens care solutions, skin care products, and as an additive in some food and drinks
    - Polysorbate 80 (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG)
    - Tromethamine (trometamol or Tris), which is a component in contrast media, oral and parenteral medications **contained in the <u>Moderna vaccine only</u>**

[1] The attending physician or specialist may recommend a different time interval based on client/patient assessment.

[2] Low-dose methotrexate (5mg to 25mg), once weekly, given orally or injected, is not a contraindication/ precaution to vaccination.

The COVID-19 vaccine should not routinely be given to:[3]

1. People who are allergic to an active substance or any of the ingredients of the COVID-19 vaccine being administered. For information about a COVID-19 vaccine's ingredients, review the vaccine manufacturer's product monograph at: www.manitoba.ca/vaccine.
2. People who have had a severe allergic reaction after the first dose of a COVID-19 vaccine should be referred to an allergist for further assessment. The National Advisory Committee on Immunization (NACI) notes that if a risk assessment deems that the benefits outweigh the potential risks for the individual; and if informed consent is provided, an authorized COVID-19 vaccine using a different platform may be considered for re-immunization. If immunization with a different platform is offered, individuals should be observed for at least 30 minutes after immunization.
3. People who have experienced major venous or arterial thrombosis with thrombocytopenia following vaccination with a viral vector COVID-19 vaccine should not receive a subsequent dose of a viral vector COVID-19 vaccine.
4. People who have experienced myocarditis or pericarditis following vaccination with a first dose of an mRNA COVID-19 vaccine should defer subsequent doses in the vaccination series until more information is available.
5. Individuals who have experienced a previous CVST with thrombocytopenia or heparin-induced thrombocytopenia (HIT) should only receive a viral vector COVID-19 vaccine if the potential benefits outweigh the potential risks. An alternate COVID-19 vaccine should be offered.
6. AstraZeneca is contraindicated in individuals who have previously experienced episodes of capillary leak syndrome.
7. People who have experienced Guillian-Barré Syndrome (GBS) 42 days following vaccination should discuss with their health care provider, the plan for subsequent doses.

For patient's who have had an allergic reaction to a COVID-19 vaccine, it is recommended to request a referral for an allergy assessment for guidance on future doses of the vaccine by faxing a referral to the appropriate allergy clinic, according to age, to either:

- The Adult Allergy Clinic of Health Sciences Centre at 204-940-2223, **OR**
- The Pediatric Allergy Department of Children's Hospital at 204-787-5040.

Include the following information in the referral request:

- Brand of COVID-19 vaccine
- First or second dose
- Details of the reaction

[3] See Appendix C for national guidance related to allergic responses to vaccination.

COVID-19 Vaccine Medical Exemption Program

The public health emergency orders issued by the Chief Provincial Public Health Officer under *The Public Health Act* require individuals in Manitoba to be fully vaccinated to attend certain public settings.

There are limited contraindications that preclude an individual from being vaccinated, or delay an individual from being (fully) vaccinated. People with contraindications, or who experience delays in vaccination due to their medical history, may be exempt from current provincial public health orders that restrict attendance at certain public settings as set out in the current provincial public health orders to fully vaccinated persons.

The following circumstances are outside of the Manitoba COVID-19 Vaccine Medical Exemption Program:

- COVID-19 vaccine requirements for travel purposes (i.e., the exemption will not be recognized by other provinces or countries).
- COVID-19 vaccine requirements for workplace purposes (e.g., unvaccinated individuals in certain sectors must adhere to regular COVID-19 testing).
- Other non-medical exemptions.

Health care providers that want to propose a new, evidence-based medical criterion for provincial consideration, may email a proposal to: COVID@gov.mb.ca.

For the purposes of the COVID-19 Vaccine Medical Exemption Program:

1. To be considered for the Program, individuals (herein referred to as "clients") must be eligible to be vaccinated against COVID-19 AND must live, work or study in Manitoba for a consecutive period of time of at least 30 days in duration.
2. College of Physicians & Surgeons of Manitoba (CPSM)-registered specialists[4], as per the following definition, are the only health care provider authorized to submit an exemption to Manitoba Health and Seniors Care, and Shared Health to process the exemption: *CPSM-registered specialists are (1) licensed by the College of Physicians and Surgeons of Manitoba; and, (2) certified by and in good standing with the Royal College of Physicians and Surgeons of Canada in the relevant speciality.*

The process for the COVID-19 Vaccine Medical Exemption Program is as follows:

- A client will connect with their primary care provider (or CPSM-registered specialist if a relationship is already in place with a specialist) and set up an appointment to review the COVID-19 Vaccine Medical Exemption Program eligibility criteria. The exemption criteria is as follows:
    - Diagnosis of myocarditis or pericarditis within seven days of an mRNA COVID-19 vaccine, **confirmed by a CPSM-registered cardiologist**.
    - Diagnosis of Guillian-Barré syndrome (GBS) within 42 days of COVID-19 vaccination, **confirmed by a CPSM-registered neurologist**.

[4] Previous terminology used was "licensed specialist." The updated terminology of "CPSM-registered" is synonymous with "licensed specialist".

- A report of a serious adverse event following immunization (AEFI) after a dose of COVID-19 vaccine where the final recommendation documented in PHIMS is for no further COVID-19 vaccination, **confirmed by a CPSM-registered provincial Medical Officer of Health.**[5]

- Acute diagnosis of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) **confirmed by a CancerCare Manitoba (CCMB) hematologist** represents an absolute contraindication to further vaccination with an adenovirus vector COVID-19 vaccine. Subsequent vaccination with an mRNA COVID-19 vaccine may be feasible but should be approved by a CCMB hematologist.

- CAR-T therapy within the last three months, **confirmed by CCMB hematologist/oncologist**.

- Allogenic or autologous stem cell transplant within the last three months, **confirmed by CCMB hematologist/oncologist**.

- Solid organ transplant recipients: pre-transplant within two weeks of transplant and post-transplant within the last month regardless of induction therapy, **confirmed by the CPSM-registered specialist supervising the transplant**.

- Active receipt of anti-cancer drug therapy may attenuate the immune response to vaccination however, given the significant risk of COVID-19 related severe complications and mortality in this patient population, the general approach has been to proceed with immunization. There may be clinical reasons in a subset of this population where deferring vaccination to a later date is appropriate, as per the **CCMB CPSM-registered oncologist/hematologist**.

- Active receipt of one or more of the following medications within the last six months may attenuate the immune response to vaccination: alemtuzumab, anti-thymocyte globulin (ATG)/thymoglobulin, basiliximab, blinatumomab, obinatuzuamb, ocrelizumab, ofatumumab, cyclophosphamide or rituximab. Given the significant risk of COVID-19 related severe complications and mortality in this patient population, the general approach has been to proceed with immunization. There may be clinical reasons in a subset of this population where deferring vaccination to a later date is appropriate, as per the **CCMB oncologist/hematologist or CPSM-registered specialist prescribing the therapy**.

- Severe allergy or anaphylactic reaction to a previous dose of a COVID-19 vaccine or any of its components that cannot be mitigated, **confirmed by a CPSM-registered allergist at the Health Sciences Centre (HSC) Allergy Clinic**.

[5] If a clinician believes that a serious AEFI occurred following a dose of COVID-19 vaccine, they must complete an AEFI form and submit it to public health for review. On the AEFI form the clinician should indicate that a request for exemption has been made by the patient. If an AEFI has already been submitted for the same event, the clinician must submit a new AEFI form that clearly communicates this is an update to include the request for exemption.

- The primary care provider will review the client's medical history and the eligibility criteria with the client and, if applicable, will refer the client to the appropriate CPSM-registered specialist.
- The specialist will meet with the client (may be virtual or in-person as required to complete the assessment) to conduct an assessment of the medical history and review the client's file to determine eligibility.
- If the client meets the eligibility criteria, the specialist will submit an exemption to Manitoba Health and Shared Health.
- Once the necessary documents are submitted to Manitoba Health and Shared Health by the specialist, the information is entered into the client's electronic public health record in PHIMS and made available in the digital QR Code. Clients would also be able to apply for a printed Vax Card as well.

*Advice to Clients who do **NOT** Meet the Medical Exemption Criteria*

- Individuals should be counselled on the material risks and expected benefits of vaccination as it pertains to their individual circumstances, taking into account their age, medical history, risk of exposure and risk of experiencing severe outcomes from a SARS-CoV-2 infection.
    - Refer to question 3 of the Clinical Practice Questions and Answers for information on communicating with vaccine hesitant clients.
- Advise individuals to continue to follow public health measures for prevention and control of SARS-CoV-2 infection and transmission.

Advice to Clients who meet the Medical Exemption Criteria

- Advise clients to continue to follow recommended public health measures for the prevention and control of SARS-CoV-2 infection and transmission.
- Advise clients to consider the public health measures in place at the public setting they are considering attending.
- Advise clients to assess their individual risk prior to attending each public setting.
    - Outdoors is lower risk than indoors.
    - When indoors, good ventilation will reduce the risk (e.g., open windows and doors).
    - Smaller group sizes are lower risk than larger group sizes.
    - Fewer contacts is lower risk than many contacts.
- Advise clients that if they are comfortable, to consider asking those who they interact with about their vaccination status. Eligible household members and other eligible close contacts of medically exempt individuals are strongly recommended to be fully vaccinated to lower the risk of transmission to the medically exempt individual as much as possible. Remind clients that the risk of acquiring COVID-19 is never zero, even for fully vaccinated people, but the risk is significantly reduced following vaccination, and further reduced by adhering to public health measures.

Guidance for use of the Viral Vector Vaccines[6]

There are two viral vector vaccines authorized for use by Health Canada among individuals ≥ 18 years of age: AstraZeneca[7] and Janssen vaccine. Manitoba has a limited supply of AstraZeneca and Janssen.

Public-facing information is available online at:
https://www.gov.mb.ca/covid19/vaccine/about.html#vvv

Recommendations for use

The National Advisory Committee on Immunization (NACI) recommends that a **primary series[8]** of a viral vector COVID-19 vaccine (AstraZeneca or Janssen) may be offered to individuals in the authorized age group without contraindications to the vaccine to initiate a series only when other authorized COVID-19 vaccines are contraindicated. **In Manitoba, only individuals aged ≥ 18 years who are unable or unwilling to receive, (1) an mRNA COVID-19 vaccine (Pfizer or Moderna), or (2) a recombinant protein subunit vaccine (Novavax/Nuvaxovid™), may receive the AstraZeneca or Janssen vaccine (while supplies last), if they provide informed consent.**

Informed consent is to include a discussion about:

1. **Clinical recommendations: NACI and Manitoba preferentially recommend that a complete series with an mRNA COVID-19 vaccine be offered to individuals in the authorized age group without contraindications to the vaccine. An authorized recombinant protein subunit COVID-19 vaccine may be offered to individuals in the authorized age group without contraindications to the vaccine who are not able or willing to receive an mRNA COVID-19 vaccine.**
2. **Vaccine safety:** individuals must be informed of the following risks, their symptoms and the need to seek immediate medical care should symptoms develop: vaccine-induced immune thrombotic thrombocytopenia (VITT), Guillain Barre syndrome (GBS), capillary leak syndrome (CLS), immune thrombocytopenia (ITP) and venous thromboembolism (VTE). **These risks do NOT appear to occur with the mRNA vaccines or protein subunit vaccine.**

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[6] On September 16, 2021, Health Canada approved the AstraZeneca/Vaxzevria™ vaccine under the Food and Drug Regulations (i.e., it is no longer issued market authorizations with the conditions for early access under the interim order, as sufficient data was made available to approve it under normal regulations). For the purposes of this document, the vaccine will continue to be referred to as "AstraZeneca." Janssen was approved under the Food and Drug Regulations on November 23, 2021.

[7] Health Canada authorized two manufacturers to produce AstraZeneca: AstraZeneca and Serum Institute of India (SII). NACI has not specifically reviewed evidence for the SII vaccine, but Health Canada has deemed SII and AstraZeneca vaccines to be comparable. AstraZeneca was previously referred to as AstraZeneca/COVISHIELD.

[8] Use of a viral vector vaccine for booster doses is **NOT** Health Canada approved nor is it recommended provincially/nationally given that there is unknown/limited data available to support this use. In situations where a client would refuse a booster if only an mRNA vaccine were available or where contraindicated, a viral vector vaccine booster can be offered provided a robust informed consent discussion takes place, noting the risks/benefits of using a viral vector vaccine in general, as well as in the context of using it as a third dose (e.g., off-label use, not clinically recommended, unknown/limited data, etc.).

3. **Vaccine effectiveness:** data from clinical trials and observational studies suggests that the viral vector vaccines may be comparatively less protective than the mRNA vaccines or the protein subunit vaccine. Clinical trials showed that beginning two weeks after the single dose, Janssen was 66% effective in protecting trial participants against COVID-19, while clinical trial data from the US showed an overall vaccine efficacy of 76% following 2-doses of AstraZeneca.

Specifically for the Janssen vaccine, in addition to the above, informed consent is to also include a discussion about:

- **Dosage:** Janssen is currently approved as a one-dose schedule in Canada. Due to the relatively lower effectiveness of a Janssen single dose schedule, individuals who received a single dose of Janssen should be offered an additional mRNA vaccine 6 months after their Janssen dose. At present, individuals with a single dose of Janssen are eligible to apply for a Vax Card through the regular process. Individuals choosing to receive a single dose of Janssen need to be advised that a 2-dose schedule may be required to ensure that their Vax Card remains valid.[9]

Viral vector vaccines are contraindicated for:

- Individuals who have experienced a previous CVST with thrombocytopenia or heparin-induced thrombocytopenia (HIT) should only receive a viral vector COVID-19 vaccine if the potential benefits outweigh the potential risks. An alternate COVID-19 vaccine should be offered. NACI recommends that persons who have experienced major venous or arterial thrombosis with thrombocytopenia following vaccination with a viral vector COVID-19 vaccine should not receive a second dose of a viral vector COVID-19 vaccine.
- Individuals who have previously experienced episodes of capillary leak syndrome.
- Individuals who are hypersensitive to the active ingredient, any other adenovirus-based vaccines, or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container:

	Dosage Form/Strength/Composition	Non-medicinal Ingredients
AstraZeneca	Solution Multidose vial (8 dose and 10 dose vial presentations)	• Disodium edetate dihydrate (EDTA) • Ethanol • L-Histidine • L-Histidine hydrochloride monohydrate • Magnesium chloride hexahydrate • Polysorbate 80 • Sodium chloride • Sucrose

[9] In rare situations where a single dose of Janssen is administered less than 28 days following a dose of mRNA vaccine, the Janssen dose can be considered valid and will end the series for as long as MB recognizes Janssen as a single-dose schedule.

		• Water for injection
Janssen	Suspension, (5 × 1010 virus particles/0.5 mL), adenovirus type 26 (Ad26) vectored COVID-19 vaccine encoding the SARS-CoV-2 Spike (S) protein in a stabilized confirmation Multi-dose vial (total fill volume 3.1 mL, containing 5 doses of 0.5 mL)	• 2-hydroxypropyl-β-cyclodextrin (HBCD) • Citric acid monohydrate • Ethanol • Hydrochloric acid • Polysorbate-80 • Sodium chloride • Sodium hydroxide • Trisodium citrate dihydrate • Water for injection

Interchangeability (i.e., vaccine product selection)

In Manitoba, clients/patients who received a first dose of AstraZeneca are recommended to be offered an mRNA COVID-19 vaccine (Pfizer or Moderna) for subsequent dose(s), eight to 12 weeks after the last AstraZeneca dose, with an absolute minimum interval of 28 days. In individual cases where a client would not otherwise be fully vaccinated if only an mRNA vaccine or protein subunit vaccine were offered for second doses, the AstraZeneca vaccine can be offered with informed consent as a second dose.

Evidence indicates that mixed COVID-19 viral vector and mRNA vaccine schedules with dosing intervals between 4 and 12 weeks have acceptable safety profiles that may be associated with short-term increased systemic reactogenicity, which is potentially increased with shorter intervals between vaccines.

Current evidence indicates that humoral and cellular immune responses (including responses against VOCs) increase when the Pfizer vaccine is administered as the second dose after AstraZeneca vaccine with an interval of 8 to 12 weeks, and are equivalent to or greater than immune responses following a homologous two-dose schedule of the AstraZeneca or Pfizer-BioNTech vaccine. Specifically, the Pfizer vaccine induced significantly higher frequencies of spike-specific CD4 and CD8 T cells and, in particular, high titres of neutralizing antibodies against the B.1.1.7, B.1.351 and the P.1 variants of concern of SARS-CoV-2. Although [the study] setup did not allow for randomization of the participants, this study demonstrated that the group boosted with Pfizer showed stronger immune responses than the group boosted with AstraZeneca.[10] **See Appendix G for a detailed summary table for clinicians to guide decision-making around intervals.**

[10] Barros-Martins J, Hammerschmidt SI, Cossmann A, Odak I, Stankov MV, Ramos GM, et al. Humoral and cellular immune response against SARS-CoV-2 variants following heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination. medRxiv. 2021 Jun 3. doi: 10.1101/2021.06.01.21258172.

Information on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT)

Health Canada has issued label changes and guidance on AstraZeneca and Janssen, following reports of rare but very serious cases of blood clots associated with low levels of blood platelets (i.e., thrombocytopenia) following immunization. This is known as Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) (previously referred to as Vaccine-Induced Pro-thrombotic Immune Thrombocytopenia (VIPIT), and would be classified as the anti-PF4 positive subgroup within the case definition for Thrombosis with Thrombocytopenia Syndrome (TTS)). The majority of cases identified so far have been in women under the age of 55 years – although cases in men and individuals between 55 and 80 years of age have also been reported, and have mostly occurred between 4 and 14 days post-vaccination. The exact mechanism by which the viral vector COVID-19 vaccines may trigger VITT is still under investigation but the mechanism appears to be similar to spontaneous heparin-induced thrombosis (HIT) / autoimmune heparin-induced thrombosis, where antibodies to platelet factor 4 (PF4)-polyanion complexes induce platelet activation, which causes thrombosis and thrombocytopenia. Due to the immune stimulus, and frequent occurrence of disseminated intravascular coagulation, clots related to VITT can be very aggressive and challenging to treat. They cannot be managed the same way as clots related to oral contraceptives, immobility, or long haul flights, and have an entirely different biologic mechanism of action. While thrombotic events have been rarely reported after vaccination with mRNA COVID-19 vaccines or after infection with SARS-CoV-2, most of these events have not been accompanied by thrombocytopenia or the other distinctive characteristics of VITT.

At this time, no other predisposing factors have consistently been identified in patients who develop VITT. The rate of VITT is most commonly estimated to be 1 per 26,000 and 1 per 100,000 persons following vaccination with a first dose of AstraZeneca vaccine. As of June 1, 2021, PHAC has estimated the rate of VITT in Canada to be 1 in 73,000 doses administered. However, as investigations continue, this rate could be as high as 1 in 50,000. For updates to the numbers of cases of TTS and VITT in Canada, please see the “Serious and non-serious adverse events reported” section of reported side effects following COVID-19 vaccination in Canada. The frequency of TTS following a second dose of AstraZeneca vaccine is currently reported between 1 per 600,000 and 1 per 750,000 individuals vaccinated with a second dose, based on vaccine safety surveillance data from the United Kingdom but this continues to evolve. The case fatality rate of VITT depends on prompt detection, diagnoses and treatment and typically ranges between 20 and 50 per cent. Many cases have been reported to have serious long-term morbidity, including neurologic injury. As of September 8, 2021, 46 VITT cases were confirmed after more than 14.5 million doses of Janssen were administered in the USA.

The outcome of VITT can be serious, including death. If diagnosed early, VITT can be treated and the risk of serious outcomes reduced. For those who have been vaccinated with a viral vector COVID-19 vaccine less than 42 days ago, be alert to the signs and symptoms of thromboembolism and thrombocytopenia. Symptoms to be vigilant for include: shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological symptoms including sudden onset of severe or persistent worsening headaches or blurred vision, skin bruising (other than at the site of vaccination) or petechiae. A decision tree to assist clinicians in the

diagnosis of VITT is included below however, specialist consultation may be required. For more information, refer to https://covid19-sciencetable.ca/sciencebrief/vaccine-induced-prothrombotic-immune-thrombocytopenia-vipit-following-astrazeneca-covid-19-vaccination/ and https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-letter.pdf.

