

An Advisory Committee Statement (ACS)

National Advisory Committee on Immunization (NACI)

NACI Rapid Response: Updated guidance on
the use of Imvamune[®] for the prevention of
mpox

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH



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prévention de la mpox

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PREAMBLE

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

TABLE OF CONTENTS

PREAMBLE	3
I. BACKGROUND.....	5
II. METHODS	6
III. EVIDENCE SUMMARY	7
III.1 BURDEN OF DISEASE	7
<i>Mpox epidemiology by clade and subclade.....</i>	7
<i>Summary of recent Canadian mpox epidemiology.....</i>	8
III.2 VACCINE CHARACTERISTICS	8
III.3 EFFECTIVENESS, SAFETY AND IMMUNOGENICITY OF IMVAMUNE® PRE-EXPOSURE VACCINATION AGAINST MPOX.....	8
<i>Effectiveness against mpox infection and moderate/severe mpox infections (including hospitalization)</i>	9
<i>Safety.....</i>	10
<i>Immunogenicity.....</i>	10
III.4 ETHICS, EQUITY, FEASIBILITY AND ACCEPTABILITY	11
III.5 ECONOMICS.....	11
IV. RECOMMENDATIONS.....	12
V. RESEARCH PRIORITIES	16
LIST OF ABBREVIATIONS.....	18
ACKNOWLEDGEMENTS	20
APPENDIX A: VACCINE EFFECTIVENESS STUDIES.....	21
REFERENCES.....	23

I. BACKGROUND

Mpox is caused by the monkeypox virus (MPXV), a mammalian *Orthopoxvirus* related to the vaccinia, cowpox, as well as variola (smallpox) viruses. The virus is transmitted either by zoonotic (animal-to-human) contact or by person-to-person contact with bodily fluids, lesions on the skin or internal mucosal surfaces (e.g., mouth, throat, anogenital region), or by contact with contaminated objects.¹ MPXV is subclassified into two distinct clades and further classified into subclades (clades Ia and Ib, and clades IIa and IIb), with clade IIb causing the 2022 global outbreak. Mpox is typically a self-limiting disease, with symptoms including rash, fever, body aches, back pain, and swollen lymph nodes. Clinical presentation during the 2022 global mpox outbreak often included oral and/or anogenital lesions, as well as lesions on the face, mouth, throat, palms of hands, and soles of feet. Potential complications of mpox include skin infections, pneumonia, sepsis, pain or difficulty swallowing, vision loss, encephalitis, myocarditis, and rarely, death.² Certain groups (i.e., young children,³ pregnant women and pregnant individuals,⁴ and immunocompromised individuals⁵) are also at higher risk of severe disease with mpox.

The World Health Organization (WHO) declared mpox a Public Health Emergency of International Concern (PHEIC) in August of 2024,⁹ following a rapid rise in cases of a novel subclade of mpox (clade Ib) in the Democratic Republic of the Congo (DRC). Travel-related cases of mpox clade Ib have since been reported in several countries outside of Africa, including Canada. The Public Health Agency of Canada (PHAC) has also issued advice, advising vaccination for Canadian healthcare professionals in advance of deployment to support the mpox clade I outbreak in countries where there is a level 2 travel health notice for mpox.¹⁰ The WHO has also designated healthcare workers at risk of being exposed to mpox, as well as mpox outbreak response team members, as priority groups recommended for vaccination.¹¹

As of March 28, 2025, ten Canadian provinces and territories have publicly reported 2,042 cases of mpox,¹² with the majority of cases occurring in Ontario (50.9%), Quebec (28.8%) and British Columbia (16.9%). Only one mpox clade I case (clade Ib) has been reported in Canada to date. Over 95% of confirmed cases with available information self-identified as gay, bisexual, and other men who have sex with men (gbMSM), and approximately 20% as living with human immunodeficiency virus (HIV).

Imvamune[®] (also called MVA-BN, Jynneos[®], Imvanex[®]) is a non-replicating, third-generation smallpox and mpox vaccine manufactured by Bavarian Nordic. Imvamune[®] was initially authorized for use in Canada on November 21, 2013, as an Extraordinary Use New Drug Submission (EUNDS) for emergency use by the government for active immunization against smallpox infection and disease in persons 18 years of age and older who have a contraindication to first- or second-generation live-replicating smallpox vaccines. Imvamune[®] was subsequently approved under a supplement to the EUNDS on November 5, 2020, for active immunization against smallpox, mpox, and related *Orthopoxvirus* infections and diseases in adults 18 years of age and older determined to be at high risk for exposure. Imvamune[®] is held within Canada's National Emergency Strategic Stockpile for the purposes of national security due to its potential efficacy against variola, the virus that causes smallpox. Imvamune[®] vaccine supply is available to provinces and territories for mpox immunization programs, upon request, by contacting PHAC's Centre for Emergency Response, Health Portfolio Operations Centre. Due to the regulatory status of this vaccine in Canada, and because the main supply is held federally, Imvamune[®] cannot be purchased by individuals on the private market and can only be accessed through provincial, territorial, or federal programs for recommended populations.