Note that active monitoring of asymptomatic immunized clients/patients is not required at this time. **To date, VITT has not been identified following receipt of mRNA COVID-19 vaccines.**

The below diagram (updated May 21, 2021) is a decision tree for diagnosing and ruling out VITT from Thrombosis Canada.[11]

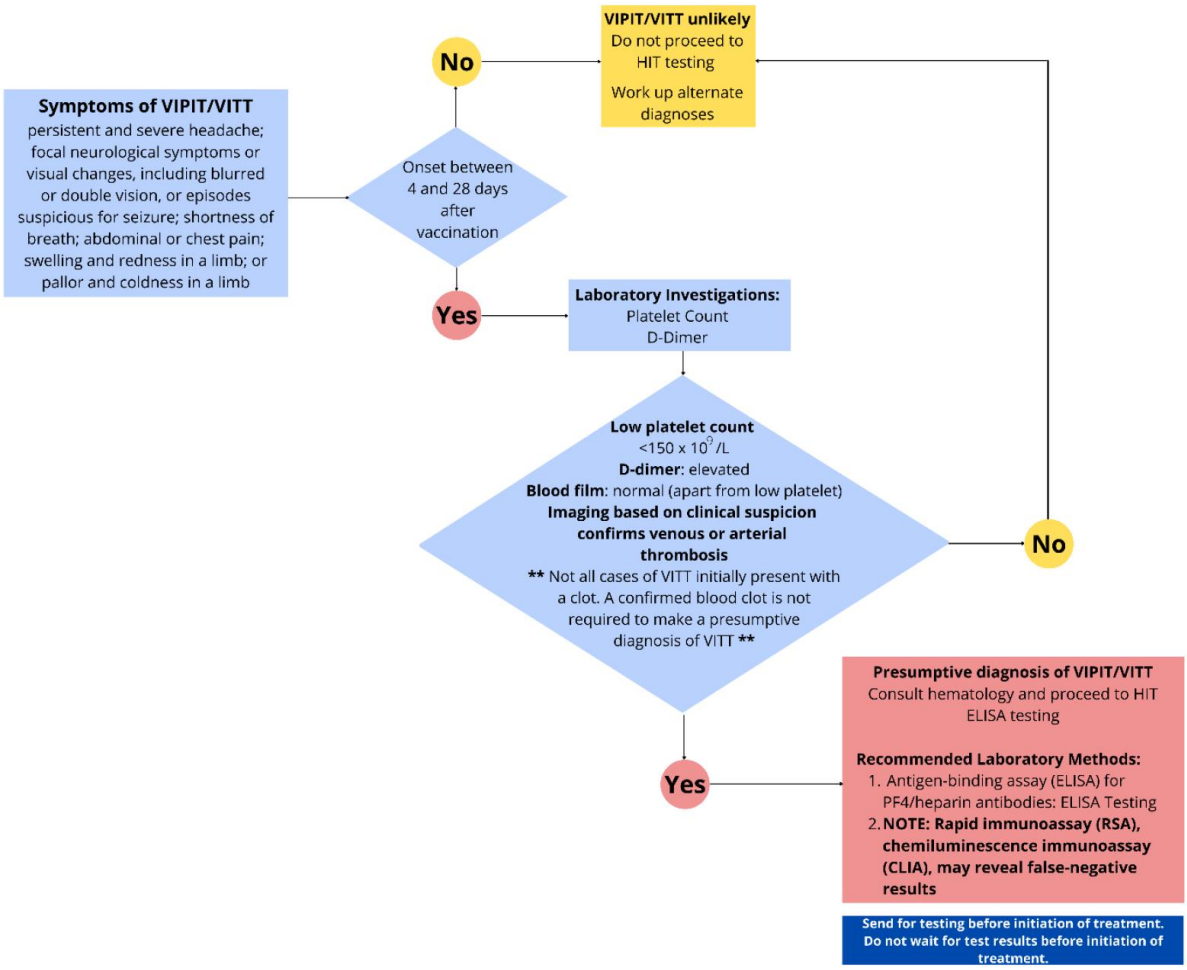

Image adapted and used with permission from Ontario's COVID-19 Science Advisory Table

Health Canada updated the AstraZeneca labelling information on June 29, 2021:

[11] Pai M, Grill A, Ivers N, et al. Vaccine-induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://covid19-sciencetable.ca/sciencebrief/vaccine-induced-prothrombotic-immune-thrombocytopenia-vipit-following-astrazeneca-covid-19-vaccination/

Thrombosis and thrombocytopenia

A combination of thrombosis and thrombocytopenia including thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with AstraZeneca COVID-19 Vaccine during post-authorization use. This includes severe cases in unusual sites such as cerebral venous sinus thrombosis (CVST) and splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. The majority of these cases occurred within the first 3 weeks following vaccination. Some cases had a fatal outcome.

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. The benefits and risks of vaccination should be considered in these patients.

Healthcare professionals should be alert to the signs and symptoms of thrombosis and thrombocytopenia. Vaccinated individuals should be instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling or pain, or persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms after vaccination including sudden onset of severe headaches, persistent or worsening headaches, blurred vision, confusion or seizures, or who experiences unusual skin bruising or petechiae beyond the site of vaccination after a few days, should seek prompt medical attention.

Individuals who have experienced a previous CVST with thrombocytopenia or heparin-induced thrombocytopenia (HIT) should only receive the AstraZeneca COVID-19 Vaccine if the potential benefits outweigh the potential risks. Patients who have experienced major venous or arterial thrombosis with thrombocytopenia following vaccination with AstraZeneca COVID-19 Vaccine should not receive a second dose of AstraZeneca COVID-19 Vaccine.

Since medical management of a post-vaccine thrombosis with thrombocytopenia may be different than medical management of other thromboses, if patients present with thrombosis with thrombocytopenia, healthcare professionals should consult with current guidance and hematologic specialists to diagnose and treat this post-vaccine event. Individuals diagnosed with thrombocytopenia within 3 weeks of vaccination with the AstraZeneca COVID-19 Vaccine should be actively investigated for signs of thrombosis, and similarly individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.

To further the understanding of a possible association of cases observed with thrombocytopenia and thrombosis following receipt of COVID-19 vaccines, Brighton Collaboration has drafted a case finding definition, available at: https://brightoncollaboration.us/thrombosis-with-thrombocytopenia-syndrome-case-finding-definition/. The purpose of this case finding definition is to identify individuals that can be studied using a common study protocol and assessment.

Resources:

- Guidance from Thrombosis Canada on diagnosis and managing VITT: https://assets.doctorsmanitoba.ca/documents/Thrombosis-Canada-VITT.pdf?mtime=20210519164602&focal=none.
- Manitoba Hematology has developed an overview that provides guidance on the presentation, diagnosis and management of VITT (current as of May 12, 2021): https://assets.doctorsmanitoba.ca/documents/Hematology-VITT.pdf?mtime=20210519164601&focal=none

Information on Guillain-Barre Syndrome (GBS)

Guillain-Barre syndrome (GBS) is a rare but potentially serious immune-mediated neurologic disorder that results in pain or numbness, muscle weakness, and paralysis in severe cases. Most people fully recover from GBS but some have residual deficits or symptoms and rarely, fatal cases can occur. GBS can result from different causes, including infections, and occurs more frequently in males and persons aged 50 years or more. Cases have been rarely reported after receipt of some vaccines. **To date, no increased risk of GBS has been identified following vaccination with the authorized mRNA COVID-19 vaccines (Pfizer and Moderna). Investigations have identified an increased risk of GBS following vaccination with the authorized viral vector COVID-19 vaccines (AstraZeneca and Janssen).**

In Canada, the number of cases of GBS following AstraZeneca vaccination is higher than would normally be expected based on rates in the general population. Up to and including September 10, 2021, PHAC had 30 reports of GBS among more than 2,750,000 doses of AstraZeneca vaccines administered (estimated rate of 1.08 cases per 100,000 doses). Symptoms occurred between 6 hours and 25 days after vaccination and the median age was 55 years (range 40 to 77 years old) and 22 (73%) were males. In the US, reports of adverse events suggest an increased risk of GBS during the 42 days following vaccination with the Janssen COVID-19 vaccine (note: AstraZeneca has not been used in the US). As of September 15, 2021, there were 201 preliminary cases of GBS reported in the US Vaccine Adverse Events Reporting System (VAERS) among more than 14.7 million doses of the Janssen vaccine administered (estimated rate of 1.37 cases per 100,000 doses). These cases have largely been reported about 2 weeks after vaccination and mostly in men, many 50 years and older.

Information on capillary leak syndrome

The following excerpt has been added to the Warnings and Precautions of the AstraZeneca and Janssen Product Monographs:

> Capillary leak syndrome
> Cases of capillary leak syndrome (CLS) have been observed very rarely in the first days after vaccination with AstraZeneca COVID-19 Vaccine. Some of the reported cases had a history of CLS. Some cases had a fatal outcome. CLS is a rare disease characterized by acute episodes of limb edema, hypotension, hemoconcentration and hypoalbuminemia. Patients with an acute episode of CLS following vaccination require prompt medical attention and treatment. Intensive supportive therapy is usually warranted. Individuals with a known history of CLS should not be vaccinated with this vaccine.

Information on immune thrombocytopenia (ITP) and venous thromboembolism (VTE)

Health Canada provided the following information on November 9, 2021 (https://recalls-rappels.canada.ca/en/alert-recall/health-canada-updating-labels-janssen-and-vaxzevria-astrazeneca-covid-19-vaccines):

Immune thrombocytopenia

Very rare cases of ITP, an autoimmune condition, have been reported internationally after receiving the Janssen COVID-19 vaccine. Similarly, cases of thrombocytopenia including ITP have been reported after receiving Vaxzevria.
ITP is a disorder that can lead to easy or excessive bruising and bleeding. The bleeding results from unusually low levels of platelets the cells that help blood clot. These cases typically occur within the first four weeks after vaccination. Some of these cases occurred in individuals with a history of ITP. Cases with a fatal outcome have been reported abroad.

Advise individuals to seek immediate medical attention if they develop symptoms, such as unexplained bleeding, unexplained bruising, or small purplish spots beyond the site of vaccination.

Venous thromboembolism

Rare cases of VTE have been reported following vaccination with the Janssen COVID-19 vaccine. VTE is a condition where a blood clot forms in a deep vein, usually in a leg, arm or groin, and may travel to the lungs causing a blockage of the blood supply, with possible life-threatening consequences.

The risk of VTE should be considered for individuals who are at increased risk for thromboembolism. Healthcare professionals should be alert to the signs and symptoms of VTE. Individuals should seek immediate medical attention if they develop symptoms, such as shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain following vaccination.

The risk of VTE should be considered for individuals who are at increased risk for thromboembolism. Healthcare professionals should be alert to the signs and symptoms of VTE. Individuals should seek immediate medical attention if they develop symptoms, such as shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain following vaccination.

Healthcare professionals are to:

- Be alert to the signs and symptoms of thromboembolism and thrombocytopenia to promptly treat these conditions according to available evidence and clinical guidelines.
- Inform people receiving the vaccine to seek medical attention if they develop any of the following symptoms:
    - ITP symptoms include spontaneous bleeding, unusual bruising or small red, purple or brown spots that appear under the skin.

    - VTE symptoms include shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain following vaccination.
- Consider consultation with a specialist if suspect the patient has post-vaccine thrombosis.
- If an individual has a history of a thrombocytopenic disorder, such as immune thrombocytopenia, the risk of developing low platelet levels should be considered before administering the vaccine and platelet monitoring is recommended after vaccination.

The Warnings and Precautions of the AstraZeneca and Janssen Product Monographs have been update accordingly.

Locations that have supply of AstraZeneca and Janssen

Hub locations have been set-up across the province to store limited supply of AstraZeneca, with some hub locations also storing Janssen. Hub locations are expected to accept appointments from anyone in Manitoba who requests AstraZeneca or Janssen following a discussion of the risks and benefits with their immunizer/health care provider, regardless of whether they are a patient of that clinic/pharmacy or where they received their first dose of AstraZeneca.

The below list includes 15 medical clinics and pharmacies that act as regional hubs. Interested individuals can be directed to use the online vaccine finder (manitoba.ca/covid19/vaccine/finder.html) to find a location with available doses, and will need to continue to check the online vaccine finder for any updates to these locations.

Location Name	Address	City
Brandon Clinic Pharmacy	4 42 Mctavish Ave. E.	Brandon
Dauphin Clinic Pharmacy	622 3rd St. SW	Dauphin
Ashern Pharmacy	43 Main St.	Ashern
Gimli Express Care Clinic	50 Center St.	Gimli
Safeway Pharmacy	318 Manitoba Ave.	Selkirk
The Medicine Shoppe Pharmacy	1 330 Fischer Ave.	The Pas
The Medicine Shoppe Pharmacy	3 602 Saskatchewan Ave. W	Portage la Prairie
Loblaw Pharmacy	175 Cargill Rd.	Winkler
Manitoba Clinic	790 Sherbrook St.	Winnipeg
Safeway Pharmacy	3393 Portage Ave.	Winnipeg
Costco	1499 Regent Ave. W	Winnipeg
Viva Care Kenaston	1665 Kenaston Blvd.	Winnipeg
Prairie Health Apothecary	600 St Anne's Rd.	Winnipeg
Loblaw Pharmacy	2132 Mcphillips St.	Winnipeg
Sobeys Pharmacy	1 178 PTH 12N	Steinbach

NOTE: a small supply of Janssen (while supplies last) is being held at the provincial distribution warehouse; any medical clinic or community pharmacy that is participating in the COVID-19 Immunization Program can request to order Janssen to meet client demand.

Guidance for use of the Protein Subunit Vaccine in the Primary Series and Booster Dose for the Adult Population

The Novavax/Nuvaxovid™ COVID-19 vaccine was the first COVID-19 recombinant protein subunit vaccine authorized as a 2-dose primary schedule by Health Canada for use in adults aged ≥ 18 years on February 17, 2022. Manitoba is scheduled to receive a small supply of the Novavax/Nuvaxovid™ COVID-19 vaccine.

This section of the Clinical Practice Guidelines is intended to provide a broad overview of the recommended use of the recombinant protein subunit COVID-19 vaccine in Manitoba. More information can be found at the original sources of information cited below:

- the National Advisory Committee on Immunization's "Recommendations on the use of the Novavax/Nuvaxovid™ COVID-19 vaccine" (www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-novavax-nuvaxovid-covid-19-vaccine.html).
- the Novavax/Nuvaxovid™ COVID-19 vaccine Product Monograph (covid-vaccine.canada.ca/info/pdf/nuvaxovid-pm-en.pdf).

Recommendations for use

Consistent with the National Advisory Committee on Immunization (NACI), Manitoba public health officials recommend that an authorized recombinant protein subunit COVID-19 vaccine may be offered to:

- Individuals in the authorized age group without contraindications to the vaccine who are not able or willing to receive an mRNA COVID-19 vaccine:
    - for the complete primary series at a recommended interval of 8 weeks between doses (authorized interval is 3 weeks; minimal interval is 21 days); or
    - for a second dose at a recommended interval of eight weeks following the administration of an authorized COVID-19 vaccine; and/or,
    - for the booster dose at a recommended interval of 6 months after a primary series for persons aged 18 years and older. **NOTE: Novavax/Nuvaxovid™ is not currently authorized for use as a booster dose in Canada.**
- Moderately to severely immunocompromised individuals in the authorized age group without contraindications to the vaccine who are not able or willing to receive an mRNA vaccine:
    - for the complete primary series (dose 1, dose 2 and dose 3) at a recommended interval of 8 weeks between dose 1 and dose 2 (authorized interval is 3 weeks; minimal interval is 21 days) and at least 28 days between dose 2 and dose 3; or,
    - for a second dose and/or third dose at a recommended interval of eight weeks after dose 1 of an authorized COVID-19 vaccine and/or at least 28 days after dose 2 of an authorized COVID-19 vaccine; and/or,
    - for the booster dose at a recommended interval of 6 months after a primary series for persons aged 18 and older. **NOTE: Novavax/Nuvaxovid™ is not currently authorized for use as a three-dose primary series or as a booster dose in Canada.**

For more information on booster dose guidance including who is recommended to be offered a booster dose, refer to the section titled, "Guidance on Booster Doses of mRNA Vaccines for Adolescents and Adults."

NACI notes that data collected over the course of the pandemic has consistently found that Canadians cite "ensuring the safety of the vaccine" as the main reason for delaying or not getting COVID-19 vaccination. For some individuals, their safety concern or vaccine hesitancy has focused on the viral vector or mRNA vaccine platforms. There is currently more experience with mRNA COVID-19 vaccines but Novavax/Nuvaxovid™ now provides another option for use. NACI took into account the available evidence on Novavax/Nuvaxovid™ and the accumulating real-world evidence on the effectiveness and safety of the mRNA COVID-19 vaccines. **The mRNA COVID-19 vaccines continue to be the preferentially recommended COVID-19 vaccine product for the primary series and booster dose.**

As per NACI, the recombinant protein subunit COVID-19 vaccine may be:

- co-administered (i.e., given simultaneously with), or at any time before/after, non-COVID-19 vaccines (including live and non-live vaccines).
- used in a homologous primary series, heterologous (mixed) primary series or as a booster dose in a homologous or heterologous prime-boost series for individuals without contraindications for whom mRNA COVID-19 vaccine is contraindicated, inaccessible, or has been refused.
    - Novavax/Nuvaxovid™ demonstrated safety and appeared immunogenic when studied in a heterologous primary series with either Pfizer (30mcg) or AstraZeneca as a first dose. When used as the second dose in a heterologous primary series, Novavax/Nuvaxovid™ is more immunogenic than two doses of AstraZeneca, but not two doses of Pfizer (30mcg).
    - There was demonstrated safety and Novavax/Nuvaxovid™ appeared immunogenic when studied as a booster dose in a homologous or heterologous prime-boost series. However, it may not be as immunogenic as a booster dose with an mRNA COVID-19 vaccine when used as a heterologous booster. **NOTE: as per the Novavax/Nuvaxovid™ product monograph, "there are no data available on the interchangeability of Nuvaxovid™ with other COVID-19 vaccines to complete the vaccination series."**

As per the product monograph, Novavax/Nuvaxovid™ is contraindicated among individuals:

- who are allergic to the active substance or any of the other ingredients of the vaccine;
- who had an allergic reaction to a previous dose of Novavax/Nuvaxovid™; and/or
- who have symptoms of COVID-19.

NACI notes that severe immediate allergic reactions (e.g., anaphylaxis) have not been reported following immunization with Novavax/Nuvaxovid™ in the clinical trials. However, given the size of the clinical trials, rare and very rare side effects of the Novavax/Nuvaxovid™ are not likely to have been identified at this time.

Vaccination of special populations

NACI notes that the safety and efficacy of Novavax/Nuvaxovid™ have not been established in the following populations:

- Individuals previously infected with SARS-CoV-2;
- Individuals who are immunocompromised due to disease or treatment;
- Individuals who are pregnant or breastfeeding;
- Individuals who have an autoimmune condition.

Informed consent should include discussion that there is currently limited evidence on the use of the Novavax/Nuvaxovid™ in these populations, while there is evidence on the safety profile and effectiveness of mRNA COVID-19 vaccines in these populations based on real world use with large numbers of individuals.

Vaccine efficacy and safety

Novavax/Nuvaxovid™ was evaluated in two pivotal Phase 3 trials: study one conducted in North America (the United States and Mexico) and study two conducted in the United Kingdom. Vaccine efficacy was also assessed in a Phase 2a/b clinical trial in South Africa. Safety was evaluated from an interim analysis of pooled data from five ongoing clinical trials conducted in Australia, South Africa, the United Kingdom, the United States and Mexico. At the time of the analysis, a total of 49,950 participants received at least one dose of Novavax/Nuvaxovid™ (n=30,058) or placebo (n=19,892). The median follow-up duration was at least 2 months post dose 2, with 66% of subjects completing at least 2 months follow-up. In all trials, eligible participants were adults aged ≥ 18 years who were healthy or were individuals with stable chronic medical conditions. Individuals with a known previous history of lab-confirmed SARS-CoV-2 infection or known immunosuppression were excluded. These trials were conducted prior to the emergence of Delta and Omicron, and there is very limited immunogenicity data, and no efficacy/effectiveness data to demonstrate what level of protection Novavax/Nuvaxovid™ offers against Omicron.

NACI summarized the clinical trial data (available as of the date of Health Canada approval) with regards to vaccine efficacy and safety.

<u>Vaccine efficacy</u>

Novavax/Nuvaxovid™ is highly efficacious (~90%) in preventing confirmed symptomatic COVID-19 disease in the short-term starting at one to two weeks after receiving the full two-dose series. Estimates of vaccine efficacy against the original SARS-CoV-2 strain were comparable to estimates in countries where the predominant circulating strain was the Alpha variant. However, vaccine efficacy was lower against the Beta variant. No efficacy or effectiveness data is available for Novavax/Nuvaxovid™ against the Delta or Omicron variants.

Vaccine safety:

Local and systemic adverse events after any dose were typically mild and transient.

Serious adverse events and other adverse events of interest: Fatal events were rare, with 21 deaths reported (13 in the vaccine group and 8 in the placebo groups). The incidence was similar in the younger age cohort between the vaccine and placebo group, but slightly higher in the vaccine group in the older age cohort. Events were mostly consistent with the morbidity associated with age and underlying medical conditions in the study population and none were assessed as related to the vaccine. No specific adverse events led to study discontinuation. Severe adverse events (about 1%) were infrequently reported and similar between the vaccine and placebo groups. Also similar between groups were serious adverse events, medically attended adverse events, and adverse events of special interest. There were no serious allergic reactions reported in the study. Serious events of Hepatobiliary Disorders were reported only in the vaccine group in participants 18 to 64 years of age, but these events (n=12) were assessed as not related to the vaccine. These were mostly reports of cholecystitis and cholelithiasis, but the majority of vaccine recipients who experienced these events had one or more risk factors for these types of outcomes.

Myocarditis and/or pericarditis: there are preliminary data on cases of myocarditis and/or pericarditis following the administration of Novavax/Nuvaxovid™ from the clinical trial data. Post-market safety surveillance data will be closely monitored to determine whether this is an adverse event of interest associated with Novavax/Nuvaxovid™, similar to myocarditis and/or pericarditis associated with mRNA COVID-19 vaccines, and to identify risk factors associated with the adverse event, and the rate at which this adverse event occurs. Per the product monograph: Myocarditis was identified in two teenage men shortly after receiving a second dose of vaccine resulting in a mild clinical course with complete resolution and no sequelae. Currently available information is insufficient to determine a causal relationship with the vaccine.

The probability of detection of very rare adverse events in clinical trials is low given clinical trial population sizes; therefore, ongoing pharmacovigilance is essential and underway.

Dosage forms, strength, composition and packaging (per Nuvaxovid™ product monograph)

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension One dose (0.5 mL) contains 5 mcg of SARS-CoV-2 recombinant spike protein (original [Wuhan] strain) Multidose vial (5 mL, containing 10 doses of 0.5 mL)	• Disodium hydrogen phosphate heptahydrate • Hydrochloric acid (for adjustment of pH) • Polysorbate 80 • Sodium chloride • Sodium dihydrogen phosphate monohydrate • Sodium hydroxide (for adjustment of pH) • Water for Injection **For adjuvant:** • Cholesterol • Disodium hydrogen phosphate dihydrate • Phosphatidylcholine • Potassium chloride • Potassium dihydrogen phosphate • Sodium chloride

Novavax/Nuvaxovid™ characteristics

Product characteristics	Novavax Nuvaxovid
Type of vaccine	Recombinant protein subunit (adjuvanted)
Age	18 years of age and older
Diluent	None
Dose	0.5 mL (5 mcg SARS-CoV-2 recombinant spike protein)
Doses per vial	10
Potential allergens	Polysorbate 80
Adjuvant	Matrix-M adjuvant (50 mcg)
Storage requirements	2°C to 8°C for a maximum of 6 months. Do not freeze. Keep the vials in the outer carton in order to protect from light.
Opened multi-dose vial storage	2°C to 25°C for up to 6 hours after first needle puncture
Adapted from the National Advisory Committee on Immunization statement; for more information/details, refer to the Novavax/Nuvaxovid™ product monograph.	

Guidance for use of the mRNA Vaccines[12] in the Primary Series for the Adolescent/Adult Population

*****The following guidance pertains to the use of Pfizer (30 mcg) and Moderna for the primary series for adolescents/adults aged ≥ 12 years*****

Recommendations for use

Manitoba public health officials and the National Advisory Committee on Immunization (NACI) preferentially recommend a complete series of mRNA COVID-19 vaccine be offered to individuals aged ≥ 12 years without contraindications to the vaccine.

Despite some evidence of increasing risk of breakthrough infections, particularly in the context of Omicron circulation, those vaccinated against COVID-19 with a two-dose series continue to demonstrate significantly lower odds of SARS-CoV-2 infection compared to unvaccinated individuals and, when infections occur, symptoms tend to be milder in vaccinated cases.

Prior to providing a COVID-19 vaccine, informed consent should include discussion about frequently occurring minor adverse events and the risks and symptoms of potential rare severe adverse events including the risk of myocarditis/pericarditis, Bell's palsy and anaphylaxis.

As a precautionary measure, NACI recommends:

- that individuals who have experienced myocarditis (with or without pericarditis) following vaccination within six weeks of receiving a first dose of an mRNA COVID-19 vaccine, should defer the second or additional dose in the vaccination series until more information is available.
    - Some people with confirmed myocarditis (with or without pericarditis) after a dose of an mRNA COVID-19 vaccine may choose to receive another dose of vaccine after discussing the risks and benefits with their immunizer/healthcare provider. If another dose of vaccine is offered, they should be offered Pfizer (30 mcg) due to the lower reported rate of myocarditis and/or pericarditis following Pfizer compared to Moderna (100 mcg). Informed consent should include discussion about the unknown risk of recurrence of myocarditis and/or pericarditis following receipt of additional doses of Pfizer in individuals with a history of confirmed myocarditis and/or pericarditis after a previous dose of mRNA COVID-19 vaccine, as well as the need to seek immediate medical assessment and care should symptoms develop.
- Those with a history compatible with pericarditis and who either had no cardiac workup or had normal cardiac investigations, can receive the next dose once they are symptom free and at least 90 days has passed since vaccination.

[12] On Sept. 16, 2021, Health Canada approved the Pfizer/Comirnaty™ and Moderna/Spikevax™ vaccines under the Food and Drug Regulations (i.e., they are no longer issued market authorizations with the conditions for early access under the interim order, as sufficient data was made available to approve them under normal regulations). For the purposes of this document, the two vaccines will continue to be referred to as Pfizer and Moderna.

Individuals who have a history of myocarditis unrelated to mRNA COVID-19 vaccination should consult their clinical team for individual considerations and recommendations. People previously diagnosed with myocarditis but who are no longer being followed by a medical professional for heart issues should receive the vaccine. Vaccination is recommended as the benefits of vaccination to prevent COVID-19 including variants of concern, outweigh rare cases of myocarditis or pericarditis. NACI advises that anyone receiving an authorized mRNA COVID-19 vaccine should be informed of the risk of myocarditis and pericarditis and advised to seek medical attention if they develop symptoms including chest pain, shortness of breath or the feeling of a fast, pounding or fluttering heartbeat. *NACI will continue to monitor the evidence and update recommendations as needed; more information about myocarditis/pericarditis is available below.*

Advise individuals to seek medical attention if they develop symptoms compatible with Bell's palsy following receipt of mRNA COVID-19 vaccines. Consider Bell's palsy in your evaluation if the patient presents with clinically compatible symptoms after an mRNA COVID-19 vaccine. Investigations should exclude other potential causes of facial paralysis. *More information about Bell's palsy is available below.*

To date, there is insufficient evidence on the receipt of both a COVID-19 vaccine and anti-SARS-CoV-2 monoclonal antibodies or convalescent plasma for treatment or prevention. Therefore, timing of administration and potential interference between these two products are currently unknown. Administration of these products close together may result in decreased effectiveness of a COVID-19 vaccine and/or anti-SARS-CoV-2 monoclonal antibodies because the monoclonal antibodies have high affinity for the spike protein expressed by the vaccines, which could prevent the production of antibodies stimulated by the vaccine. **Manitoba public health officials recommend that COVID-19 vaccination be deferred for 90 days after receiving a passive antibody product (anti-SARS-CoV-2 monoclonal antibody) to avoid potential interference of the product with vaccine-induced immune response.**[13] However, if passive antibody products and a COVID-19 vaccine dose are administered within 90 days, the vaccine does not need to be repeated. The Centres for Disease Control (CDC) also note that:

- There is no recommended minimum interval between antibody therapies not specific to COVID-19 treatment and COVID-19 vaccination.
- Vaccines other than COVID-19 vaccines, including inactivated and live vaccines, may be administered without regard to timing of anti-SARS-CoV-2 monoclonal antibodies.

Interchangeability of the primary series (i.e., vaccine product selection)

Manitoba public health officials and the National Advisory Committee on Immunization (NACI) recommend that when the first dose in a COVID-19 vaccine series is an mRNA vaccine, the same mRNA vaccine product should be offered for the second dose if readily available. When the same mRNA vaccine product is not readily available, or is unknown, or there is a need to preserve sufficient Pfizer supply for the 12 to ≤ 29 year old population, another mRNA COVID-

[13] This current guidance applies to all COVID-19 vaccine products and is under active review.

19 vaccine product can be considered interchangeable and should be offered. There are two exceptions to this general guidance:

1. **Individuals aged 12 to 29 years:** Manitoba public health officials recommend Pfizer (30 mcg) to start or continue the vaccine series (i.e., individuals aged 12 to 29 years who received dose 1 of Moderna should complete their series with Pfizer). Pfizer is preferred to Moderna because of a lower reported rate of myocarditis/pericarditis following Pfizer (30 mcg) compared to Moderna (100 mcg). Analyses of Canadian data suggests that with the primary series, the incidence of myocarditis is rare with either mRNA vaccine, but higher following Moderna (100 mcg) compared to Pfizer (30 mcg). The reported rates of myocarditis/pericarditis among males aged 18 to 29 years after the second dose were 15.9 per 100,000 for Moderna (100 mcg) and 2.6 per 100,000 for Pfizer (30 mcg). Among individuals aged ≥ 30 years, either mRNA vaccine should be used given that this age group has a lower risk of vaccine-associated myocarditis/pericarditis.

2. **Individuals who have contraindications to an mRNA vaccine:** rarely, individuals are advised not to receive additional doses of an mRNA vaccine. In these situations, a person may be recommended on a case-by-case basis to receive a non-mRNA authorized COVID-19 vaccine.

For moderately to severely immunocompromised adults aged ≥ 30 years (where three doses are recommended for the primary series): Manitoba public health officials recommend that when the first dose in a COVID-19 vaccine primary series is an mRNA vaccine (Moderna or Pfizer), the same mRNA vaccine product should be offered for subsequent doses if readily available. When the same mRNA vaccine product is not readily available, or is unknown, or there is a need to preserve sufficient Pfizer supply for the 12 to ≤ 29 year old population, another mRNA COVID-19 vaccine product can be considered interchangeable and should be offered. Moderna (100 mcg) induces somewhat higher antibody levels compared to Pfizer (30 mcg). Protection against infection and severe disease from a primary series with Moderna (100 mcg) may be more durable than Pfizer (30 mcg).

When the first dose in a COVID-19 vaccine series is AstraZeneca: either AstraZeneca or an mRNA vaccine product may be offered for the second dose to complete the series however, an mRNA vaccine product is preferred and Manitoba public health officials recommend that an mRNA vaccine be offered as a second dose due to evidence suggesting a better immune response and the safety of heterologous schedules.

When the first dose in a COVID-19 vaccine series is a non-mRNA vaccine: either mRNA vaccine product (e.g., Moderna and Pfizer) may be offered for the second dose to complete the series.

Guidance on the recommended interval for the primary series

Manitoba has adopted the NACI recommendation with respect to the optimal interval of eight (8) weeks between dose 1 and dose 2 for all populations. Data show that the very good protection provided by mRNA vaccines may be further improved when the interval between the first and second doses are extended beyond the authorized intervals. NACI makes the following cautionary notes:

- There is no change to the recommended interval between second (and third doses for immunocompromised individuals).
- There is no change to the authorized minimum interval of 21 days for Pfizer and 28 days for all other mRNA schedules (Pfizer and Moderna, Moderna and Moderna, and Moderna and Pfizer).
- This recommendation does not replace clinical judgement; clinicians should continue to select a shorter interval (21 or 28 days) at their discretion in discussion with the client, informed by local transmission of the SARS-CoV-2 virus; the degree of individual risk of exposure to the virus; and, the need of a second dose for earlier protection (e.g., travel requirements).
- People who completed their primary vaccine series using 21 or 28 day interval also have very good protection against severe COVID-19 disease and do not need to restart their vaccine series.

For moderately to severely immunocompromised populations aged ≥ 12 years, a three dose primary series is recommended (see Appendix F for the list of conditions/definition of individuals who are moderately to severely immunocompromised). Studies have demonstrated that some people who do not respond after two doses, particularly those who are moderately to severely immunocompromised, develop antibodies after a third dose of an mRNA vaccine; and that there are increases in antibody titres following a third dose for some of those who do respond to an initial primary series. There is increasing evidence that antibody titres are related to vaccine effectiveness, (including against viral variants) and may relate to the duration of protection and protection against severe disease. However, a correlate of protection has not yet been defined. The third dose for moderately to severely immunocompromised persons should be distinguished from that of a booster dose. The intent of a booster dose is to restore protection that may have waned over time in individuals who responded adequately to an initial primary vaccine series. Additional doses beyond the standard primary vaccine series provide an opportunity for individuals who may not have achieved an adequate level of protection from the standard primary series to develop a better immune response.

For guidance on vaccination timing for individuals previously infected with SARS-CoV-2, see question 25 of the Clinical Practice Questions and Answers.

The three dose primary series schedule for moderately to severely immunocompromised people is as follows:

	Interval between dose 1 & dose 2		Interval between dose 2 & dose 3	
	Min.	**Recommended**	**Min.**	**Recommended**
Ages 12 years and older	21 or 28 days (product specific)	8 weeks	≥ 28 days	As per clinical discretion [a]

NOTES:

[a] There is limited data to determine the optimal interval for the third dose. It is recommended to consider the risk factors for exposure and severe disease when deciding on the time interval. At this time, the minimum interval of the third dose from the preceding dose is 28 days. In general, NACI recommends that immunocompromised individuals be immunized at the time when maximum immune response can be anticipated:

- Immunize prior to any planned immunosuppression such that optimal immunogenicity is achieved, if possible.
- Delay immunization if the immunodeficiency is transient (if this can be done safely because exposure is unlikely in the individual's setting and circumstance).
- Stop or reduce immunosuppression to permit better vaccine response, if appropriate. Consult the Canadian Immunization Guide for more detail on the timing of vaccination in relation to immunosuppressive therapy: **www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25**.

Rare and very rare adverse events following immunization

Rare and very rare adverse events occur in 0.01% to less than 0.1% and less than 0.01% of vaccine recipients, respectively.

Information about myocarditis and pericarditis

NACI advises that health care providers should consider myocarditis and/or pericarditis in their evaluation if the patient presents with clinically compatible symptoms (chest pain, shortness of breath, palpitations) after the second dose of an mRNA COVID-19 vaccine but should be investigated regardless of timing from vaccination to onset. Investigations include electrocardiogram, serum troponins and echocardiogram with frequent abnormal electrocardiogram findings and elevated troponin levels. Consultation with a cardiologist, infectious disease specialist, internal medicine specialist and/or rheumatologist may be advisable to assist in this evaluation, particularly to investigate the many potential causes of myocarditis and pericarditis. Investigations may include diagnostic testing for acute COVID-19 infection (e.g., PCR testing), prior SARS-CoV-2 infection (e.g., detection of SARS-CoV-2 nucleocapsid antibodies), and consideration of other potential infectious or non-infectious etiologies including auto-immune conditions.

Rare cases of myocarditis and pericarditis following vaccination with COVID-19 mRNA vaccines have been reported in Canada and internationally, including from Israel, the United States and Europe. Canadian and international data suggests cases of myocarditis and/or pericarditis occur more often in adolescents and adults under 30

years of age, more often in males than in females, and more often after a second dose of an mRNA vaccine than after a first dose. The association of myocarditis and pericarditis with mRNA vaccination and a mechanism for inflammation remain under investigation.

There are many potential causes for myocarditis and pericarditis including both infectious and non-infectious causes. Disease severity can be variable. The cases of myocarditis and pericarditis that have been reported after vaccination with an mRNA COVID-19 vaccine to date have responded well to conservative therapy, and tend to recover quickly. Canadian and international data suggests there is a lower reported rate of myocarditis/pericarditis following Pfizer (30 mcg) compared to Moderna (100 mcg) for individuals aged 12 to ≤ 29 years.

The risk of myocarditis and/or pericarditis associated with an additional dose after a 1- or 2-dose primary series of an mRNA vaccine when given to immunocompromised individuals is unknown at this time. NACI is continuing to monitor the evidence and will update recommendations as information becomes available. Health Canada, PHAC and the provincial/territorial health authorities continue to monitor closely.

On June 30, 2021, Health Canada updated the Pfizer-BioNTech and Moderna Product Monographs:

- **Moderna Product Monograph:** https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf
- **Pfizer Product Monograph:** https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf

The following has been added to *Section 7: Warning and Precautions* of the Product Monographs for both Moderna and Pfizer (below is the excerpt from the Pfizer Product Monograph):

> **Cardiovascular**
> Myocarditis and Pericarditis
>
> Very rare cases of myocarditis and/or pericarditis following vaccination with Pfizer-BioNTech COVID-19 Vaccine have been reported during post-authorization use. These cases occurred more commonly after the second dose and in adolescents and young adults. Typically, the onset of symptoms has been within a few days following receipt of the Pfizer-BioNTech COVID-19 Vaccine. Available short-term follow-up data suggest that the symptoms resolve in most individuals, but information on long-term sequelae is lacking. The decision to administer the Pfizer-BioNTech COVID-19 Vaccine to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances.

Healthcare professionals are advised to consider the possibility of myocarditis and/or pericarditis in their differential diagnosis if individuals present with chest pain, shortness of breath, palpitations or other signs and symptoms of myocarditis and/or pericarditis following immunization with a COVID-19 vaccine. This could allow for early diagnosis and treatment. Cardiology consultation for management and follow up should be considered.

The Canadian Pediatric Society provides clinical guidance on myocarditis and pericarditis following mRNA COVID-19 vaccination, available at: https://cps.ca/en/documents/position/clinical-guidance-for-youth-with-myocarditis-and-pericarditis.

Information about Bell's palsy

Very rare cases of Bell's palsy (typically temporary weakness or paralysis on one side of the face) have been reported following vaccination with COVID-19 mRNA vaccines (Pfizer or Moderna) in Canada and internationally among individuals aged ≥ 12 years. Bell's palsy is an episode of facial muscle weakness or paralysis. The condition is typically temporary. Symptoms appear suddenly and generally start to improve after a few weeks. The exact cause is unknown. It's believed to be the result of swelling and inflammation of the nerve that controls muscles on the face.

Symptoms of Bell's palsy may include:

- uncoordinated movement of the muscles that control facial expressions, such as smiling, squinting, blinking or closing the eyelid
- loss of feeling in the face
- headache
- tearing from the eye
- drooling
- lost sense of taste on the front two-thirds of the tongue
- hypersensitivity to sound in the one ear
- inability to close an eye on one side of the face

Individuals should be advised to seek medical attention if they develop symptoms of Bell's palsy following receipt of mRNA COVID-19 vaccines. Consider Bell's palsy in your evaluation if a patient presents with clinically compatible symptoms after an mRNA COVID-19 vaccine. Investigations should exclude other potential causes of facial paralysis.

See Appendix C for information and precautions for vaccinating allergic persons.

Guidance on Booster Doses of mRNA Vaccines for Adolescents and Adults

The Delta variant of concern continues to circulate in some parts of the province. A two-dose primary series continues to offer good protection against severe outcomes against Delta, with waning seen against symptomatic infection. Evidence suggests a third dose provides increased protection (approximately 90%) against symptomatic disease from Delta.

Evidence continues to emerge and evolve with respect to how well the mRNA vaccines protect against Omicron. Emerging evidence suggests:

- A few weeks after the second dose, the mRNA vaccines offer little protection against symptomatic disease but good protection (approximately 70 per cent) against severe outcomes.
- A third dose of mRNA vaccine appears to offer some level of protection against symptomatic disease in the short term, although estimates of effectiveness vary by study and continue to evolve (approximately 50 to 60 per cent vaccine effectiveness against infection). The duration of protection against symptomatic disease is currently unknown after a third dose, but the limited evidence available suggests protection wanes quicker against Omicron compared to other variants (e.g., Delta).
- A third mRNA dose appears to offer some increased protection against severe outcomes. A study from England suggests a third dose is 88% effective at preventing hospitalizations from Omicron compared to being unvaccinated.[14] Duration of protection is unknown.

The intent of a booster dose is to restore protection that may have decreased over time to a level that is no longer deemed sufficient in individuals who initially responded adequately to a complete primary vaccine series.

General booster dose guidance for adults[15]

Manitoba public health officials recommend a booster dose of mRNA vaccine be offered to adults at increased risk of serious illness from COVID-19, their caregivers and close/household contacts 6 months after their last COVID-19 vaccine. This includes[16]:

- people aged 50 years and older
- residents of personal care homes or congregate elderly person housing sites (e.g., assisted living)
- individuals with the following chronic health conditions:

[14] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf

[15] General booster dose guidance for adults also applies in situations where adults are unable or unwilling to receive an mRNA vaccine and are therefore being offered a protein subunit vaccine.

[16] As evidence continues to emerge in the context of Omicron with respect to vaccine effectiveness of a booster dose against the epidemiology/disease severity of Omicron, the list of who is recommended to receive a third dose may change.

    - an immune system moderately to severely weakened by disease or medical treatment (see appendix F for the list of conditions/definition of individuals who are moderately to severely immunocompromised)
    - cardiac or pulmonary disorders (ex: cystic fibrosis)
    - neurologic or neurodevelopmental conditions
    - diabetes and other metabolic diseases
    - renal or liver disease
    - anemia or hemoglobinopthy
    - asplenia or hyposplenism (including sickle cell disease)
    - obesity (body mass index = 40)
    - tuberculosis disease (current or previous) OR latent tuberculosis (LTBI) where treatment has not been completed
    - human immunodeficiency virus (HIV), irrespective of CD4 count
- pregnant individuals
- health care personnel who have direct contact with patients, residents or clients
- First Nation, Métis and Inuit people
- individuals living north of the 53rd parallel of latitude or in a remote/isolated community
- individuals living or working in a congregate living facility (e.g., correctional facilities, group homes, homeless shelters)
- individuals experiencing homelessness
- individuals receiving homecare OR receiving any level of Community Living Disability Service support (or, as per family physician determination of equivalent levels of family support)
- individuals who have only received a viral vector vaccine (e.g., AstraZeneca or Janssen); OR
- or as recommended by a health care provider

All other individuals 18 to ≤ 49 years of age who are fully vaccinated against COVID-19 <u>can</u> further reduce their individual risk by getting a booster dose of an mRNA vaccine six months after their last COVID-19 vaccine, after considering the risks and benefits of vaccination.

Guidance for clients who have received non-Health Canada approved vaccines is provided below.[17]

[17] The guidance for clients who have received non-Health Canada approved vaccine(s) also applies to adults who are unable or unwilling to receive an mRNA vaccine and are therefore being offered a protein subunit vaccine.

In making the decision to proceed with a booster dose, clients must acknowledge they understand the following risks and benefits as part of the informed consent process:

- **Risk of getting sick from COVID-19 and experiencing complications.** Emerging evidence suggests that overall the risk of serious illness from Omicron is lower compared to other variants of concern. Based on past experience, some groups of people continue to be at increased risk of experiencing serious illness from Omicron. The need for and benefits of a booster dose among individuals aged 18 to ≤ 49 years who are not from a group recommended to be offered a booster dose should be made on an individual basis, taking into account an individual's personal aversion to risk.
- **The evidence on the safety of a booster dose.** The evidence on the risk of myocarditis/pericarditis in adults is limited but suggests a lower risk than what has been seen following dose two. In Israel and the United States, the rates of myocarditis following a booster dose in adults are generally falling between the rates post-dose 1 and post-dose 2.
- **The limited and evolving evidence on the effectiveness of a booster dose.** In general, there is some decline noted in older adults (such as those 80 years of age and over) and residents in long term care homes in overall effectiveness over time after two doses, although protection against severe outcomes appears to be more durable than protection against infection. Observational studies show a reduction in vaccine effectiveness against COVID-19 in immunocompromised adults when compared to the general population with a 2-dose vaccine series. Current evidence suggests that overall, a booster dose improves protection from Omicron illness among adults; it is not yet known how long this increased protection lasts. Finally, people who are vaccinated remain less likely to spread COVID-19 to others even if they are infected however, risk of further spread is not fully mitigated through vaccination.
- **What is known and unknown at this time** (e.g., it is unknown what future variants of concern may emerge, and how the vaccine will work against them). Variant-specific vaccines are in development and may be available in the coming months.