NACI first issued guidance on the use of Imvamune® (Modified vaccinia Ankara-Bavarian Nordic [MVA-BN]) on June 10, 2022, in the context of a rapidly evolving mpox outbreak among countries previously non-endemic for mpox.⁶ Initial interim NACI recommendations were centered around the use of Imvamune® for post-exposure vaccination against mpox. NACI subsequently updated interim guidance on the use of Imvamune® on September 23, 2022, recommending pre-exposure vaccination against mpox in risk groups,⁷ and on May 24, 2024, NACI provided updated recommendations on the use of Imvamune® for the prevention of mpox.⁸

OBJECTIVE

In the context of the evolving global mpox outbreak and emerging evidence on vaccine effectiveness, this rapid response was undertaken to provide additional guidance on the use of the Imvamune® vaccine for the prevention of mpox.

DEFINITIONS

MSM: Man or Two-Spirit identifying individual who has sex with another person who identifies as a man, including but not limited to individuals who self-identify as trans-gender, cis-gender, Two-Spirit, gender-queer, intersex, and non-binary.

II. METHODS

On November 25, 2024, and January 20, 2025, the NACI mpox Working Group (WG) convened to discuss and review NACI recommendations regarding the use of Imvamune® (May, 2024), considering reports of ongoing mpox clade I outbreaks globally. The NACI mpox WG reviewed data on the current epidemiology of mpox, both in Canada and internationally, current evidence on Imvamune® vaccination coverage in Canada, and published scientific literature regarding the effectiveness, immunogenicity and safety of Imvamune®. Knowledge synthesis was performed by the NACI Secretariat and supervised by the NACI mpox WG. Following critical appraisal of individual studies, summary tables with ratings of risk of bias informed by Cochrane 2.0 or ROBINS-I, as appropriate, were prepared (see [Appendix A](#)). NACI considered feedback obtained from a stakeholder group representing gbMSM communities. Input was provided by the National Emergency Strategic Stockpile (NESS) and the Canadian Immunization Committee (CIC). NACI recommendations related to travel were developed in collaboration with the Committee to Advise on Tropical Medicine and Travel (CATMAT). NACI approved these updated recommendations on February 18, 2025.

The main policy question addressed in this rapid response is:

1. Following the emergence of MPXV clade I, the WHO PHEIC declaration, and recent changes in international and Canadian guidance on Imvamune® use for the prevention of mpox in the context of international travel, should guidance related to international travellers be updated?
 - a. Should this guidance, if needing an update, be specific to areas of ongoing mpox transmission, or to specific populations (i.e., healthcare workers, participation in high-risk activities, etc.)?

Additional topics for updated guidance include:

2. Given the current data regarding the duration of protection of Imvamune®, should groups currently recommended to receive Imvamune® be considered for a third dose (i.e., a booster dose), and if so, at what interval?
 - a. Are there specific sub-populations within the current recommendations where this may/may not be warranted?
3. Are any changes needed to the populations/groups recommended to receive Imvamune® for the prevention of mpox, including whether to consider healthcare workers for vaccination, given the current mpox epidemiology internationally and in Canada?

III. EVIDENCE SUMMARY

III.1 Burden of disease

The WHO first declared mpox a PHEIC in July 2022 due to a rapid global outbreak of mpox cases, including in countries where MPXV is not endemic. From January 1, 2022, to January 31, 2025, 129,172 laboratory-confirmed cases of mpox and 283 deaths from 128 member states in all six WHO regions have been reported to the WHO.¹³ The PHEIC was declared over in May of 2023 after a sustained decline in global cases. In September 2023, a novel variant of MPXV (clade Ib) was identified in the Democratic Republic of the Congo (DRC), which was responsible for a rapid increase in reported and suspected cases of mpox in central Africa, leading to a second mpox-related PHEIC being declared on August 14, 2024.⁹ Between January 1, 2024, and January 26, 2025, a total of 19,837 confirmed mpox cases have been reported in Africa, including 93 deaths due to mpox.¹⁴ The number of suspected mpox cases and mpox-related deaths is considerably higher. Since the WHO PHEIC declaration, clade Ib mpox cases have been reported in several countries outside of Africa, including Canada (1 case as of April 16, 2025).¹⁵