General booster dose guidance for adolescents

As per the National Advisory Committee on Immunization (NACI), a booster dose of an mRNA vaccine may be offered to adolescents 12 to 17 years of age who may be at higher risk of severe outcomes from COVID-19 infection. This includes adolescents:

- with an underlying medical condition at high risk of severe illness due to COVID-19*;
- who are residents of congregate living settings (e.g., shelters, group homes, quarters for migrant workers, correctional facilities); and/or,
- who belong to a racialized and/or marginalized community disproportionately affected by COVID-19.

NOTE: no recommendations for booster doses for the general adolescent population 12 to 17 years of age are being made at this time. Health Canada has not received a submission or clinical trial data from a vaccine manufacturer for a COVID-19 booster for people under 18 years of age.

*Adolescents with one or more of the following underlying medical conditions may be at high risk of severe illness due to COVID-19:

- cancer – active treatment
- chronic kidney disease
- chronic lung disease, including uncontrolled asthma
- cystic fibrosis
- neurodevelopmental and other chronic neurological conditions including epilepsy and cerebrovascular disease
- diabetes (type 1 & 2)
- Down syndrome
- congenital heart disease or other chronic heart diseases, including pulmonary hypertension
- chronic liver disease
- obesity (BMI ≥ 30)
- pregnancy
- sickle cell disease or thalassemia
- substance use disorders
- immunocompromised state, including primary immune deficiency, solid organ or hematopoietic stem cell transplant, HIV infection, or immunosuppressive therapy. **See Appendix F for the full definition.**
- medically fragile/having medically complex needs

In making the decision to proceed with a booster dose, clients must acknowledge they understand the following risks and benefits as part of the informed consent process (considering that booster doses are only authorized for individuals aged ≥ 18 years in Canada; the use of a booster dose in adolescents is off-label):

- **Risk of getting sick from COVID-19 and experiencing complications.** The relative risks and benefits of a third dose of Pfizer (30 mcg) in adolescents, including duration and level of protection compared to infection from Omicron, are largely unknown at this time. And the need for and benefit of a booster dose in the general adolescent population is unclear. Although being highly transmissible, Omicron appears less severe (<1% of national cases among adolescents 12 to 19 years of age are hospitalized) than earlier variants of concern, and adolescents who have received two doses continue to be at very low risk for severe outcomes due to infection. However, based on past experience in this pandemic, some groups of people due to various biological and/or social factors, have been demonstrated to be at increased risk of serious illness. Young people also appear to be at lower risk of long-COVID, with two doses of vaccine further reducing that risk. Myocarditis can also occur as a complication of SARS-CoV-2 infection, including, very rarely, in adolescents.
- **The limited and evolving evidence on the safety of a booster dose.** Preliminary post-market data shows no additional safety concerns beyond those reported after two doses. For dose one and dose two, adolescents are among the age groups at highest risk for the rare event of myocarditis/pericarditis following mRNA vaccination. Preliminary

data suggests this rate may be similar, or higher, for booster doses as it is for the primary series among adolescents.

    - As of early January 2022, two cases of myocarditis have been reported in Israel among 41,610 third doses of Pfizer (30 mcg) administered to adolescents aged 12 to 15 years. However, preliminary data from the UK compared the risk of myocarditis post COVID-19 vaccines to the baseline risk and observed that among males aged 13 to 39 years, the estimated association between myocarditis and Pfizer (30 mcg) was higher post vaccine dose 3 (Incidence rate ratio [IRR]: 7.60 [1.92 - 30.15]) compared to post vaccine dose 2 (IRR: 3.41 [2.44 - 4.78]).

- **The limited and evolving evidence on the effectiveness of a booster dose.** Current evidence suggests a booster dose improves protection from Omicron illness among adults. It is not yet known how long this increased protection lasts. There is currently limited evidence on the effectiveness of a booster dose against Omicron among adolescents. Finally, studies have shown that 2 doses provides high vaccine effectiveness at preventing the rare but serious complication of MIS-C. There is no data regarding the impact of a third dose on the risk of MIS-C.
    - As per NACI, preliminary data from a recent large pharmacovigilance study in adolescents 12 to 17 years of age in France reported a rate of 1.1 (95% CI: 0.5-2.1) MIS-C cases per 1,000,000 doses administered, compared to 113 (95% CI: 95-135) cases per 1,000,000 SARS-CoV-2 infections in this age group. Data from pediatric patients 12-18 years of age diagnosed with MIS-C in France between September 1, 2021 and October 31, 2021 found the hazard ratio for MIS-C was 0.09 (95% CI: 0.04-0.21; P <.001) after the first vaccine dose compared with unvaccinated adolescents.
- **What is known and unknown at this time** (e.g., it is unknown what future variants of concern may emerge, and how the vaccine will work against them). NACI notes that a vaccination strategy based on repeated booster doses with the original vaccine composition without consideration of the evolution of the virus and vaccine coverage in the global context is unlikely to be effective. In addition, variant-specific vaccines are in development and may be available in the coming months.

Interchangeability (i.e., vaccine product selection)

Consistent with the National Advisory Committee on Immunization (NACI), Manitoba public health officials recommend that:

- **For adolescents/young adults aged 12 to ≤ 29 years (including those with moderate to severe immunocompromise):** Pfizer is recommended to mitigate the risk of myocarditis/pericarditis.
- **For adults aged ≥ 30 years:** either mRNA vaccine (Moderna or Pfizer) may be used, regardless of which COVID-19 vaccine was previously given for the primary series.
- **For moderately to severely immunocompromised adults aged ≥ 30 years:** either mRNA vaccine (Moderna or Pfizer) may be used, regardless of which COVID-19 vaccine

was previously given for the primary series. As per NACI guidance, Moderna/Spikevax™ (100 mcg) may be preferred; this is based on clinical discretion.

- *Rarely, individuals may be advised not to receive additional doses of an mRNA vaccine. In these situations, a person may be recommended on a case-by-case basis to receive another authorized COVID-19 vaccine.*

Recommended interval

Principles of immunology indicate that a longer interval between priming and booster doses of a vaccine results in a better and more durable response. Most studies on mRNA COVID-19 vaccine booster doses have used an interval of ≥ 6 months following the completion of the primary series.

While evidence demonstrates that six to eight months is optimal for the strongest immune response, there may be times where this recommendation must be balanced against the local context. Ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving a booster dose.

It is recommended that all eligible individuals receive their booster dose 6 months after their primary series. However, there may be some circumstances where logistical concerns may make an earlier booster (no sooner than 5 months) a reasonable decision for some adults (for example, if it is unlikely the adult will return for a booster dose at a later date). The only exception to this general guidance is for people who received one or two doses of a COVID-19 vaccine that is not approved by Health Canada, as these individuals do not need to wait six months to receive a booster dose; these individuals can receive a booster dose ≥ 28 days after their last dose.

For guidance on vaccination timing for individuals previously infected with SARS-CoV-2, see question 25 of the Clinical Practice Questions and Answers.

Immunization Schedule for Adolescent/Adult (General) Population

	Interval between dose 1 and dose 2		**Interval between dose 2 and the booster dose**	
	Minimum	**Recommended**	**Minimum**	**Recommended**
Ages 12 to ≤ 17 years	21 or 28 days (product specific)[a]	8 weeks	Not authorized and/or recommended at this time for the general adolescent population [d]	
Ages 18 years and older	21 or 28 days (product specific)[a]	8 weeks	≥ 28 days	6 months [b,c]

NOTES:

[a] The minimum interval between two Pfizer doses is 21 days; all other mRNA primary series schedules (with Moderna and/or a combination of Pfizer and Moderna) is 28 days.

[b] A booster dose of Pfizer or Moderna is recommended for adults at increased risk of serious illness from COVID-19, their caregivers and close/household contacts.

[c] Booster doses given earlier than an interval of 5 months since the last dose require a prescription.

[d] A booster dose of an mRNA vaccine may be offered ≥ 6 months since the last dose to adolescents 12 to 17 years of age who may be at higher risk of severe outcomes from COVID-19 infection.

Immunization Schedule for Immunocompromised Individuals						
	Interval between dose 1 and dose 2		Interval between dose 2 and dose 3		Interval between dose 3 and booster (4th) dose	
	Min.	Recommended	Min.	Recommended	Min.	Recommended
Ages 12 years and older	21 or 28 days (product specific)	8 weeks	≥ 28 days	As per clinical discretion [a]	≥ 28 days	6 months

NOTES:
[a] There is limited data to determine the optimal interval for the third dose. It is recommended to consider the risk factors for exposure and severe disease when deciding on the time interval. At this time, the minimum interval of the third dose from the preceding dose is 28 days. In general, NACI recommends that immunocompromised individuals be immunized at the time when maximum immune response can be anticipated:

- Immunize prior to any planned immunosuppression such that optimal immunogenicity is achieved, if possible.
- Delay immunization if the immunodeficiency is transient (if this can be done safely because exposure is unlikely in the individual's setting and circumstance).
- Stop or reduce immunosuppression to permit better vaccine response, if appropriate. Consult the Canadian Immunization Guide for more detail on the timing of vaccination in relation to immunosuppressive therapy: www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25.

Dosage

Generally, older adults have a dampened immune function, and may need to receive a higher dose formulation of a vaccine to improve their response to vaccines. Manitoba is therefore adopting the following NACI recommendations with respect to dosage of the Moderna vaccine for booster doses (following any combination of valid primary series vaccines):

- For adults aged ≤ 69 years who are living in community: **use a half dose (50 mcg; 0.25ml)** of Moderna for third/booster doses.
- For adults aged ≥ 70 years who are living in community: **use a full dose (100 mcg; 0.5ml)** of Moderna for third/booster doses.
- For adults of any age who are moderately to severely immunocompromised: **use a full dose (100 mcg; 0.5ml)** of Moderna for fourth/booster doses. (NOTE: persons aged 12 to ≤ 29 years are recommended to receive the Pfizer product).
- For adults of any age who are living in a personal care home or congregate elderly person housing site: **use a full dose (100 mcg; 0.5ml)** of Moderna for third/booster doses.
- For adults of any age who have two non-Health Canada approved vaccines: **use a full dose (100 mcg; 0.5ml)** of Moderna for third/booster doses.

There is no change to the Pfizer dosage. The full dosage (100 mcg; 0.5ml) is to be used for the Moderna primary series. When using the Moderna vaccine for booster doses, the maximum number of vial punctures permitted is 20. After 20 punctures, the vial should be discarded.

Below is specific information pertaining to some of the populations recommended to be offered a booster dose. Individuals who are recommended to be offered a booster dose should continue to be counselled on the risks/benefits of a booster dose, particularly where recommendations are made from a population perspective (e.g., health care workers) as opposed to an individual perspective (e.g., peopled aged 50 years and older). ***Adults aged ≥ 18 years who are unable or unwilling to receive an mRNA vaccine may be offered a protein subunit vaccine following a review/discussion of the risks and benefits of vaccination. See the section "Guidance for the use of protein subunit vaccines in the Primary Series and Booster Dose for the Adult Population" for more information.***

Guidance on a booster dose for immunocompromised individuals aged ≥ 12 years

To date, people with moderately to severely compromised immune systems have been observed to generally have lower antibody responses and lower vaccine effectiveness from COVID-19 vaccines than immunocompetent individuals, although this varies depending on the underlying condition or immunosuppressive agents. Individuals with various conditions associated with immune compromise were excluded from the manufacturer-conducted randomized controlled COVID-19 vaccine efficacy trials and it is uncertain what vaccination strategy will most optimally protect these individuals from illness and severe outcomes.

While data on a fourth dose of a COVID-19 vaccine after the recommended three-dose primary series in moderately to severely immunocompromised individuals are currently limited, many of these individuals are at a higher risk of severe outcomes of COVID-19 and also at increased risk of decreasing protection over time since vaccination. Therefore, immunocompromised individuals who already received an additional dose in the COVID-19 vaccine primary series are included in those recommended to be offered a booster dose six months from their last dose. **Manitoba public health officials recommend that moderately to severely immunocompromised individuals aged ≥ 12 years should be offered a primary series of three doses of an authorized mRNA vaccine followed by a fourth/booster dose.**

- If any dose in the series is with Moderna, a full dose (100 mcg; 0.5ml) should be used. (NOTE: Pfizer is the recommended product for those aged 12 to ≤ 29 years).
- For those aged ≥ 30 years, either mRNA vaccine may be used, regardless of which COVID-19 vaccine was previously given for the primary series. Moderna (100 mcg) may be preferred; this is based on clinical discretion.
- **See Appendix F for the list of conditions/definition of individuals who are moderately to severely immunocompromised.**

Ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving a fourth/booster dose, including:

- Evidence used to inform the additional dose recommendations is based on safety and immunogenicity data in adolescents; evidence on efficacy/effectiveness of an additional dose after a primary series will be reviewed when it is available.
- Safety data of small studies available to this point, suggests the reactogenicity of an additional dose of a COVID-19 mRNA vaccine was similar to that of prior doses. (Note:

due to small sizes and limited follow-up times, the impact of additional doses on rare adverse events is unknown).

- Evidence in some immunocompromised populations indicates that humoral immune responses increase after an additional dose of COVID-19 vaccine is administered to these individuals and that this is associated with a modest increase in overall proportion of individuals who seroconvert.
- Due to the unknown efficacy/effectiveness of an additional dose, immunocompromised individuals should continue to follow recommended public health measures.
- Immunocompromising conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the progression of disease and use of medications that suppress immune function.
- The risk of myocarditis and/or pericarditis following a third dose of mRNA vaccine is limited at this time but suggests a lower risk than what has been seen following dose two in the general population.
- Health Canada has approved the use of a booster dose for both Pfizer (30 mcg) and Moderna (50 mcg) with an interval of at least six months for individuals aged ≥ 18 years. (NOTE: NACI and Manitoba public health officials recommend a full dose (100 mcg) when Moderna is given for booster doses in immunocompromised individuals). Booster doses administered earlier than six months and/or administered to individuals between 12 and ≤ 17 years of age would be considered an off-label use at this time.

Guidance on an additional dose for travel purposes (i.e., individuals who request an additional dose to meet travel requirements of their destination) for adults aged ≥ 18 years

Individuals who received a mixed COVID-19 vaccine series may request two doses of a homologous mRNA COVID-19 vaccine, as per travel guidance from the destination. **There is no clinical recommendation that individuals who received a mixed schedule (dose one with a viral vector vaccine followed by dose two with an mRNA vaccine) should be offered an additional dose, unless they are part of a group recommended to be offered a booster dose (e.g., individuals aged ≥ 50 years, pregnant individuals, etc.). However, in recognition that there may be broader considerations at play beyond the effectiveness of the vaccine series, the province of Manitoba is permissive of an additional dose being provided for travel purposes alone, earlier than the recommended interval (six months since the last dose) taking into consideration the following:**

- The minimum interval between the preceding dose and the additional dose is 28 days.
- There should be specific travel plans to a destination that requires people to be fully immunized with two doses of the same COVID-19 vaccine. In situations where an individual received a complete viral vector vaccine series but needs a complete mRNA vaccine series as per the travel requirements of their destination, third and fourth doses of an mRNA vaccine is permitted provided the discussion required to obtain consent acknowledges that there is no effectiveness or safety data to support this use. Note: the absolute minimum interval between doses is 28 days.
- Individuals without specific travel plans or, where their destination does not require them to receive an additional dose, should not receive an additional dose earlier than the recommended interval (i.e., six months following their last dose) for the purpose of travel.

For example, at this time, the USA and Mexico do NOT have any vaccine requirements for entry although local jurisdictions within the country may have their own specific rules. Individuals should therefore thoroughly review the requirements of their destination as these rules are regularly changing.

Ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving an additional dose. (NOTE: Health Canada approved the use of a booster dose of Pfizer (30 mcg) and Moderna (50 mcg) provided they are administered at least six months after the last COVID-19 vaccine dose AND to individuals aged 18 years of age and older. Use outside of these indications is considered to be off-label at this time).

Guidance for individuals aged ≥ 12 years who received non-Health Canada approved COVID-19 vaccines

The vaccine immunogenicity, efficacy and effectiveness of authorized vaccines available worldwide vary. While many of the vaccines appear to be performing very well based on available data, others have lower effectiveness. The Public Health Agency of Canada (PHAC) considered a number of approaches for updating the vaccinations for those who received only non-Health Canada authorized COVID-19 vaccines and are planning to stay in Canada for longer periods of time. PHAC's selected approach aimed to balance the following:

- Optimal protection against COVID-19, recognizing that the vaccine effectiveness of the non-Health Canada authorized vaccines may vary. Optimal effectiveness helps to protect the individual and those they may interact with (including in health care settings, congregate living settings, educational settings, workplaces and the community);
- Limit the reactogenicity by minimizing the number of additional doses provided, recognizing the safety and reactogenicity of extra doses is not yet studied for a number of these vaccines;
- Provide a simple and straightforward approach that is easy to implement.

Consistent with PHAC's approach and to be considered fully vaccinated for individuals planning to stay in MB for longer periods of time (i.e., to live, work or study), Manitoba public health officials recommend:

- one additional dose of an mRNA COVID-19 vaccine be offered to those who have received one or two doses of a non-Health Canada approved vaccine.
    - The minimum interval between the preceding dose and the additional dose is 28 days.
    - No additional doses are recommended for individuals who have received three doses (but they are recommended to be offered a booster dose if they fall into one of the recommended groups, as outlined below).[18]
- a booster dose of an mRNA COVID-19 vaccine following the additional mRNA dose (or following three doses) for adults at increased risk of serious illness from COVID-19, their caregivers and close/household contacts (e.g., individuals aged ≥ 50 years, pregnant individuals).

[18] Some clients have reportedly received a second mRNA dose (following 1 or 2 non-Health Canada approved vaccine plus an mRNA dose series). The second mRNA dose should be validated provided it was administered 21 days (or 19 days in the case of two Pfizer doses) after the previous mRNA dose.

- The minimum interval between the additional dose and the booster dose is six months.
- A booster dose may be offered to adolescents who may be at higher risk of severe outcomes, including adolescents with an underlying medical condition at high risk of severe illness due to COVID-19, residents of congregate living settings and/or adolescents who belong to a racialized and/or marginalized community disproportionately affected by COVID-19.

Residents of personal care homes and congregate elderly person housing sites

Protection from vaccination might not persist as long in this population compared to other populations, because these residents are at high risk of exposure to SARS-CoV-2 due to their congregate living environment and at high risk of severe outcomes due to age and underlying health status. Longer time since last dose and shorter intervals between doses in the primary series, as well as older age/immunosenescence, also contribute to waning vaccine protection against infection and severe outcomes in this population. Due to the possibility of decreased protection over time from a complete COVID-19 vaccine series in residents of personal care homes and of congregate elderly person housing sites, Manitoba recommends that residents of personal care homes and congregate elderly person housing sites be offered a booster dose of a COVID-19 vaccine. This includes First Nation personal care home residents, as well as First Nation personal care home staff.

Health care personnel aged ≥ 18 years

Emerging evidence suggests that immunity to a complete series of COVID-19 vaccination wanes over time, at least with respect to symptomatic infection. Effectiveness for healthy individuals remains high against severe outcomes (e.g., hospitalization and death). Health care personnel who have direct contact with patients, residents or clients, are recommended to be offered a booster dose of an mRNA vaccine.

People aged ≥ 18 years who had a viral vector vaccine series

Data from clinical trials and observational studies suggest that the viral vector vaccines may be comparatively less protective than the mRNA vaccines. Manitoba recommends that individuals who received a viral vector vaccines series (two doses of AstraZeneca at least 28 days apart, or one-dose of Janssen) be offered an additional dose of an mRNA vaccine at least 6 months after their second dose of a viral vector vaccine. Individuals who had a mixed vaccine series (i.e., one dose of a viral vector vaccine, one dose of an mRNA vaccine) are not recommended at this time to be offered any additional mRNA doses (unless they are already recommended to be offered a booster dose for other reasons–e.g., residents of personal care homes, etc.).

First Nation, Métis and Inuit adults

Across Canada, the rate of active COVID-19 cases started rising in First Nations communities in August 2021 and was 4.2 times higher than the rate in the general population as of October. Racialized and marginalized populations such as Indigenous Peoples have been disproportionately affected by COVID-19 due to a number of intersecting equity factors. The proportion of Canadians who identify as Indigenous and have at least one underlying medical

condition associated with severe COVID-19 is higher compared to other Canadians for every age category above 20 years of age. This increases the risk of severe outcomes for COVID-19 in this population. Adults in or from Indigenous communities were included in the earliest stages of initial COVID-19 immunization and may be at increased risk of waning of protection because for some of them, more time has elapsed since their second dose and a number of them were vaccinated with a very short interval between doses to optimize protection as quickly as possible. Manitoba recommends that First Nation, Métis and Inuit adults regardless of residence be offered a booster dose.

People aged 50 years of age and older living in community

Older adults are at increased risk for severe disease because of their age and underlying medical conditions and, there is emerging evidence of decreased vaccine effectiveness against severe disease in elderly adults, particularly those aged 80 years and older. The data suggests that compared to fully vaccinated younger age groups, fully vaccinated cases 80 years of age and over have the highest rates of hospitalizations and deaths, followed by those aged 70 to 79 years. Manitoba recommends that adults aged ≥ 50 years be offered a booster dose.

Individuals aged ≥ 12 years living, or adults aged ≥ 18 years working, in a congregate living facility (e.g., correctional facilities, group homes, homeless shelters)

Outbreaks continue to occur in multiple settings, including long-term care homes and retirement residences and as well as other congregate living settings that are enclosed and crowded, and can be a significant source of spread of SARS-CoV-2 infection.

Ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving an additional dose.

Where should I direct clients to access booster doses?

- Booster doses can be offered at any location that currently offers COVID-19 vaccine. There are two scenarios when a prescription is required:
    1. Individuals who require an additional dose for travel purposes earlier than the recommended interval of six months, must have a prescription if receiving the vaccine outside of their physician's office.
    2. Individuals who are immunocompromised must have a prescription if receiving a third dose in the primary series outside of their physician or pharmacist's office.
- Further details on where clients can access a booster dose as well as situations that require a prescription, are available at www.gov.mb.ca/covid19/vaccine/eligibility-criteria.html.

Guidance for use of the mRNA Vaccine in the Pediatric Population

On November 19, 2021, Pfizer (10 mcg) was the first COVID-19 vaccine authorized by Health Canada for use in children aged five to ≤ 11 years. On March 17, 2022, Health Canada authorized Moderna (50 mcg) for the use in children six to ≤ 11 years.

***** NOTE: only this section of the Clinical Practice Guidelines includes recommendations/guidance for children aged five to ≤ 11 years, with the exception/addition of Appendix C (guidance on precautions of vaccinating allergic persons) and Appendix D (managing administration errors) which are for individuals aged ≥ 5 years.*****

While additional data are required to fully determine the disease severity caused by the Omicron variant in specific populations including unvaccinated individuals and young children (<5 years of age), several reports and emerging studies are reporting reduced frequencies of severe outcomes from COVID-19 for the Omicron variant compared to the Delta variant.

Consistent with previous SARS-CoV-2 variants of concern, children 5 to 11 years of age remain at low risk of severe outcomes from Omicron. While COVID-19 associated hospitalizations among children 5 to 11 years of age have increased, which is consistent with all other age groups in Canada during the Omicron wave, the proportion of COVID-19 cases among children 5 to 11 years of age that have been hospitalized or admitted to ICU remains low.

Recommendations for use

Manitoba public health officials and the National Advisory Committee on Immunization (NACI) recommend that a complete series of mRNA vaccine be offered to children in the authorized age group* without contraindications to the vaccine, with a dosing interval of at least eight weeks between the first and second dose.

***Please NOTE:** Pfizer (10 mcg) pediatric vaccine is approved for use in children **aged 5 to 11 years** and Moderna (50 mcg) is approved for use in children **aged 6 to 11 years.**

Manitoba public health officials recommend that either mRNA product, Pfizer (10 mcg) or Moderna (50 mcg), can be offered as a primary series in the authorized age group. When the first dose in a COVID-19 vaccine series is an mRNA vaccine, the same mRNA vaccine product should be offered for the second dose if readily available. When the same mRNA vaccine product is not readily available, or is unknown, another mRNA COVID-19 vaccine product can be considered interchangeable and should be offered.

Because there is more data available from the real-world use of the Pfizer vaccine, NACI preferentially recommends the following:

- For children 6 to 11 years of age (which is the age group in which the Moderna (50 mcg) primary series vaccine is authorized):
    - **Moderna (50 mcg dose) may be offered as an alternative to Pfizer (10 mcg dose), however the use of Pfizer (10 mcg dose) is preferred to Moderna (50 mcg dose) to start or continue the primary vaccine series.**

NACI states that indirect data from the adult populations (≥18 years of age) suggest Moderna (100 mcg) may result in higher vaccine effectiveness after a 2-dose primary series compared to Pfizer (30 mcg) and is associated with a higher seroconversion rate among adult immunocompromised patients. Given this potential benefit, administration of the Moderna (50 mcg) vaccine as a 3-dose primary series may be considered for some immunocompromised individuals 6 to 11 years of age, as outlined in the product monograph. Each dose would be provided 4 to 8 weeks apart, as per the NACI recommended schedule for immunocompromised populations.

Clinical trial data demonstrated the vaccine to be safe and effective:

- **Safety:** Overall, Pfizer and Moderna were well tolerated in children aged 5 (or 6 for Moderna) to 11 years. No serious adverse events related to the vaccine, no cases of MIS-C, myocarditis/pericarditis or deaths were reported in either clinical trial.

- **Efficacy:** The estimated efficacy of the Pfizer vaccine against symptomatic COVID-19 from 7 days after dose 2 was 90.7% (95% CI: 67.7 to 98.3%; 3 cases identified in the vaccine group and 16 cases in the placebo group). Preliminary Moderna efficacy against symptomatic COVID-19 was 88% (95% CI: 70.0 to 95.8%) starting 14 days after dose 1. None of the identified cases met the pre defined criteria for a severe case of COVID-19, therefore the data did not include estimates of vaccine efficacy against severe outcomes such as hospitalization, MIS-C or death.

Real world safety surveillance data shows that:

- In the US, about 8.7 million doses of Pfizer (10 mcg) had been administered to individuals aged 5 to 11 years as of December 19, 2021. The US uses the manufacturer's recommended 21-day interval between doses. Reactogenicity data from the v-safe surveillance system are consistent with the clinical trial results; overall, Pfizer is well tolerated, where individuals aged 5 to 11 years report adverse reactions less frequently than individuals aged 12 to 15 years who received Pfizer (30mcg). Overall, 12 confirmed cases of myocarditis (including 8 of 12 reports among males and 9 of 12 reports after dose 2) in individuals aged 5 to 11 years had been reported to the Vaccine Adverse Event Reporting System (VAERS). The cases of myocarditis among the 5 to 11 year-old population appeared to have similar characteristics to those reported in older age groups (onset usually within a week after vaccination, more often after dose 2, more often in males than females, and the majority of individuals tend to recover quickly). However, after dose 2, the reported rate of myocarditis in males aged 5 to 11 years (4.3 cases per million doses administered) is substantially lower than in males aged 12 to 15 years (45.7 cases per million doses administered) and males aged 16 to 17 years (70.2 cases per million doses administered).
- At this time, the risk of myocarditis or pericarditis after dose 2 when using an extended interval (at least 8 weeks) among children ages 5 to 11 years and the safety of a third dose of COVID-19 vaccine in individuals aged 5 to 11 years are unknown. To date, after months of real world usage of vaccine in this age group, no increased risk of myocarditis or pericarditis has been observed.

- Moderna vaccine has more recently been approved for use in children 6 to 11 years of age. In clinical trials, no safety issues were detected. Data on the safety of COVID-19 vaccines will continue to be monitored (i.e., real world use) to detect and respond to potential safety signals that may arise, including myocarditis/pericarditis.
- Although risk of myocarditis/pericarditis with the Moderna (50 mcg) in children 6 to 11 years of age is unknown, with a primary series in adolescents and young adults the rare risk of myocarditis/pericarditis with Moderna (100 mcg) was higher than with Pfizer (30 mcg).
- Vaccine related myocarditis/pericarditis is a much milder condition than infection related myocarditis/pericarditis. The majority of cases have responded well to treatment and recovered quickly.

Children must be at minimum 5 years of age at the time of immunization to be considered eligible to receive the Pfizer (10 mcg) pediatric vaccine. Children must be at minimum 6 years of age at the time of immunization to be considered eligible to receive the Moderna (50 mcg) vaccine. Children should receive the vaccine they are eligible for at the time of immunization. That means children who are soon turning 12 years of age, should receive the Pfizer pediatric vaccine (10 mcg) or Moderna (50 mcg) for dose 1 when they are 11 years of age and then the Pfizer adolescent/adult vaccine (30 mcg) for dose 2 (as Pfizer remains the recommended vaccine for those 12 to <30 years of age) if they turn 12 years of age and have yet to receive their second dose.

Consistent with current recommendations for adolescents/adults with previous infection, an mRNA **vaccine may be offered to children with a previous history of SARS-CoV-2 infection,** assuming they are asymptomatic and outside of the period of self-isolation. The suggested interval between symptom onset or positive test (if asymptomatic) and vaccination is 2 to 3 months.

For children with a previous history of MIS-C, vaccination should be postponed until clinical recovery has been achieved or until it has been ≥ 90 days since diagnosis, whichever is longer.

As a precautionary measure, NACI recommends waiting 14 days before or after the administration of another vaccine before administering a COVID-19 vaccine to prevent an erroneous attribution of an adverse event to one particular vaccine over another. Concomitant administration or a shortened interval is acceptable in certain circumstances (e.g., when school vaccines are already scheduled).

Burden of disease in children aged five to 11 years

Children aged five to 11 years of age generally present with mild or asymptomatic SARS-CoV-2 infection. Since the start of the pandemic, Manitoba data shows that (current as of March 29, 2022):

- Over 12,056 children have tested positive for COVID-19. NOTE: this is likely to be an underestimate of the exact prevalence given the frequency of mild/asymptomatic infections in children, as well as changes in testing guidelines.
- A total of 68 children have been hospitalized and 10 have been admitted to ICU.
    - With just under half of hospitalizations attributed to COVID-19 (as opposed to incidental and/or hospital-associated infections).
- One child has died.
- Thirteen children aged five to 11 years have been diagnosed with MIS-C.

The National Advisory Committee on Immunization (NACI) also notes that:

- Myocarditis can also occur as a complication of SARS-CoV-2 infection, including [very rarely] in children.
- While evidence is limited in pediatric populations, children may also be at risk of a post-COVID-19 condition (i.e., long COVID or post acute COVID-19 syndrome). However, current evidence suggests the risk is lower in children compared to older age groups.
- Children are also at risk of collateral harms of the COVID-19 pandemic. Prolonged schooling disruptions, social isolation and reduced access to academic and extra-curricular resources have had profound impact on the mental and physical well-being of children and their families. These harms can disproportionately affect some Canadian children and families as compared to others, and the impacts of these harms may further exacerbate social inequities among racialized and Indigenous communities, refugees and other newcomers to Canada, persons living in low-income settings, as well as children with disabilities.

NACI also notes that the relative risk for severe outcomes of COVID-19 may be substantial for children with comorbidities, but the magnitude of the absolute excess risk remains small. The clinical risk factors for severe COVID-19 in children aged five to 11 years includes:

- Down Syndrome
- End-stage kidney disease
- Epilepsy
- Neurological disorders
- Type 1 and 2 diabetes
- Obesity (BMI > 40)
- Living in congregate living settings
- Feeding tube dependence

Guidance on the recommended interval for the primary series

Manitoba public health officials, the Manitoba COVID-19 Vaccine Pediatric Advisory Committee and the National Advisory Committee on Immunization (NACI) recommend that the interval for children aged 5 to ≤ 11 years is 8 weeks after dose one. This is because:

- The benefit of a longer interval is expected to outweigh any benefit of a shorter interval, even in the current context of community transmission of Omicron.
- Emerging evidence suggests that longer intervals between the first and second doses of COVID-19 vaccines result in more robust and durable immune response and higher vaccine effectiveness, and may be associated with a lower risk of myocarditis and/or pericarditis in adolescents and young adults.

Vaccine product	Pediatric schedule	Absolute minimum interval	Authorized minimum interval	Recommended interval
Pfizer	2 doses of 0.2 mL (10 mcg)	19 days	21 days	At least 8 weeks
Moderna	2 doses of 0.25 mL (50 mcg)	21 days	28 days	At least 8 weeks

In some situations, doses may be given closer together, but no sooner than 21 days for Pfizer (10 mcg) or 28 days for Moderna (50 mcg), after discussing the risks and benefits with the parent/guardian or as recommended by the relevant public health authority on current epidemiologic trends.

For children living in First Nations communities, the Manitoba First Nations Pandemic Response and Coordination Team and public health officials from the First Nations and Inuit Heath Branch (FNIHB) recommend that children living in First Nation communities receive their second dose no sooner than, but as close to 21 days for Pfizer and 28 days for Moderna, as possible. Given the higher risk context in First Nation communities, the benefits of achieving full protection sooner outweigh the risks of a shorter dose interval.

For guidance on vaccination timing for individuals previously infected with SARS-CoV-2, see question 25 of the Clinical Practice Questions and Answers.

Guidance for children who are immunocompromised

People with moderately to severely compromised immune systems have been observed to generally have lower antibody responses and lower vaccine effectiveness from COVID-19 vaccines than immunocompetent individuals, although this varies depending on the underlying condition or immunosuppressive agents. **See Appendix F for the list of conditions/definition of individuals who are moderately to severely immunocompromised.**

Consistent with the Canadian Pediatric Society and the National Advisory Committee on Immunization (NACI), Manitoba public health officials recommend a three dose primary series for moderately to severely immunocompromised children aged 5 to ≤ 11 years.

NACI notes that while vaccine effectiveness data for children who are immunocompromised are limited, and waiting for more evidence would increase the certainty of this recommendation, it is still possible to extrapolate based on adolescent data. Available evidence on immunogenicity and safety in adolescent populations supports offering an additional vaccine dose to children 5 to 11 years of age who are moderately to severely immunocompromised, to optimize direct protection conferred by vaccine. The additional dose provides an opportunity to obtain protective immunity against COVID-19.

NACI states that indirect data from the adult populations (≥18 years of age) suggest Moderna (100 mcg) may result in higher vaccine effectiveness after a 2-dose primary series compared to Pfizer (30 mcg) and is associated with a higher seroconversion rate among adult immunocompromised patients. Given this potential benefit, administration of the Moderna (50 mcg) vaccine as a 3-dose primary series may be considered for some immunocompromised individuals 6 to 11 years of age, as outlined in the product monograph. Each dose would be provided 4 to 8 weeks apart, as per the NACI recommended schedule for immunocompromised populations.

Ensure a robust informed consent process that clearly communicates both what is known and unknown about the risks and benefits of receiving a third dose in children aged five to ≤ 11 years, including:

- Evidence used to inform the additional dose recommendations is based on safety and immunogenicity data in adolescents; evidence on efficacy/effectiveness of an additional dose after a primary series will be reviewed when it is available.
- Safety data of small studies available to this point, suggests the reactogenicity of an additional dose of a COVID-19 mRNA vaccine was similar to that of prior doses primarily in adolescents.
- Due to the unknown efficacy/effectiveness of an additional dose, immunocompromised individuals should continue to follow recommended public health measures.
- Immunocompromising conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the progression of disease and use of medications that suppress immune function.
- The risk of myocarditis and/or pericarditis following a third dose of mRNA vaccine in this population is unknown at this time.
- Pfizer and Moderna are approved for use as a 3-dose primary series in individuals who are immunocompromised.

Recommended Immunization Schedule for Immunocompromised Children						
		INTERVAL				
		Interval between dose 1 and dose 2		**Interval between dose 2 and dose 3**		**Interval between dose 3 and dose 4 (booster)**
		Minimum	**Recommended**	**Minimum**	**Recommended**	
Ages 5 to ≤ 11 years	Pfizer (10 mcg)	21 days	8 weeks	≥ 28 days	Unknown; use clinical discretion*	Not authorized/recommended at this time; may be updated in future based on
Ages 6 to ≤ 11 years	Moderna (50 mcg)	28 days	8 weeks			

						emerging evidence
	***There is limited data to determine the optimal interval for the third dose. It is recommended to consider the risk factors for exposure and severe disease when deciding on the time interval. At this time, the minimum interval of the third dose from the second dose is 28 days. In general, NACI recommends that immunocompromised individuals be immunized at the time when maximum immune response can be anticipated:** • **Immunize prior to any planned immunosuppression such that optimal immunogenicity is achieved, if possible.** • **Delay immunization if the immunodeficiency is transient (if this can be done safely because exposure is unlikely in the individual's setting and circumstance).** • **Stop or reduce immunosuppression to permit better vaccine response, if appropriate. Consult the Canadian Immunization Guide for more detail on the timing of vaccination in relation to immunosuppressive therapy: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25.**					

Information about myocarditis and pericarditis

Emerging Canadian safety surveillance data suggest an extended interval between the first and second dose may reduce the risk of myocarditis/pericarditis associated with the second dose of an mRNA COVID-19 vaccine. Data from the US suggest the risk of myocarditis/pericarditis following mRNA COVID-19 vaccination may be higher in older adolescents aged 16 to 17 years compared to younger adolescents aged 12 to 15 years.

Currently, the risk of myocarditis/pericarditis in children age 5 to 11 following immunization with the Pfizer-BioNTech (10 mcg) or Moderna (50 mcg) vaccine is unknown. Safety surveillance data from individuals aged 12 and older does not suggest the risk of myocarditis/pericarditis following mRNA COVID-19 vaccination would be greater in children aged 5 to 11 years compared to older populations. Additionally, the impact of a reduced vaccine dose (Pfizer: 10 mcg vs 30 mcg; Moderna: 50 mcg vs 100 mcg) is also unknown. To date, after months of real world usage of vaccine in this age group, no increased risk of myocarditis or pericarditis has been observed.

NACI recommends deferring the second dose in children who experience myocarditis or pericarditis following the first dose of mRNA vaccine until more information is available.

- Some people with confirmed myocarditis (with or without pericarditis) after a dose of an mRNA COVID-19 vaccine may choose to receive another dose of vaccine after discussing the risks and benefits with their immunizer/healthcare provider. If another dose of vaccine is offered, they should be offered Pfizer due to the lower reported rate of myocarditis and/or pericarditis following Pfizer compared to Moderna in the 12 to <30 year old population. Informed consent should include discussion about the unknown risk of recurrence of myocarditis and/or pericarditis following receipt of additional doses of Pfizer in individuals with a history of confirmed myocarditis and/or pericarditis after a previous dose of

mRNA COVID-19 vaccine, as well as the need to seek immediate medical assessment and care should symptoms develop.

Children who have a history of myocarditis unrelated to mRNA COVID-19 vaccination should consult their clinical team for individual considerations and recommendations. If they are no longer followed clinically for cardiac issues, they may receive the vaccine. Parents/guardians/caregivers must be advised to seek medical attention if a child develops symptoms including chest pain, shortness of breath, or palpitations following vaccination.

Information on MIS-C

Very rare cases of MIS-C/A (multisystem inflammatory syndrome; in children and in adults, respectively) have been reported following vaccination with COVID-19 mRNA vaccines in Canada and internationally among individuals aged 12 years and older. However, on October 29, 2021, the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (EMAPRAC) issued a statement that there is currently insufficient evidence on a possible link between mRNA COVID-19 vaccines and very rare cases of MIS-C/A.

For children with a previous history of MIS-C, vaccination should be postponed until clinical recovery has been achieved or until it has been ≥ 90 days since diagnosis, whichever is longer.

Differences between Pfizer's pediatric and adolescent/adult formulations

	Adolescent/Adult Formulation	Pediatric Formulation
Age	Aged ≥ 12 years	Aged 5 to ≤ 11 years
Packaging color	Purple cap (note: at this time, there is no color on the packaging)	Orange on vial cap and packaging
Buffer	Phosphate	Tris/sucrose
Known potential allergens[1]	Polyethylene glycol (PEG) Polysorbate 80	Polyethylene glycol (PEG) Polysorbate 80 Tromethamine (trometamol or Tris)
Diluent volume to add to vaccine vial	**1.8 ml**	**1.3 ml**

Injection volume (Dose)[2]	**0.3 ml** (30 micrograms)	**0.2 ml** (10 micrograms)
Doses per vial	6 doses/vial; low dead volume needle/syringe required	10 doses/vial; low dead volume needle/syringe required
Time to discard after dilution	6 hours	12 hours
Storage - ultra low freezer (-90ºC to -60ºC)	9 months	6 months
Storage - freezer (-25ºC to -15ºC)	2 weeks	Not recommended at this time
Storage - refrigerator (2ºC to 8ºC)	1 month (mark on vial or packaging date to be discarded)	10 weeks (mark on vial or packaging date to be discarded)
Storage - room temperature prior to dilution (up to 25ºC)	2 hours	12 hours
NOTES: [1] See Appendix C for guidance on managing allergic pediatric clients (consistent with guidance for managing allergic clients aged ≥ 12 years). [2] In the Phase 1 dose finding trial, due to the frequency and severity of reactogenicity observed with a 30 mcg dose in the first 4 children 5-11 years of age that received two doses, 30 mcg each, the internal review committee (IRC) recommended that the 30 mcg dose be discontinued and the remaining participants who received 30 mcg as dose 1 received 10 mcg for dose 2 instead (n=12).		

Differences between Moderna's pediatric and adolescent/adult dosage

Product specification	Use in children (6 to ≤11 years of age; primary series)	Use in adults/adolescents (≥12 years of age; primary series)
Age	**6 to 11 years**	**12 years of age and over**
Dose	**50 mcg (0.25 mL)**	**100 mcg (0.5 mL)**

Doses per vial	**20**	**10**
Diluent	No dilution required	
Potential allergens	Polyethylene glycol (PEG) Tromethamine (Tris, Trometamol)[1]	
Storage[2,3,4,5]	• Frozen[3] until expiry date printed on the label • Refrigerated[3,4] for up to 30 days • Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 24 hours • Once needle-punctured, vials can be stored at room temperature4 or refrigerated3,4 up to 24 hours but should not be punctured more than 20 times	
Transport[3]	• Frozen[3] full cartons containing vials[5] • Refrigerated[3,4] thawed vails can be transported up to 12 hours (included in 30-day limit for refrigerated storage)	

NOTES:

[1]Tromethamine (Tris or trometamol) is used as a buffer in vaccines and medications, including those for use in children, to improve stability and prevent pH fluctuations in the solution. No safety concerns have been identified with tromethamine. While tromethamine has been identified as a potential allergen, a review of existing evidence did not identify any cases of allergic reactions to tromethamine in children.

[2]Regardless of storage condition, vaccines should not be used after date of expiry printed on the vial and cartons.

[3]Frozen is -25°C to -15°C; Refrigerated is +2°C to +8°C; Room temperature is +15°C to +25°C.

[4]Once vials are thawed, they should not be refrozen. Thaw in refrigerated conditions between +2° to +8°C (36° to 46°F) for 2 hours and 30 minutes. After thawing, let vial stand at room temperature for 15 minutes before administering. Alternatively, thaw at room temperature for 1 hour.

[5]During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Vials must be kept frozen and protected from light, in the original cartons, until ready to thaw.

Guidance on an additional dose for individuals who received non-Health Canada approved COVID-19 vaccines for individuals aged 5 to ≤ 11 years

The vaccine immunogenicity, efficacy and effectiveness of authorized vaccines available worldwide vary. While many of the vaccines appear to be performing very well based on available data, others have lower effectiveness.