Mpox epidemiology by clade and subclade

Evidence comparing the virulence and transmissibility of various clades of MPXV is still emerging, however reports have identified several potential epidemiological differences.^{16–20} In non-endemic areas, clade Ib transmission continues to largely occur in high-contact sexual networks, primarily the gbMSM community, and therefore the majority of cases reported have been amongst adult males. Historically, the majority of MPXV clade Ia infections were acquired through zoonotic transmission,²¹ but evidence of sustained human-to-human transmission (both through sexual and non-sexual contact) has been accruing.^{17,22,23} Given the novel nature of MPXV clade Ib, data are still emerging, however available data suggest MPXV clade Ib is primarily transmitted via close person-to-person contact, including both sexual and non-sexual contact. Unlike clade Ib, the strain responsible for the 2022 global outbreak, there is considerable transmission of both MPXV clade Ia and Ib outside of gbMSM sexual networks. There is a large disease burden in heterosexual males and females, as well as children (where the majority of MPXV clade Ia cases occur).^{16–20,24} Evidence to date suggests clade Ia is potentially less transmissible than clade Ib, however unlike clade Ib and Ib, clade Ia cases are predominantly reported in children under the age of 15 (usually as a result of close household contact with infected individuals). A PHAC rapid risk assessment has determined that the most likely spread scenario for clade Ia or Ib in Canada would be through close contacts, including sexual contacts, with the potential for domestic amplification through high-contact sexual networks, including among gbMSM, sex workers and their close contacts.²⁵

Compared to MPXV clade IIb, clade I strains, particularly clade Ia, may be associated with a higher rate of severe disease, as well as a potentially elevated case fatality rate (CFR).^{26–28} Of the two clade I subclades, clade Ia appears to be associated with greater disease severity and a higher mortality rate compared to clade Ib. Given the limitations to available data from MPXV endemic countries, it is also possible that observed differences between MPXV clades and subclades are driven by differences in demographic variables (including the populations affected, access to healthcare, nutrition etc.) between infected individuals. Recent preliminary data suggest that the CFR among people with a clade I mpox infection is lower when they are hospitalized and provided high-quality supportive care.²⁹ Evidence directly comparing the severity of MPXV clades and subclades, including any data stratified by age, sex or other risk factors (i.e., immunocompromised status) are still emerging.

Summary of recent Canadian mpox epidemiology

The majority of mpox cases observed to date in Canada occurred during the initial outbreak in 2022 (≈75%, n=1,477 cases), with most cases having been reported in Ontario, Quebec and British Columbia.¹² There have been 494 mpox cases reported in Canada since the start of 2024 (as of March 28, 2025), compared to only 69 mpox cases reported in 2023, indicating a recent increase in mpox activity nationally. Severe disease remains relatively rare, with 52 hospitalizations (6 since the start of 2024), three ICU admissions (0 since the start of 2024) and no deaths recorded to date in Canada. Most cases continue to be reported in gbMSM (≈95%) between the ages of 18 and 49 (≈85%), with sexual contact as the predominately reported mode of transmission. In addition, individuals living with HIV have been disproportionately affected by mpox (≈20% of cases). There have been 102 mpox cases in healthcare workers in Canada, as of October 17, 2024. Based on available information, most cases among healthcare workers were likely acquired through community exposures.

III.2 Vaccine characteristics

Imvamune[®] (also called MVA-BN, Jynneos[®], Imvanex[®]) is a non-replicating, third-generation smallpox and mpox vaccine manufactured by Bavarian Nordic. Imvamune[®] was initially authorized for use in Canada on November 21, 2013, as an Extraordinary Use New Drug Submission (EUNDS) for emergency use by the government for active immunization against smallpox infection and disease in persons 18 years of age and older who have a contraindication to first- or second-generation live-replicating smallpox vaccines. Imvamune[®] was subsequently approved under a supplement to the EUNDS on November 5, 2020, for active immunization against smallpox, mpox, and related *Orthopoxvirus* infections and diseases in adults 18 years of age and older determined to be at high risk for exposure. Further information on Imvamune[®] can be found in the product monograph available through Health Canada's [Drug product database](#), as well as the [Canadian Immunization Guide \(CIG\)](#), Part 4 Smallpox and mpox vaccines chapter.