Consistent with PHAC's approach for adults**,** Manitoba public health officials recommend one additional dose of an approved mRNA COVID-19 vaccine be offered for individuals in the authorized age groups planning to stay in MB for longer periods of time (i.e., to live or study) who have received one dose of a non-Health Canada approved vaccine. The recommended interval between the preceding dose and the additional dose is 8 weeks.

Clinical practice questions and answers

1. What information is available for parents/guardians/clients who are concerned about the vaccine effect on fertility?

There is no evidence that any vaccines, including COVID-19 vaccines, cause fertility problems. On March 18, 2021, the Society of Obstetricians and Gynecologists of Canada (SOGC) released a statement in response to the rumours suggesting that COVID-19 vaccination may affect future fertility:

> There is absolutely no evidence, and no theoretic reason to suspect that the COVID 19 vaccine could impair male or female fertility. These rumors are unfounded and harmful.
>
> The widespread social media concern stems from misinformation about the similarities between syncytin-1 (used for placental implantation) and the SARS-CoV-2 spike protein. While the two proteins have several similar amino acids, they remain vastly different. The antibodies produced against the SARS-CoV-2 spike protein would not have cross-reactivity with syncitin-1 (sogc.org/common/Uploaded%20files/Latest%20News/EN_SOGCStatement_COVID-19Vaccination-Fertility.pdf).

The SOGC also developed a document with references on "COVID-19 Vaccine: Myths and Facts" as it pertains to the affect of COVID-19 vaccination on pregnancy, fertility and the menstrual cycle: sogc.org/common/Uploaded%20files/Covid%20Information/FAQ_Myth-Fact_17Sept2021.pdf.

Researchers, physicians and safety regulators are monitoring the COVID-19 vaccines very carefully for side effects and they will report findings if anything new arises.

Clinical Practice Questions and Answers

The COVID-19 vaccine landscape is rapidly evolving. Clinical trials are ongoing and emerging data from post-marketing studies, often in pre-print, are released daily. The following is a list of evidence-based sources of information that immunizers and health care providers can refer to for the most current information and evidence about the COVID-19 vaccines authorized in Canada.

- the National Advisory Committee on Immunization (NACI) releases statements with guidelines and recommendations around the use of the COVID-19 vaccines authorized in Canada as well as priority population sequencing: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html.
    - To subscribe for notification of updates, go to: https://health.canada.ca/en/health-canada/services/healthy-living/immunization-and-vaccines/canadian-immunization-guide/subscribe.html.
- the manufacturer product monograph is available online at: https://www.gov.mb.ca/covid19/vaccine/resources.html, and include:
    - Pfizer/Comirnaty™
    - Moderna/Spikevax™
    - AstraZeneca/Vaxzevria™
    - Janssen
    - Novavax/Nuvaxovid™
- information about Health Canada's regulatory approval processes and other regulator-role specific information is available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html.
- the Public Health Agency of Canada (https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/vaccines.html) develops resources as well as prepares national summary statistics on population coverage and summary reports of adverse events following immunization (AEFI).
- provincial resources, guidelines and information for immunizers and health care providers can be found online at: https://www.gov.mb.ca/covid19/vaccine/index.html. Questions and answers specifically for community pharmacists and physicians that are participating in the COVID-19 Immunization Program can be found at: https://manitoba.ca/covid19/vaccine/partners/faq.html.

The following questions and answers are intended to supplement information from NACI, the product monographs, Health Canada, the Public Health Agency of Canada and the Government of Manitoba. Where available, links to new studies will be provided in the footnotes. Please note that this is not intended to be an exhaustive list of questions and answers but rather, is a central repository of emerging evidence and information that is being highlighted for your attention and action. Should you have a clinical question that is not addressed below or in one of the aforementioned resources linked above, please email your question to COVID@gov.mb.ca.

General Vaccine Information

1. ***This question/answer has been removed as it is no longer current or relevant****

2. What should I do if I receive a fraudulent offering of COVID-19 vaccine?

Please be advised that Health Canada and other Canadian jurisdictions are reporting fraudulent offers to procure COVID-19 vaccines direct from manufacture. Please be advised that all COVID-19 vaccines are procured federally; any direct offering is fraudulent and should be reported to the police or RCMP, whichever has jurisdiction in your area.

3. How should I communicate with vaccine hesitant clients/patients?

As per the Canadian Immunization Guide, vaccine hesitancy is a term used to describe a refusal of vaccination or a delay in an immunization schedule due to concerns about immunization. Vaccines evoke concerns different from other health interventions because vaccines are generally offered to individuals who are healthy, as opposed to other health interventions that are predominantly intended for individuals with a disease. Vaccine hesitancy is a complex issue with multiple determinants, the most important being:

- lack of understanding about the vaccine being given and about immunizations in general
- conflicting information from a variety of sources (for example, alternative medicine practitioners, anti-vaccination websites);
- mistrust of the source of information (for example, perceptions of business and financial motives of the vaccine industry)
- perceived risk of serious adverse events and concerns regarding injections (for example, pain and anxiety associated with immunization; coincidental rather than causal adverse events that are perceived as vaccine-related)
- lack of appreciation of the severity and incidence of vaccine preventable diseases;
- sociocultural beliefs (for example, religious beliefs)

With respect to COVID-19 vaccines, the hesitancy could focus specifically around:

- the speed in which the vaccines are being developed
- perceived perception that regulators and manufacturers are cutting corners (i.e. lack of transparency of the process in which a vaccine is approved and what is required from manufacturers)
- new technology of vaccine manufacturing
- reports of adverse events following immunization
- perceived perception that one vaccine is better than another vaccine

It is therefore vital that immunizers and health care providers endeavor to address these concerns at an individual level, to ensure completion of the COVID-19 vaccine series as

well as eliminate the spread of misinformation that can impact decision-making of other people. Health care providers can use different techniques of addressing vaccine hesitancy with their clients/patients, by:

- using presumptive and motivational interviewing techniques to identify and address specific vaccine concerns
- using effective and clear language to present evidence for disease risks and vaccine benefits fairly and accurately
- respecting differences of opinion about immunization in a non-judgemental, open dialogue approach
- managing pain from immunization[19]

Health care providers should have a multitude of evidence-based resources available that are tailored to a range of socio-cultural groups, including:

- factsheets
- product monographs
- information on Health Canada's independent drug authorization process[20]

4. What is the process for obtaining and documenting informed consent?

A provincial COVID-19 Vaccine Consent Form is available for immunizers and health care providers to use for the purposes of obtaining and documenting informed consent from clients/patients. Informed consent can be given verbally or in writing, and must be documented. A consent form or client/patient medical chart or electronic health record may be used to document informed consent. For more information, review the provincial Informed Consent Guidelines for Immunization (https://www.gov.mb.ca/health/publichealth/cdc/protocol/consentguidelines.pdf).

The COVID-19 vaccine may be offered to people who fall into one or more of the following categories, provided that the risks and benefits of immunization are adequately conveyed to the client/patient:

a. Immunosuppressed due to disease or treatment
b. Autoimmune disorder

The process of obtaining informed consent from persons who fall into one or more of the above categories as well as for those who require a third/booster dose, requires the immunizer or health care provider to review the pertinent information contained in the factsheets and have a risk-benefit discussion with the client/patient that is guided by the information in the Clinical Practice Guidelines.

Only in situations where the client/patient who is immunosuppressed or has an autoimmune disorder AND is getting immunized at a Super-Site or Pop-up Clinic,

[19] Clinician focused immunization pain management resources are available through Immunize Canada at: https://immunize.ca/immunization-pain-management-clinician.
[20] For more information on vaccine hesitancy and communicating effectively about immunization, go to: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-5-communicating-effectively-immunization.html.

is a health care provider required to provide a hard copy of the completed form back to the client/patient.

5. What is the process for approving COVID-19 vaccines in Canada?

As per Health Canada, to market a vaccine in Canada, manufacturers must file an application to Health Canada via one of the following regulatory processes:

a. the interim order for COVID-19 drug authorization
b. the Food and Drug Regulations

The interim order regulatory process is a fast-tracked review process that allows Health Canada to start the review process as evidence becomes available instead of waiting until all studies are complete. Health Canada authorizes a vaccine under the interim order if the evidence demonstrates that the vaccine is:

- safe, effective and of good quality **AND**
- the intended benefits outweigh the material risks.

On September 16, 2021, Health Canada approved the Pfizer (Comirnaty™), Moderna (Spikevax™) and AstraZeneca (Vaxzevria™) vaccines under the Food and Drug Regulations (i.e., they are no longer issued market authorizations with the conditions for early access under the Interim Order, as sufficient data was made available to approve them under normal regulations). On November 23, 2021, Health Canada approved Janssen under the Food and Drug Regulations. On February 17, 2022, Health Canada approved Novavax/Nuvaxovid™ under the Food and Drug Regulations.

6. What is the interval between COVID-19 vaccine doses that I should follow?

As per NACI, there is no data on a maximum interval between doses or on medium or long-term efficacy of COVID-19 vaccines. In general, interruption of a vaccine series resulting in a greater than recommended interval between doses does not require restarting the series as delays between doses do not result in a reduction in final antibody concentrations for most multi-dose (prime-boost) products. For many other multi-dose vaccines provided in adulthood using other vaccine technologies, the greatest proportion of short-term protection is achieved with the first dose with additional doses primarily intended to extend protection over the longer term.

Morbidity and mortality from COVID-19 is ongoing. Based on emerging evidence of the protection provided by the first dose of a two-dose series for COVID-19 vaccines authorized in Canada, in the context of limited COVID-19 vaccine supply and ongoing pandemic disease, Manitoba maximized the number of individuals benefiting from the first dose by extending the interval between doses up to four months (16 weeks). When supply increased, this extended interval was no longer adhered to.

As per NACI, the primary immunization schedule is as follows:

Vaccine	Schedule	Minimum interval	Authorized interval	Optimal interval[d]
Pfizer	2 doses*	19 days [a]	21 days	8 weeks
Moderna	2 doses*	21 days [b]	28 days	8 weeks
AstraZeneca	2 doses	28 days	4 to 12 weeks [c]	at least 8 weeks
Janssen	1 dose	N/A		
Novavax	2 doses	21 days	3 weeks	8 weeks

NOTES:

[a] pre-protocol design for the Pfizer-BioNTech vaccine clinical trial was 19-23 days.

[b] majority of participants in the Moderna clinical trial received the second dose 21 to 42 days after the first dose.

[c] AZ clinical trial demonstrated optimal efficacy when the interval between doses was ≥ 12 weeks.

[d] there is emerging evidence that longer intervals between the first and second doses of COVID-19 vaccines result in more robust and durable immune response and higher vaccine effectiveness.

* certain populations are eligible to receive a third/booster dose; for third dose interval, see "Guidance on Subsequent Doses."

At this time, it is recommended that people receive only one COVID-19 vaccine series (i.e., there is no recommendation to receive a second COVID-19 vaccine series with a different product at this time). In situations where an additional dose is recommended after the 1- or 2-dose primary series, the minimum interval between the preceding dose and the additional dose is 28 days.

NACI recommends that persons who received a first dose of an mRNA vaccine (Pfizer-BioNTech or Moderna) should be offered the same mRNA vaccine for their second dose. If the same mRNA vaccine is not available or unknown, another mRNA vaccine can be considered interchangeable and should be offered to complete the vaccine series. There are two exceptions to this general guidance:

1. **Individuals aged 12 to 29 years:** Manitoba public health officials recommend Pfizer (30 mcg) to start or continue the vaccine series (i.e., individuals aged 12 to 29 years who received dose 1 of Moderna should complete their series with Pfizer). Pfizer is preferred to Moderna because of a lower reported rate of myocarditis/pericarditis following Pfizer (30 mcg) compared to Moderna (100 mcg). Analyses of Canadian data suggests that with the primary series, the incidence of myocarditis is rare with either mRNA vaccine, but higher following Moderna (100 mcg) compared to Pfizer (30 mcg). The reported rates of myocarditis/pericarditis among males aged 18 to 29 years after the second dose were 15.9 per 100,000 for Moderna (100 mcg) and 2.6 per 100,000 for Pfizer (30 mcg). Among individuals aged ≥ 30 years, either mRNA vaccine should be used given that this age group has a lower risk of vaccine-associated myocarditis/pericarditis.

2. **Individuals who have contraindications to an mRNA vaccine:** rarely, individuals are advised not to receive additional doses of an mRNA vaccine. In these situations, a person may be recommended on a case-by-case basis to receive a non-mRNA authorized COVID-19 vaccine.

To ensure minimum intervals, immunizers and health care providers are to review client immunization records via eChart or the Public Health Information Management System (PHIMS) before immunizing.

Certain populations are recommended to be offered a booster dose; for information on recommended and minimum intervals, see "Guidance on Subsequent Doses." Generally, the interval for booster doses are recommended to be given ≥ six months after the last dose for individuals aged 12 years and older. Previously, based on community level risk, it had been recommended that certain populations receive their booster dose ≥ five months (individuals aged ≥ 50 years and older and adults living in First Nation community).

See Appendix G for a detailed summary table for clinicians to guide decision-making around primary series intervals, including recommended and minimum intervals.

7. *****This question/answer has been removed as it is no longer current or relevant*****

8. *****This question/answer has been removed as it is extensively covered in the clinical guidance*****

9. ******This question/answer has been removed as it is extensively covered in the clinical guidance******

10. **Do Health Canada-approved COVID-19 vaccines protect against variants of concern?**

Yes, although the level of protection (i.e., efficacy) varies by vaccine and variant of concern. COVID-19 variants of concern, such as those first identified in the United Kingdom, South Africa and Brazil, continue to spread globally, and new variants can emerge at any time.

As per NACI, the Pfizer-BioNTech and AstraZeneca vaccines protect against the B.1.1.7 (Alpha) variant first identified in the UK. There is emerging evidence that Pfizer and AstraZeneca also offer good protection against the B.1.617.2 (Delta) VOC, but only after the second dose; emerging estimates suggest two doses of Pfizer vaccine are 87.9% effective and two doses of AstraZeneca vaccine are 59.8% effective. There are also emerging data on the efficacy or effectiveness of mRNA vaccine against B.1.351 (Beta) VOC. There is also evidence that the Janssen vaccine offers protection against the B.1.351 variant of concern first identified in South Africa as well as the P.2 variant of interest first identified in Brazil.

Evidence continues to emerge and evolve with respect to how well the mRNA vaccines protect against the Omicron variant. Emerging evidence suggests:

- A few weeks after the second dose, the mRNA vaccines offer little protection against symptomatic disease but good protection (approximately 70 per cent) against severe outcomes.
- A third dose of mRNA vaccine appears to offer some level of protection against symptomatic disease in the short term, although estimates of effectiveness vary by study (approximately 50 to 60 per cent vaccine effectiveness against infection). The duration of protection against symptomatic disease is currently unknown after a third dose, but the limited evidence available suggests protection wanes quicker against Omicron compared to other variants (e.g., Delta).
- A third mRNA dose appears to offer increased, albeit marginal, protection against severe outcomes. A study from England suggests a third dose is 88% effective at preventing hospitalizations from Omicron compared to being unvaccinated.[21]

The Novavax/Nuvaxovid™ trials were conducted prior to the emergence of Delta and Omicron, and there is very limited immunogenicity data, and no efficacy/effectiveness data to demonstrate what level of protection Novavax/Nuvaxovid™ offers against Omicron.

11. ***This question/answer has been removed as it is no longer current or relevant****

Vaccine Safety

12. Is there an increased risk of thromboembolic events with the AstraZeneca vaccine?

On March 8, 2021, Health Canada was informed by the European Medicines Agency (EMA) that Austria stopped using a batch of AstraZeneca (AZ) following three reports of thromboembolic events following vaccination. As a result, several countries in Europe including Denmark, temporarily paused the use of specific batches of AZ in their campaigns as a precautionary measure, pending investigation.

On March 18, 2021, following their investigation, the EMA and the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) issued a statement that the benefits of the use of AZ continue to outweigh the risks. EMA's safety committee reports that overall the number of thromboembolic events reported after vaccination, both in studies before licensing and in reports after rollout of vaccination campaigns, was lower than that expected in the general population. This allows EMA's safety committee to confirm that there is no increase in overall risk of blood clots. However, in younger

[21] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf

patients there remain some concerns, related in particular to these rare cases. The reported cases were almost all in women under 55 years of age.[22]

On March 18, Health Canada issued a statement that it had assessed the available data on the reported events and determined that the AZ vaccine has not been associated with an increase in the overall risk of blood clots. On March 24, Health Canada updated the AstraZeneca and COVISHIELD Product Monographs, as well as issued a Health Product Risk Communication to health care professionals. These updates highlight a combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely following vaccination with the AstraZeneca COVID-19 vaccine, and provides further guidance for health care professionals and vaccine recipients.

- AstraZeneca Product Monograph: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf

- Health Product Risk Communication: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-letter.pdf

On March 29, 2021, the National Advisory Committee on Immunization (NACI) recommended that AstraZeneca should not be used in adults < 55 years of age while the safety signal of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) following vaccination with AstraZeneca COVID-19 vaccine is investigated further. Since then, several jurisdictions in Canada, including Manitoba, lowered the age to ≥ 40 years for the general population, and ≥ 30 years of age for people with health conditions. Now, AstraZeneca and Janssen (which also carries the risk of VITT) are available for people aged 18 years and older who would otherwise decline an mRNA vaccine or, are contraindicated to receive an mRNA vaccine. For more information on VITT and viral vector vaccines, see the section on “Guidance for use of Viral Vector Vaccines.”

13. I have a client/patient who experienced an AEFI; what do I do?

An adverse event following immunization (AEFI) is any untoward medical occurrence in a vaccinee that follows immunization. It may be any unfavorable and/or unintended sign, abnormal laboratory finding, symptom or disease.

Report AEFIs as per www.gov.mb.ca/health/publichealth/cdc/div/aefi.html#rrp. In accordance with Section 59 of The Public Health Act, health care providers are to report a reportable AEFI within seven days of becoming aware of the AEFI. Furthermore, health care providers should report a serious AEFI within one business day, which can be by telephone, followed by the complete written report within 72 hours.

A reportable AEFI is an event that:

1. is temporally associated with a vaccine AND
2. has no other clear cause at the time of reporting

[22] https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots

Of particular interest are AEFIs that are serious, unexpected and/or of special interest. But all AEFIs that meet (1) or (2) above should be reported, unless they are only mild local reactions that are not overly concerning to the vaccine recipient.

An AEFI is considered "unexpected" if either of the following criteria is met:

- it is not listed in the most current Health Canada-approved product monograph for vaccines marketed in Canada
- listed in the product monograph but is different in nature, severity, frequency, specificity or outcome

Provide clients/patients with the following factsheet before immunization: What to do if you experience an adverse reaction after receiving the COVID-19 vaccine (https://www.gov.mb.ca/asset_library/en/covid/covid19_vaccine_reaction_factsheet.pdf).

Recommendations around future COVID-19 vaccine doses will depend on the type and severity of reaction. If there is any ambiguity, consult a relevant specialist.

14. Can a client/patient who had a previous anaphylactic reaction to a vaccine and underwent allergy testing thereafter, receive a COVID-19 vaccine?

Yes. History of a prior anaphylactic reaction to vaccine is a precaution but not a contraindication to receiving a COVID-19 vaccine, provided the client does not have any known allergies to any of the ingredients found in the vaccine (or other known contraindications). If no component of the vaccine was identified by an allergist as a cause for the previous reported anaphylactic reaction, it is deemed safe to proceed. However, it is recommended that the client/patient be observed for 30 minutes post-vaccination (as opposed to the routine recommendation of 15 minutes post-vaccination).

If the client/patient did not undergo allergy testing following the previous anaphylactic reaction to a vaccine which has shared ingredients to the COVID-19 vaccine to be given, it would be prudent to consult allergy/immunology.

15. I have a client/patient who experienced a mild, non-anaphylactic, allergic reaction following the first dose of COVID-19 vaccine; should I proceed to offer the second dose?

Generally speaking, subsequent doses can be offered provided that the client/patient is not allergic to an active substance or allergic to any of the ingredients of the vaccine. The client/patient should be counselled prior to vaccination on the possibility of experiencing another allergic reaction, and may need to stay in the clinic for at least 30 minutes post-vaccination to monitor for signs of a more severe allergic reaction. If there is any ambiguity, consult a relevant specialist.

16. I have a client/patient who experienced an anaphylactic reaction following their first dose of COVID-19 vaccine; what does this mean for future doses?

A referral to the COVID-19 Vaccine Allergy Clinic at Health Sciences Centre from the general practitioner or nurse practitioner is recommended. The consult can be sent to the Adult Allergy Clinic of Health Sciences Centre at 204-940-2223, **OR** the Pediatric Allergy Department of Children's Hospital at 204-787-5040.

17. Should I counsel patients to take acetaminophen or ibuprofen <u>before</u> getting immunized to mitigate or minimize potential side-effects or pain from immunization?

No. NACI recommends that acetaminophen or ibuprofen should not be routinely used before or at the time of vaccination, but their use is not a contraindication to vaccination. There is currently no evidence on the benefit from administration of oral analgesics for the prevention of immunization injection pain or systemic reactions.

Acetaminophen or ibuprofen after vaccination may be used for the management of pain and/or fever after vaccination.

18. If a client/patient experiences side effect(s) after vaccination that mimic COVID-19, should they isolate and get tested for COVID-19?

Public health officials urge anyone who has cold or flu-like symptoms, such as a cough, fever, runny nose, sore throat, headache, or any of the symptoms listed in the screening tool to isolate and follow public health guidance.

Vaccine Efficacy

19. What should I tell my patients who received AstraZeneca for their first dose, and want to receive AstraZeneca for their second dose?