III.3 Effectiveness, safety and immunogenicity of Imvamune[®] pre-exposure vaccination against mpox

NACI reviewed available evidence on efficacy/effectiveness, safety and immunogenicity of Imvamune[®] as pre-exposure vaccination for the prevention of mpox and mpox-associated morbidity, leveraging an evergreen PHAC database of published and pre-printed studies related to Imvamune[®] and mpox. A detailed list of recently published vaccine effectiveness studies

reviewed can be found in [Appendix A](#). For an overview of previously analyzed studies, please see [Interim guidance on the use of Imvamune® in the context of a routine immunization program, Appendix A: Vaccine effectiveness studies](#).

Effectiveness against mpox infection and moderate/severe mpox infections (including hospitalization)

Imvamune® administered as pre-exposure prophylaxis for the prevention of mpox continues to demonstrate a high degree of effectiveness, after either one or two doses. Current vaccine effectiveness (VE) data from available real-world observational studies has demonstrated the VE against infection of a single-dose of Imvamune® ranges from 36% (95% confidence intervals [CI]: 22 to 47%) to 86% (95% CI: 59 to 95%) and the VE of a two-dose series ranges from 66% (95% CI: 47 to 78%) to 89% (95% CI: 44 to 98%). Results from these analyses are in agreement with a recent systematic review and meta-analysis, evaluating the VE of third generation mpox vaccines against mpox infection.³⁰ A meta-analysis of available data (search run November 3rd, 2023) found the VE of a single dose was 76% (95% CI: 64 to 88%) and the VE of a two-dose schedule was 82% (95% CI: 72 to 92%).

Data on the effectiveness of Imvamune® against moderate to severe mpox infection (including hospitalization) is less robust, but data are encouraging. In studies providing estimates of effect, even a single dose of Imvamune® was effective at reducing moderate to severe mpox infection (VE 82%; 95% CI: -50 to 98%)³¹ and at reducing the odds of hospitalization due to mpox (OR 0.27; 95% CI: 0.08 to 0.65).³² Similarly, a two-dose schedule was also associated with a significant decrease in the odds of hospitalization due to mpox (OR 0.20; 95% CI: 0.01 to 0.90 and OR 0.20; 95% CI: 0.0 to 0.5).^{32,33} Several additional studies have demonstrated the rarity at which hospitalizations due to mpox occur in individuals who have been vaccinated with Imvamune®, even with a single dose.^{34–37} When breakthrough infection does occur, the severity of infection appears considerably reduced following vaccination with Imvamune®, with fewer lesions, less mucosal involvement, and fewer systemic symptoms.^{33,34,36}

The duration of protection provided by Imvamune® remains unclear at this time, against both infection and moderate/severe infection. As mpox vaccination campaigns generally started in non-endemic countries experiencing outbreaks (i.e., Canada, USA, UK, etc.) in the summer of 2022, continued population-level monitoring of VE will be critical. However, no signs of a decrease in VE have been observed in the literature to date, and the most recent data available suggest continued high VE. Disparate time intervals between vaccination and infection among fully vaccinated individuals also suggests that breakthrough infections are not due to waning immunity. Modelling studies conducted to date estimate the duration of protection of a two-dose series of Imvamune® to be at least 10 years.^{38,39} Combining VE data with antibody kinetic data following vaccination, the level of long-term effectiveness was estimated to be 59.2% (95% CI 38.7 to 74.2%) for a single dose and 66.6% (48.8 to 78.2%) for a complete two-dose series (with a 28-day interval) 10 years following vaccination.³⁸ Consistent with other vaccines, an extended interval between the first and second dose was predicted to lead to higher effectiveness over time. NACI will continue to monitor emerging evidence of the VE of Imvamune® against mpox infection, to evaluate the duration of protection of both a single dose and a complete, two-dose series.

Currently available VE data comes from studies conducted in countries where mpox is non-endemic, where MPXV clade IIb is responsible for virtually all mpox cases and therefore the effectiveness of Imvamune® against MPXV clade Ia and Ib is unclear at this time. Unpublished

data from a CDC study in the DRC that began in 2017 and vaccinated approximately 1,600 healthcare workers with two doses of Imvamune[®], observed only one laboratory-confirmed infection, indicating significant effectiveness against mpox in an area of high clade I transmission.^{40,41} In addition, several challenge studies in non-human primates have demonstrated significant protection against MPXV clade I associated with MVA-BN vaccination.^{42–45} There is currently no evidence and no biological rationale to suggest a decrease in vaccine effectiveness against MPXV clade Ia or Ib.