Advise your patient that although the AstraZeneca vaccine is safe and effective, it does carry the risk of VITT, Guillain Barre syndrome (GBS) and capillary leak syndrome (CLS),), immune thrombocytopenia (ITP) and venous thromboembolism (VTE) which do not appear to occur with the preferentially recommended mRNA vaccines. In addition, emerging evidence suggests that mixed schedules with AstraZeneca as the first dose, followed by an mRNA (Pfizer or Moderna) with the second dose, is safe and produces a stronger immune response (compared to a vaccine series using only the AstraZeneca vaccine). This is why persons who received AstraZeneca for the first dose, are recommended to receive an mRNA vaccine for the second dose, and why viral vector vaccines are not permitted for use as third/booster doses in Manitoba.

20. What is the difference between vaccine efficacy and effectiveness, and what does the data tell us about the efficacy and effectiveness of the COVID-19 vaccines authorized for use in Canada?

Vaccine efficacy provides an estimate of how well a vaccine works under optimal conditions (e.g., clinical trial). **Vaccine effectiveness** provides an estimate of how well a vaccine works in the real world, under “normal” conditions (e.g., observational data). Estimates of efficacy or effectiveness can be expressed in differing ways, such as the vaccines affect on lab-confirmed (a)symptomatic disease or in reducing hospitalizations or death.

As per NACI,[23] vaccine effectiveness estimates, which are obtained from observational studies, are typically lower than vaccine efficacy estimates from clinical trials. Differences between observational data and clinical trial data may be due to the following:

- Observational studies include populations generally excluded from clinical trials (e.g., elderly residents in long term care facilities).
- Both symptomatic and asymptomatic infection are often being studied in observational studies, whereas the clinical trials looked mainly at symptomatic disease.
- It is also possible that relaxing of public health measures and precautions by vaccinated people in the real world may be increasing their risk of infection, leading to lower vaccine effectiveness estimates.

The following is a summary of efficacy estimates (against the original SARS-CoV-2 strain):

- **mRNA vaccines:** Clinical trail data for both Pfizer and Moderna demonstrated approx. 95 per cent **efficacy** in preventing lab-confirmed COVID-19 after two doses among adult participants. On May 5, 2021, Health Canada authorized the use of the Pfizer COVID-19 mRNA vaccine in adolescents 12 to 15 years of age, following the results of a phase 3 clinical trial in this population. Clinical trial evidence showed 100% efficacy in adolescents 12 to 15 years of age against confirmed COVID-19 illness. On November 19, 2021, a series of Pfizer (10 mcg) was approved for use in children aged 5 to 11 years. On March 17, 2022, Moderna (50 mcg) was approved for use in children aged 6 to 11 years. The estimated efficacy of the Pfizer vaccine against symptomatic COVID-19 from 7 days after dose 2 was 90.7% (95% CI: 67.7 to 98.3%; 3 cases identified in the vaccine group and 16 cases in the placebo group). Preliminary Moderna efficacy against symptomatic COVID-19 was 88% (95% CI: 70.0 to 95.8%) starting 14 days after dose 1.
- **Viral Vector Vaccine:** early clinical trial data for **AstraZeneca** demonstrated an average **vaccine efficacy** of 81.6% in participants aged 18 to ≤ 64 years with ≥ 12 week interval. On March 22, 2021, AstraZeneca released interim safety and efficacy analysis from the AZD1222 US Phase III trial[24], suggesting 76 to 79% efficacy at preventing symptomatic COVID-19 and 100% efficacy against severe or critical disease and hospitalization. Clinical trial data for Janssen has demonstrated it to be 67% efficacious against moderate to severe/critical symptomatic disease at least two weeks after receiving one dose.
- **Protein subunit vaccine:** clinical trial data available to date have shown that Novavax/Nuvaxovid™ is highly efficacious (~90%) in preventing confirmed

[23] https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/extended-dose-intervals-covid-19-vaccines-early-rollout-population-protection.html
[24] https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/astrazeneca-us-vaccine-trial-met-primary-endpoint.html

symptomatic COVID-19 disease in the short-term starting at one to two weeks after receiving the full two-dose series.

21. How long does protection after vaccination last (i.e., duration of protection)?

The duration of protection of mRNA or viral vector COVID-19 vaccine is currently unknown although current evidence suggests fully immunized people are protected for at least six months, if not longer.

Vaccine Storage, Handling and Transport

22. In some situations, I am able to draw more vaccine from a multi-dose vial than what is listed on the label. Is this okay?

Yes, provided doses administered and inventory is updated accordingly, and all administration-related infection, prevention and control guidelines are followed. The Province recommends that only additional doses from a multi-dose vial should be drawn if the full dose can be drawn from one vial (i.e., it is recommended that health care providers do not pool vaccine and draw from multiple vials to make additional doses).

23. What are some general storage and handling guidelines?

- Ensure empty vaccine vials are properly disposed of in sharps containers (i.e., do not discard empty vials in garbage cans or bins) and the box that doses are shipped in that comes from a manufacturer should be shredded (this is to avoid fraudulent claims).
- The storage requirements of all COVID-19 authorized vaccines in Canada is as follows:

	Primary storage requirements pre-puncture	**Additional Storage options pre-puncture**	**Usage limit post-puncture**
Pfizer ***MDV (6 doses)***	-90˚C to -60˚C	-25˚C to -15˚C for up to 2 weeks[a] 1 month at +2˚C to +8˚C 2 hours up to +25˚C	6 hours at +2˚C to +25˚C
Moderna ***MDV (10 doses)***	-25˚C to -15˚C	30 days at +2˚C to +8˚C **and/or** 24 hours at +8˚C to +25˚C	24 hours at +2˚C to +25˚C **OR** after max. number of vial punctures (20 punctures)

AstraZeneca ***MDV (10 doses)***	+2˚C to +8˚C	+2˚C to +8˚C	6 hours at room temperature (up to +30˚C) **OR** 48 hours at +2˚C to +8˚C[b]
Janssen ***MDV (5 doses)***	+2˚C to +8˚C	+2˚C to +8˚C	3 hours at room temperature (up to +25˚C) **OR** 6 hours at +2˚C to +8˚C
Novavax ***MDV (10 doses)***	+2˚C to +8˚C	+2˚C to +8˚C	2°C to 25°C for up to 6 hours after first needle puncture

24. What do I do if I experience a cold chain break?

Please refer to Manitoba Health Adverse Storage Condition (ASC) Form and Procedure (https://www.gov.mb.ca/health/publichealth/cdc/docs/ccf.pdf) for detailed information on what constitutes a cold chain break and protocols for reporting the excursion to MH and handling the affected product.

New clinical questions raised about general vaccine administration practices

25. Should clients/patients who have had SARS-CoV-2 infection get immunized, and when should they get immunized?

Clients previously infected with COVID-19 (and no longer symptomatic and/or isolating) can be immunized against COVID-19. NACI recommends that previously infected individuals may be offered a complete vaccine series. Individuals with previous infection who receive a single dose of vaccine generate a comparable immune response (and therefore may have similar levels of protection) to SARS-CoV-2 naïve individuals who receive 2 doses. However, comparative vaccine effectiveness data between these 2 groups are lacking and protection against most variants of concern in this scenario is unknown. Effectiveness studies comparing previously infected people who receive 1 or 2 doses of COVID-19 vaccines are not currently available.

The optimal time from infection to a dose of vaccine is largely unknown at this time as there is insufficient clinical or real-world data. Based on a review of the NACI guidance (released February 4, 2022), Manitoba public health officials advise waiting two to three months to immunize clients following a SARS-CoV-2 infection. Clients can be immunized earlier than two months but must at minimum be outside the period of isolation/communicability before immunization.

26. Can tuberculin skin testing (TST) or Interferon Gamma Release Assay (IGRA) be done at the same time as the COVID-19 vaccine is administered?

If tuberculin skin testing or an IGRA test is required it should be administered and read before immunization or delayed for at least 4 weeks after vaccination. This is because there is a theoretical risk that mRNA or viral vector vaccines may temporarily affect cell-mediated immunity, resulting in false-negative TST or IGRA test results. Vaccination with COVID-19 vaccines may take place at any time after all steps of tuberculin skin testing have been completed.

In cases where an opportunity to perform the TST or IGRA test might be missed, the testing should not be delayed since these are theoretical considerations. However, retesting (at least 4 weeks post immunization) of individuals with negative results for whom there is high suspicion of tuberculosis infection may be prudent.

27. Can other vaccines be given at the same time as, or before or after, the COVID-19 vaccine?

Effective October 1, 2021, Manitoba is adopting the NACI guidance on co-administration of COVID-19 vaccines with other vaccines for individuals aged ≥ 12 years.

NACI recommends that COVID-19 vaccines may be given concomitantly with, or at any time before or after, other vaccines.*

***including live, non-live, adjuvanted, or unadjuvanted vaccines.**

NACI has concluded that a precautionary approach to co-administration of the COVID-19 vaccine is now no longer necessary (i.e., waiting 14 or 28 days between vaccines depending on which vaccine was administered first), and recommends that vaccines may be administered concomitantly with (i.e. same day), or any time before, non-COVID-19 vaccines (including live, non-live, adjuvanted, or unadjuvanted). The concomitant administration of COVID-19 with non-COVID-19 vaccines will facilitate influenza vaccine programs in the fall and winter months and other routine vaccine programs that were disrupted due to the COVID-19 pandemic.

Informed consent should include a discussion of the benefits and risks given the limited data available on administration of COVID-19 vaccines with other vaccines. Studies to assess the safety and immunogenicity of concurrent administration of COVID-19 vaccines with other vaccines are ongoing.

It is currently not known if the reactogenicity of COVID-19 vaccines is increased with concomitant administration of other vaccines. While no specific safety concerns have been identified for various other vaccines with concomitant administration regimens, there is potential for increased reactogenicity with concomitant administration of COVID-19 vaccines with other vaccines, particularly those known to be more reactogenic, such as newer adjuvanted vaccines.

If more than one type of vaccine is administered at a single visit, they should be administered at different injection sites using separate injection equipment. NACI will continue to monitor the evidence and update recommendations as needed.

28. Are there specific training materials or requirements for mRNA vaccines?

Any provider that will be administering an mRNA vaccine MUST complete the necessary training materials as per the Vaccine Implementation Task Force. mRNA vaccines fall under a new vaccine technology platform that comes with unique storage and handling requirements. For participating physicians and pharmacists, these materials have been shared via email; if you require the materials to be resent, please email COVID@gov.mb.ca.

29. What do we know about breakthrough infections in fully immunized individuals?

Emerging evidence suggests that a complete two-dose vaccine series with an mRNA vaccine remains effective against severe health outcomes including hospitalization and death; a third dose may provide enhanced protection against mild-to-moderate disease as well as severe outcomes. This is true for both the Delta and Omicron variants. Two doses of an mRNA vaccine appear to offer little protection against symptomatic disease after a number of weeks have passed since vaccination. Three doses of an mRNA vaccine may provide enhanced protection against infection from Omicron, but two doses remain effective against severe health outcomes.

Appendix A: Advisability and timing of COVID-19 vaccination in cancer/serious blood disorder patients

The current strategy is to provide a first dose of vaccine as soon as possible. The second dose may be delayed for up to 4 months. The recommendations below reflect this strategy. These recommendations are subject to change, particularly if the strategy for second dose delivery changes again.

Specific recommendations for cancer patients is as follows:

- When a patient's age group becomes eligible, they should get vaccinated as soon as possible.
- The patients CCMB clinical team should be made aware that the patient will be getting vaccinated, when, and with what product.
- As a general principle, the first dose of vaccine should be administered at least 5-6 weeks before commencing anti-cancer drug treatment or radiation treatment. Given current eligibility guidelines, this is likely not feasible, and vaccination should take place when possible, using the following guidelines:

Type of Treatment	Suggested Timing of Vaccination
Cyclical chemotherapy	During active chemotherapy treatment, vaccine should be administered within a few days prior to next chemotherapy cycle (away from the neutrophil and platelet nadir), if possible. Vaccine should not be administered on the same day as chemotherapy If neutrophil count is not anticipated to recover, vaccination can occur at any time during the cycle, avoiding the day of chemotherapy administration.
Tyrosine kinase inhibitors Endocrine therapy (including PARP inhibitors) Continuous oral chemotherapy	No specific timing required
Immune checkpoint inhibitors Proteasome inhibitors Immunomodulatory agents	Avoid vaccinating on day of treatment
Monoclonal antibodies (including those targeting CD19 , CD 20 and CD 22)	No specific timing; avoid vaccinating on day of treatment.

Corticosteroids[25]	If administered cyclically, aim to vaccinate when not receiving the steroids. If continuous, no specific timing
Auto and allo HSCT and CAR-T	Delay vaccination until > 3 months post HSCT
IVIG	No specific timing
Patients due to commence radiotherapy	If delaying radiotherapy will not compromise outcomes, consider delaying radiotherapy until immunity is likely to have occurred post immunization. If outcomes could be compromised by delay, immunization should proceed, preferably as early in the course of radiotherapy as possible.

Important points:

1. Although many cancer treatments may impair vaccine effectiveness, there is currently no evidence that vaccines will harm patients on such treatments. As such, the default should be to proceed with vaccination if there is no other contraindication.
2. Vaccination should generally be avoided on the day a cyclical therapy is administered to minimize the chance of ascribing a treatment-related adverse event to the wrong agent.

[25] Low-to-moderate dose of prednisone (equivalent of less than 2 mg/kg/day or less than 20 mg/day if weight > 10 kg) is not a contraindication/precaution to vaccination.

Appendix B: AstraZeneca Eligibility Criteria

Appendix B is included here for historical purposes only.

The following is a list of health conditions that were used to determine priority for eligible persons (as per the authorized age category) for the AstraZeneca vaccine in Manitoba's first shipments of AstraZeneca vaccine. ***(NOTE: these priority health conditions have since been modified under the revised eligibility criteria, effective April 30, 2021).***

Priority 1:[26]

- Individuals with the following chronic health conditions:
    - end stage renal disease undergoing hemodialysis **OR** peritoneal dialysis
    - cirrhosis due to any cause **OR** portal hypertension
    - heart failure (class III/IV), ventricular assist device **OR** adult congenital heart disease stage C and D
    - severe COPD, pulmonary hypertension, pulmonary fibrosis, interstitial lung disease **OR** cystic fibrosis
    - history of cerebral vascular accident with residual deficits
    - malignant hematologic disorders including leukemia and lymphoma **OR** clonal blood disorder
    - malignant neoplasms (solid tissue) who will receive or are currently receiving immunosuppressive therapy including chemotherapy
    - severe obesity (BMI ≥ 40)
    - receiving one or more of the following immunosuppressive therapies: B cell therapies (e.g., rituximab, ocrelizumab), cyclophosphamide, alemtuzumab, calcineurin inhibitors, chronic dose prednisone >=20mg/day, mycophenolate, sulfasalazine and JAK inhibitors (e.g., tofacitinib)[27]
    - solid organ or hematopoietic stem cell transplant (candidate or recipient)
    - trisomy 21 (Down's syndrome)
    - asplenia or hyposplenism (including sickle cell disease)
- Individuals receiving home care ≥ 4 times/week **OR** receive 24/7 support from Community Living Disability Services.

Priority 2:

- Individuals with the following chronic health conditions:
    - Chronic cardiovascular disease including heart failure (class I/II), coronary artery disease, malignant tachyarrythmia **OR** cardiomyopathies
    - chronic liver disease
    - chronic neurologic **OR** neurodevelopmental conditions including cerebral palsy, Parkinson's disease, multiple sclerosis, ALS **OR** dementia (including Alzheimer's disease)

[26] Pregnant individuals (18 to ≤ 64 years of age) with one of: aged ≥ 35 years, BMI ≥ 30, pre-existing diabetes, pre-existing hypertensions, cardiac or pulmonary disease, were originally eligible under priority 1 but were removed on March 29, 2021 due to rare incidents of VITT following vaccination in those aged < 55 years.
[27] The attending physician or specialist may recommend a different time interval based on client/patient assessment.

    - chronic pulmonary disease including COPD **OR** severe and/or uncontrolled asthma
    - chronic renal disease
    - HIV (CD4 cell count ≥ 200 x 106/L and CD4 percentage ≥ 15%)
    - severe systemic autoimmune disorders (e.g., systemic lupus erythematosus, scleroderma, myocarditis, rheumatoid arthritis)
    - type 1 or 2 diabetes mellitus (poorly controlled and/or with complications)
    - active tuberculosis (current or previous) **OR** current latent tuberculosis (LTBI)
    - receiving immunosuppressing therapy*
- Individuals receiving homecare ≤ 3 times/week **OR** any level of Community Living Disability Services supports (or as per family physician determination of equivalent levels of family support).
- Household contacts of individuals with Priority 1 chronic health conditions **OR** designated family caregiver(s) for personal care home residents.

** See the Canadian Immunization Guide: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25*

Appendix C: Precautions of vaccinating allergic persons aged ≥ 5 years.

The below information is subject to change; refer to the Public Health Agency of Canada's (PHAC's) online Quick Reference Guide on use of COVID-19 Vaccines for the most up-to-date information/guidance: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/quick-reference-guide-covid-19-vaccines.html.

Severe Immediate Allergic Reaction (e.g., anaphylaxis) to an authorized COVID-19 vaccine or a vaccine excipient

In individuals with a history of a severe, immediate (≤ 4h following vaccination) allergic reaction (e.g., anaphylaxis) after previous administration of an mRNA COVID-19 vaccine, re-vaccination (i.e. administration of a subsequent dose in the series when indicated) may be offered with the same vaccine or the same mRNA platform if a risk assessment deems that the benefits outweigh the potential risks for the individual and if informed consent is provided. The risk of a severe immediate allergic reaction after re-immunization appears to be low and no long-term morbidity has been associated with re-vaccination.

- Consultation with an allergist or other appropriate physician should be sought prior to re-vaccination.
- If re-vaccinated, vaccine administration should be done in a controlled setting with expertise and equipment to manage anaphylaxis. Individuals should be observed for **at least** 30 minutes after re-vaccination. For example, a longer period of observation is warranted for individuals exhibiting any symptom suggestive of an evolving AEFI at the end of the 30 minute observation period.

For those with a previous history of allergy to an mRNA vaccine, re-vaccination with an mRNA vaccine is preferred over a viral vector vaccine due to the better effectiveness and immunogenicity of mRNA vaccines and the possible adverse effects specifically associated with viral vector vaccines (e.g., Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), capillary leak syndrome and Guillain-Barré Syndrome).

In individuals with a history of a severe, immediate (≤4h following vaccination) allergic reaction (e.g., anaphylaxis) after previous administration of a viral vector COVID-19 vaccine, re-vaccination may be offered with an mRNA platform if a risk assessment deems that the benefits outweigh the potential risks for the individual and if informed consent is provided. If re-vaccinated, individuals should be observed for at least 30 minutes after re-vaccination.

In individuals with a confirmed severe, immediate (≤4h following exposure) allergy (e.g., anaphylaxis) to a component of a specific COVID-19 vaccine or its container (e.g., PEG), consultation with an allergist is recommended before receiving the specific COVID-19 vaccine. Individuals who are allergic to tromethamine (found in the Moderna product) should be offered the Pfizer vaccine which does not contain this excipient. Individuals who are allergic to polysorbates (found in viral vector vaccines), should be offered an mRNA vaccine.

Mild to moderate immediate allergic reactions

Re-vaccination may be offered with the same vaccine or the same (mRNA) platform in individuals with mild to moderate immediate allergic reactions (defined as limited in the scope of symptoms and involvement of organ systems or even localized to the site of administration)

after a previous dose of authorized COVID-19 vaccines or any of its components. Offering an mRNA vaccine is preferred over a viral vector vaccine (see above). Assessment by a physician or nurse with expertise in immunization may be warranted prior to re-immunization. Most instances of anaphylaxis to a vaccine begin within 30 minutes after administration of the vaccine. Therefore, if re-vaccination is chosen, an extended period of observation post-vaccination of at least 30 minutes should be provided for the aforementioned individuals.

Other allergies or concerns relating to allergies

Individuals with proven severe allergic reaction (e.g., anaphylaxis) to injectable therapy not related to a component of authorized COVID-19 vaccines (e.g., intramuscular, intravenous, or subcutaneous vaccines or therapies) may be routinely vaccinated and do not need to be assessed. Most instances of anaphylaxis to a vaccine begin within 30 minutes after administration of the vaccine. Therefore, an extended period of observation post-vaccination of 30 minutes should be provided for the aforementioned individuals.

Individuals with suspected but unproven allergy to a vaccine component (e.g., PEG) may be routinely vaccinated and do not need a specific assessment regarding this suspected allergy. Most instances of anaphylaxis to a vaccine begin within 30 minutes after administration of the vaccine. Therefore, an extended period of observation post-vaccination of 30 minutes should be provided for the aforementioned individuals.

Individuals with a history of allergy not related to a component of authorized COVID-19 vaccines or other injectable therapy (e.g., foods, oral drugs, insect venom or environmental allergens) can receive COVID-19 vaccines without any special precautions. Individuals should be observed for a minimum of 15 minutes following vaccination.

Appendix D: Managing Inadvertent Vaccine Errors

***Below are two guidance tables on the Management of Inadvertent Vaccine Errors, adapted from the Public Health Agency of Canada (PHAC), one for adolescents/adults, and one table for the pediatric population*. Updated January 18, 2022.**

The below information is subject to change; refer to PHAC's online Quick Reference Guide on use of COVID-19 Vaccines for the most up-to-date information/guidance: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/quick-reference-guide-covid-19-vaccines.html.

Overview

This document is intended to assist healthcare providers by providing an approach to managing COVID-19 vaccines that are administered in a manner that differs from the recommendations of the manufacturer and/or the National Advisory Committee on Immunization (NACI) (referred to as vaccine administration errors). This document builds on guidance developed by CDC's Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States and the guidance developed by Public Health Ontario, with input from the Canadian Immunization Committee and the National Advisory Committee on Immunization.

There is limited evidence to guide the management of these situations. This document provides guidance only. Clinical judgement in particular situations may also result in different management decisions than outlined below.

Note that this document is to be used only to manage errors that have already occurred. The product monograph and recommendations from the National Advisory Committee on Immunization should be followed when administering COVID-19 vaccines. Refer to Appendix G to guide the decision-making around recommended and minimum intervals.

Steps to be taken after an error is recognized

Following the identification of an inadvertent vaccine administration error, healthcare providers should:

- Inform the recipient of the vaccine administration error as soon as possible after it is identified. The recipient should be informed of any implications/recommendations for future doses, and possibility for local or systemic reactions and impact on the effectiveness of the vaccine (if applicable and as known).
- Report all errors or near miss incidents in accordance with the institutional medication error or professional body's reporting process. Errors can also be reported to the Canadian Medication Incident Reporting and Prevention System (CMIRPS).
- If an inadvertent vaccine administration error results in an adverse event following immunization (AEFI), complete the jurisdiction's AEFI form and submit it to the local public health authority.
- Determine how the vaccine administration error occurred and implement strategies to prevent it from happening again.
- Serologic testing to assess vaccine-induced immunity following COVID-19 vaccine errors to guide management decisions is generally not recommended. Providers are

encouraged to contact their local public health authority for advice if considering using serology to investigate an error.

- Additional resources on vaccine administration practices can be found in the Canadian Immunization Guide.

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
Site/route	• Incorrect site (that is, site other than the deltoid muscle [preferred site] or anterolateral thigh [alternate site])	• Consider this a valid dose • Inform the parent/guardian and child of the error or deviation and the potential for local and systemic adverse events and that the dose is acceptable
	• Incorrect route (for example, subcutaneous)	• Consider this a valid dose • Inform the parent/guardian and child of the error or deviation and potential for local and systemic adverse events and that the dose is acceptable
Age	• Dose or product administered to a client who is younger than the minimum age authorized by Health Canada to receive the product (this includes children 5 to 11 years of age who received 10 micrograms/0.1mL or more of the adult formulation)	• Consider this a valid dose • Give the second dose with the recommended age-appropriate dosage, product and interval (NACI recommends an interval of at least 8 weeks) once the child reaches the age that they can receive an authorized mRNA vaccine • Inform the parent/guardian and child of the potential for local and systemic adverse events[1]
COVID-19 vaccine administered within 14 days before or after a non-COVID-19 vaccine	• COVID-19 vaccine dose administered on the same day, or up to 14 days before or after another vaccine (a non-COVID-19 vaccine)	• Both the COVID-19 and the other vaccine are valid.

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**

Intervals	• Two doses of a COVID-19 vaccine given too close together in time (including on the same day)	• Inform the parent/guardian and child of the potential for local and systemic adverse events
		• If the second dose was administered 19 or more days after the first for Pfizer, consider both doses valid and the series complete
		• If the second dose was administered less than 19 days after the first for Pfizer, consider the second dose invalid.
		  ○ For invalid doses, repeat with at least an 8 week interval from the date of the invalid dose
		  ○ If a significant local or systemic reaction from the invalid dose occurs, consult with a physician or nurse with expertise in immunization before repeating. When repeating the dose, inform the parent/guardian and child of the potential for local and systemic adverse events

	• Second dose administered later than the suggested optimal interval of at least 8 weeks	• There is no interval that is too long and all doses would be considered valid • No further doses are required
Dosage (see Diluent section below for specific information on	• Higher-than-authorized dose volume administered	• Consider this dose valid • If that was the first dose, and the child needs a second dose, use the age-appropriate dose given at least 8 weeks later. • Inform the parent/guardian and child of the potential for local and

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
Pfizer-BioNTech and the diluent)		systemic adverse events Table 4 Footnote

	• Lower-than-authorized dose volume administered (for example, leaked out, equipment failure, client pulled away)	• If less than a full dose may have been administered, consider it invalid.
		• If the error is discovered on the same clinic day, administer a full repeat dose immediately in another appropriate site.
		• If error is discovered after the clinic day and:
		  ○ The invalid dose was a first dose, administer a full repeat dose when the error is discovered.
		  ○ The invalid dose was not the first dose, wait 8 weeks to offer the repeat dose (unless the amount administered is likely to be very small, in which case repeat immediately).
		• Inform the parent/guardian and child of the potential for local and systemic adverse events Table 4 Footnote 1

	• More or less than the authorized number of doses obtained from the vial	• As long as the correct volume was drawn up per dose (and the correct amount of diluent was used), the doses are valid.
Storage and handling	• Dose administered after improper storage and handling (for example, temperature excursion)	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting the dose should be considered invalid and if that seems appropriate based on clinical judgment, a repeat

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose. • Inform the parent/guardian and child of the potential for local and systemic adverse events. Table 4 Footnote 1
	• Dose administered past the expiration/beyond use date	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting the dose should be considered invalid and if that seems appropriate based on clinical judgment, a repeat dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose. • Inform the parent/guardian and child of the potential for local and systemic adverse events Table 4 Footnote 1
Diluent (Pfizer only)	• Incorrect diluent type	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting that the dose be considered invalid and if that seems appropriate based on clinical judgment, a repeat dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose. • Inform the parent/guardian and child of the potential for local and systemic adverse events. Table 4 Footnote 1

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
	• ONLY diluent administered	• Inform the parent/guardian and child that no vaccine was administered • Administer the authorized (appropriately diluted) dose as soon as possible in another appropriate site

	• Too much diluent administered (more than 1.3ml of diluent was added to the vial, based on 0.2ml dose administered)	• If more than 1.3 ml of diluent was added to the vial, consider this an invalid dose. If the error is discovered on the same clinic day, administer a full repeat dose immediately in another appropriate site.
		• If error is discovered after the clinic day and:
		  ○ The invalid dose was a first dose, administer a full repeat dose when the error is discovered.
		  ○ The invalid dose was not the first dose, wait 8 weeks to offer the repeat dose.
		• Inform the parent/guardian and child of the potential for local and systemic adverse events Table 4 Footnote 1

	• No diluent or less than the recommended diluent, resulting in higher than the authorized dose (based on 0.2 ml dose administered)	• Consider this dose valid • Inform the parent/guardian and child of the potential for local and systemic adverse events Table 4 Footnote 1

Table 4 Footnote 1

This footnote applies to children who have had an invalid dose that has been repeated with a valid dose or a dose that was too high:

If the child requires a second dose to complete the initial series, the suggested optimal interval to receive the second dose in the initial series is at least 8 weeks from the valid dose. Advise the parent/guardian and child about the potential for local and systemic

Types of administration errors and recommended actions for each error for the pediatric population aged five to ≤ 11 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
	adverse events following the second dose. If a child who requires a second dose has developed a significant local or systemic reaction from an earlier dose, base the decision to administer the second dose on a case-by-case basis in consultation with an allergist/immunologist or other appropriate physician.	

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
Site/route	• Incorrect site (that is, site other than the deltoid muscle [preferred site] or anterolateral thigh [alternate site])	• Consider this a valid dose • Inform the client of the error or deviation and the potential for local and systemic adverse events and that the dose is acceptable
	• Incorrect route (for example, subcutaneous)	• Consider this a valid dose • Inform the client of the error or deviation and potential for local and systemic adverse events and that the dose is acceptable
Age	• If a 10 mcg dose of Pfizer is used for a client 12 years of age and older	• Please see recommendation for lower-than-authorized dose
	• Dose or product administered to a client who is younger than the minimum age authorized by Health Canada to receive the product	• Inform the client of the potential for local and systemic adverse events[1] Pfizer and Moderna vaccines: • Consider this a valid dose • Give the subsequent dose with the recommended age-appropriate dosage, product

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		and interval once the client reaches the age that they can receive an authorized mRNA vaccine. • NACI recommends an interval of at least 8 weeks between the first and second dose and that Pfizer is the preferred product for the primary series for those 12 to 29 years of age and may be the preferred product for the booster dose for those 18 to 29 years of age. AstraZeneca vaccine: • Consider this a valid dose • Preferentially give an mRNA vaccine for the second dose • Preferentially give an mRNA vaccine for the second dose with the recommended age-appropriate dosage, mRNA product and interval once the client reaches the age that they can receive an authorized mRNA vaccine. • NACI recommends an interval of at least 8 weeks between the first and second dose and that Pfizer is the preferred product for the primary series for those 12 to 29 years of age and may be the preferred product for the booster dose for those 18 to 29 years of age. Janssen vaccine • Consider this a valid dose • When the client has reached the age that they are eligible to

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		receive an mRNA vaccine, provide an age-appropriate mRNA dose 6 months after the Janssen dose. • NACI recommends Pfizer vaccine for those 12 to 29 years of age.
Intervals	• First two doses of a COVID-19 vaccine given too close together in time (including on the same day)	• Inform the client of the potential for local and systemic adverse events • If the second dose was administered 19 or more days after the first for Pfizer or 21 or more days after the first for Moderna or AstraZeneca, consider both doses valid and the series complete. • If the second dose was administered less than 19 days after the first for Pfizer or less than 21 days after the first for Moderna or AstraZeneca, consider the second dose invalid. ○ For invalid doses, repeat with at least a 21 or 28 day interval, with a recommended 8 week interval, from the date of the invalid dose.If a significant local or systemic reaction from the invalid dose occurs, consult with a physician or nurse with expertise in immunization before repeating. When repeating the dose, inform the client of the potential for local and

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		systemic adverse events.
	• Second dose administered later than the NACI-recommended optimal interval of 8 weeks	• There is no interval that is too long and all doses would be considered valid
	• Third dose in the primary series administered earlier than the 28 day minimum interval for moderately to severely immunocompromised individuals	• Invalidate any dose given ≤ 27 days. • Offer a booster dose at least 6 months from the date of the invalid dose.
	• Booster dose given at less than a 6 month interval from the last dose in the primary series	• As long as at least 8 weeks has passed since the last dose in the primary series, consider the booster dose valid. • If less than 8 weeks has passed between the last dose in the primary series and the booster dose, consider the booster dose invalid and repeat the booster dose at least 6 months from the invalid dose
Mixed COVID-19 vaccines for first, second or additional/booster doses	• A different COVID-19 vaccine used for the first, second or additional/booster doses[2]	• Consider all doses valid regardless of the type of vaccine • See footnote for those who received only non-Health Canada authorized vaccines. [2]
Dosage (see Diluent section below for specific information on Pfizer-	• Higher-than-authorized dose volume administered	• Consider this dose valid • Inform the client of the potential for local and systemic adverse events[1]

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**

BioNTech and the diluent)	• Lower-than-authorized dose volume administered (for example, leaked out, equipment failure, client pulled away, or pediatric dose administered to an adult 18 years of age or older)	• If less than a full dose may have been administered, consider it invalid (see notes below for exceptions).
		• If the error is discovered on the same clinic day, administer a full repeat dose immediately in another appropriate site.
		• If error is discovered **after the clinic day** and:
		  • The invalid dose was a first dose, administer a full repeat dose when the error is discovered.
		  • The invalid dose was not the first dose, wait 8 weeks to offer the repeat dose (unless the amount administered is likely to be very small, in which case repeat immediately).
		• Inform the client of the potential for local and systemic adverse events[1]
		• **Note**: if Moderna is being used as a booster or additional dose and the full 100 microgram dose is recommended by NACI (e.g., for specific populations) and only 50 micrograms was inadvertently administered, consider the dose valid and **do not repeat.**
		• **Note:** If a child/adolescent 12 to 17 years of age inadvertently received a Pfizer (10 mcg) dose for dose 1, consider this dose **valid** and **do not repeat**. The second dose should be a Pfizer (30 mcg) dose 8 weeks later
		• If a child/adolescent 12 to 17 years of age inadvertently

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		received a Pfizer (10 mcg) dose for dose 2, consider this dose **invalid** and **repeat** with correct dosing for age Pfizer (30 mcg) with at least an 8 week interval from the date of the invalid dose • If a child/adolescent 12 to 17 years of age inadvertently received a Moderna (50 mcg) dose (for dose 1 or 2), consider the dose(s) **valid** and **do not repeat** (even if both doses were 50 mcg). If this was their first dose, the second should be Pfizer (30 mcg) for individuals 12 to 29 years of age or should be Moderna (100 mcg) for individuals ≥ 30 year of age.
	• More or less than the authorized number of doses obtained from the vial	• As long as the correct volume was drawn up per dose (and the correct amount of diluent was used, if applicable), the doses are valid
Storage and handling	• Dose administered after improper storage and handling (for example, temperature excursion)	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting the dose should be considered invalid and if that seems appropriate based on clinical judgment, a repeat dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose.

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		• Inform the client of the potential for local and systemic adverse events[1]
	• Dose administered past the expiration/beyond use date	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting the dose should be considered invalid and if that seems appropriate based on clinical judgment, a repeat dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose. • Inform the client of the potential for local and systemic adverse events[1]
Diluent (Pfizer-BioNTech only)	• Incorrect diluent type	• Contact the manufacturer for guidance. Your local public health authority can also be consulted for advice. • If the manufacturer provides information suggesting that the dose be considered invalid and if that seems appropriate based on clinical judgment, a repeat dose may be given. Consider delaying the repeat dose until 8 weeks from the invalid dose. • Inform the client of the potential for local and systemic adverse events[1]
	• ONLY diluent administered (that is, 0.9% sodium chloride)	• Inform the client that no vaccine was administered • Administer the authorized (appropriately diluted) dose as

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
		soon as possible in another appropriate site.

	• Too much diluent administered (more than 2.0 ml of diluent added to the vial, based on 0.3 ml dose administered)	• If more than 2.0 ml of diluent was added to the vial, consider this an invalid dose.
		• If the error is discovered on the same clinic day, administer a full repeat dose immediately in another appropriate site.
		• If error is discovered after the clinic day and:
		  ○ The invalid dose was a first dose, administer a full repeat dose when the error is discovered.
		  ○ The invalid dose was not the first dose, wait 8 weeks to offer the repeat dose.
		• Inform the client of the potential for local and systemic adverse events[1]

	• No diluent or less than the recommended diluent, resulting in higher than the authorized dose (based on 0.3 ml dose administered)	• Consider this dose valid • Inform the client of the potential for local and systemic adverse events[1]

Table 4 Footnote 1

This footnote applies to people who have had an invalid dose that has been repeated with a valid dose or a dose that was too high:

If the client requires a subsequent dose in the initial series (e.g., second dose or, for those who are moderate to severely immunocompromised, the third dose), the suggested optimal interval is at least 8 weeks from the last valid dose. Advise the client about the potential for local and systemic adverse events following the subsequent dose.

Type of administration errors or deviations and recommended actions for adolescents/adults aged ≥ 12 years		
Type	**Administration error or deviation**	**Interim guidance on how to consider the dose and recommended action**
	If the client requires a booster dose, wait 6 months from the last valid dose in the initial series. If the client has developed a significant local or systemic reaction from an earlier dose, base your decision to administer future doses on a case-by-case basis in consultation with an allergist/immunologist or other appropriate physician.	
Table 4 Footnote 2		
	Note that if no Health Canada authorized vaccine has been received and less than 3 doses of COVID-19 vaccines have been received, a dose of an mRNA vaccine is recommended for those planning to live, work or study in Canada. See COVID-19: Recommendations for those vaccinated with vaccines not authorized by Health Canada for those staying in Canada to live, work or study.	

References

Centres for Disease Control and Prevention (CDC). Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States. Available from: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

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Public Health England. COVID-19 vaccination programme Information for healthcare practitioners Republished 20 May 2021 Version 3.7. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/988091/COVID-19_vaccination_programme_guidance_for_healthcare_workers_20_May_2021_v3.7.pdf

Appendix E: Manitoba's Second Dose Plan

Appendix E is included here for historical purposes only.

Manitoba's plan for launching second doses of COVID-19 vaccine

Based on emerging evidence of the protection provided by the first dose of a two dose series for COVID-19 vaccines currently authorized and available in Canada, the National Advisory Committee on Immunization (NACI) recommended that:

- Jurisdictions maximize the number of individuals benefiting from the first dose of vaccine by extending the second dose of COVID-19 vaccine up to four months after the first.
- Second doses be offered as soon as possible after all eligible populations have been offered first doses, with priority given to those at highest risk of severe illness and death from COVID-19 disease after or concurrent with, first doses for all remaining eligible populations.

Eligibility Criteria of Second Doses

Some clients/patients may have a health condition that affects their ability to mount an acceptable immune response. Effective May 21, 2021, people with one or more of the conditions (listed below) are the first group prioritized to receive the second dose of COVID-19 mRNA vaccine 28 days from the first dose:

- end stage renal disease undergoing hemodialysis or peritoneal dialysis
- cirrhosis due to any cause **OR** portal hypertension
- heart failure (class III or IV)
- malignant hematologic disorders including leukemia and lymphoma or clonal blood disorders, or malignant neoplasms (solid tumors) who will receive or are currently receiving immunosuppressive therapy including chemotherapy or immunomodulatory therapy
- receiving one or more of the following immunosuppressive therapy: B cell therapies (e.g., rituximab, ocrelizumab), cyclophosphamide, alemtuzumab, calcineurin inhibitors (cyclosporine, tacrolimus), chronic dose prednisone >=20mg/day, mycophenolate, and JAK inhibitors (e.g., tofacitinib)
- solid organ transplant (candidate or recipient)
- hematopoietic stem cell transplant (recipient)
- trisomy 21 (Down's syndrome)
- human immunodeficiency virus (HIV)
- receiving home care ≥ 4 times/week **OR** receiving 24/7 Community Living Disability Services supports (or as per family physician determination of equivalent levels of family support).

Effective May 24, all Indigenous people born on or before December 31, 2009 are eligible to schedule their second dose appointments (provided they meet the minimum time interval between doses). It is anticipated that the remainder of second dose eligibility will follow the order in which first dose vaccines were given. For up-to-date information on second dose eligibility for the remainder of the population, visit: https://www.gov.mb.ca/covid19/vaccine/eligibility-criteria.html#second-dose.

Appendix F: Definition of Immunocompromised

The following definition of moderately to severely immunocompromised includes individuals aged ≥ five years with one or more of the following conditions:

- Active treatment for solid tumor or hematologic malignancies, OR
- Receipt of solid organ transplant and taking immunosuppressive therapy, OR
- Receipt of CAR-T therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), OR
- Moderate to severe primary immunodeficiency, OR
- Stage 3 or advanced untreated human immunodeficiency (HIV) infection and those with acquired immunodeficiency syndrome, OR
- Anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (defined as the equivalent to greater than or equal to 20 mg of prednisone for 4 or more weeks), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) blockers and other biologic agents that are significantly immunosuppressive). For clarity, this includes the following drugs: active treatment with immunosuppressive medications such as cancer chemotherapeutic agents (chemotherapy, immunotherapy or targeted therapies), TNF blockers, certain biologic agents (e.g., rituximab), mycophenolate, tacrolimus, Jak inhibitors, methotrexate, fingolimod, azathioprine and leflunomide.
- Individuals in end stage renal disease undergoing hemodialysis or peritoneal dialysis, those on the transplant list and people with a ventricular assist device have been shown to be at increased risk of experiencing severe outcomes from COVID-19. There is limited data available on the safety and effectiveness of providing additional doses to these relatively small patient populations. Additional dose recommendations for these patient populations should be made on a case-by-case basis, taking into account the patient's risks of exposure, level of immunocompromise, risk of experiencing severe outcomes as well as the lack of evidence.

Appendix G: Summary Table of Recommended and Minimum Intervals

Appendix G is included here for historical purposes only and is no longer being updated.

This summary table is to be used by clinicians to guide decision-making around recommended and minimum intervals for the primary series for adolescents/adults. Last updated: Nov. 4, 2021.

Dose 1	Dose 2*	Manitoba Health's Recommended Interval	Recommended Minimum Interval for Optimal Immune Response	Absolute Minimum Interval - Not Recommended	PHIMS Forecaster**
		MB Health's recommended interval between dose 1 and dose 2 is 28 days for all COVID-19 vaccine combinations. This allows for consistent messaging to the public. If all clients book at 28 days or later, and there is an inadvertent vaccine product change at a clinic, it will not impede the ability to immunize clients. If clients present to clinic 28 days after 1st dose of vaccine, immunize.	Recommended minimum interval for optimal immune response which is supported by data from clinical trials. If clients present to clinic at this time, immunize.	Absolute minimum interval for immunization to be counted as a second dose but is not a recommended practice. **Recommended Minimum Interval for Optimal Immune Response is preferred.** *These doses are not automatically validated within PHIMS and are considered errors. These doses require manual override in PHIMS to count as a valid second dose.* Vaccine administered earlier than this interval would not be considered a valid second dose.	Parameters that have been set in the PHIMS Forecaster.
Pfizer	Pfizer	8 weeks	21 days	19 days	Eligible 19 days Due at 21 days Overdue 16 weeks
Pfizer	Moderna	8 weeks	28 days	19 days	PHIMS will forecast Pfizer
Moderna	Moderna	8 weeks	28 days	21 days	Eligible 21 days Due at 28 days Overdue 16 weeks
Moderna	Pfizer	8 weeks	28 days	21 days	PHIMS will forecast Moderna
AstraZeneca	Pfizer	At least 8 weeks	8-12 weeks	21 days	Eligible 28 days Due at 8 weeks Overdue 16 weeks
AstraZeneca	Moderna	At least 8 weeks	8-12 weeks	21 days	PHIMS will forecast Pfizer
AstraZeneca	AstraZeneca	At least 8 weeks	12 weeks	21 days	PHIMS will forecast Pfizer

Note: When calculating vaccine interval, dose 1 is administered on day 0 of the schedule.

***PHIMS will only forecast one product for dose 2. However, in situations where a different product was administered for second dose, the second dose will still be validated provided the minimum interval is met. As of November 1, 2021 the PHIMS forecaster is currently under review given MB's recent adoption of the NACI recommendation of eight weeks of the recommended interval between doses.*