Safety

Available post-marketing safety surveillance data on Imvamune[®] suggests that the vaccine is well-tolerated. For more information regarding the safety of a two-dose series of Imvamune[®], please refer to the [CIG, Part 4 Smallpox and mpox vaccines chapter](#). The most common adverse events (AEs) reported by adults following one and/or two doses were non-serious injection-site and systemic reactions, consistent with clinical trial findings. Generally, the second dose was slightly better tolerated than the first. No serious AEs were reported after either dose, including no signals for increased risks of myocarditis/pericarditis following vaccination. A recent National Institutes of Health trial of MVA-BN in adolescents 12 to 17 years of age found that the vaccine was well tolerated through day 210 of the study, with the overall frequency of AEs in the adolescent trial participants was similar to what has been observed in adults.⁴⁶ In Canada specifically, data from the Canadian National Vaccine Safety Network (CANVAS) showed that Imvamune[®] was well tolerated, and most reported AEs were mild or moderate.⁴⁷ The majority of participants in this study (99%) were ≥20 years of age.

Data regarding the safety and tolerability of a third dose of Imvamune[®] are limited. A randomized, phase II trial in adults living with HIV administered a booster dose of Imvamune[®] to 31 participants, 12 weeks following the second dose.⁴⁸ Compared to a group of participants receiving the standard two-dose regimen, those receiving a booster dose reported a higher incidence of solicited local adverse events and overall adverse events related to study vaccination. However, no serious adverse events or adverse events of special interest related to study vaccine were reported. Unpublished results from a phase II clinical trial in Germany⁴⁹ reported similar results, with no serious adverse events related to the vaccine being observed following a booster dose two years following completion of the primary series (n=75 participants). One participant (1.3%) reported an unsolicited grade ≥3 adverse event within 29 days of vaccination. A recent study of healthcare workers from the DRC, who received a third dose five years after completion of the primary series, demonstrated elevated rates of local and systemic reactions following the administration of the third dose, compared to the first or second dose of the primary series. However, there were no severe adverse events observed.⁵⁰

Immunogenicity

Recent data have suggested that the antibody titres produced by Imvamune[®] vaccination in mpox-naïve individuals wane over time, usually within six to 12 months.^{51–53} The clinical significance of declining antibody levels over time remains unclear due to the lack of a clearly defined correlate of protection. It is possible that the level of circulating titres may not be the only marker of protection, as the role of innate and cell-mediated immunity is not currently fully understood. In addition, the robustness of memory responses may potentially influence the disease outcome. The disparate time intervals observed between vaccination and breakthrough infection among fully vaccinated individuals supports this theory.³³ A recent study of healthcare workers from the

DRC, who received a third dose five years after completion of the primary series, demonstrated a rapid and robust increase in both binding and neutralizing antibody levels, seven days following the third dose, suggesting that protection may not wane during this period of time. This response was observed irrespective of circulating antibody levels before third vaccine dose, indicating durable B-cell memory.⁴⁰

III.4 Ethics, equity, feasibility and acceptability

NACI considered the importance of transparency, in terms of acknowledging any uncertainties or knowledge gaps, in fostering and maintaining public trust. Additionally, as mpox transmission generally requires close and prolonged contact (including, but not limited to, sexual contact), NACI recommendations have been made based on need and risk, rather than solely other criteria such as gender or sexual orientation.

During the development of initial recommendations for Imvamune[®] use for the prevention of mpox, PHAC consulted with stakeholder groups representing impacted communities. Overall, gbMSM communities communicated positive attitudes towards mpox vaccination. However, since 2022, the majority of Imvamune[®] recipients have only had their first dose. This could potentially be due to factors such as perceived lower risk of infection compared to the spring/summer of 2022 when case numbers were high across many Canadian urban centers, or perceived risk of adverse events following immunization (AEFI) after the first dose of Imvamune[®].^{54–56}

All Canadian provinces and territories continue to offer Imvamune[®] to individuals considered at high risk of mpox. Implementation as an ongoing immunization program for populations at a high risk of mpox may have improved feasibility compared to ad hoc pop-up clinics employed during the 2022 mpox outbreak. However, understanding potential barriers and challenges to vaccination from the end-user perspective is critical to improving vaccine uptake.⁵⁷ It has been noted that identification of travel-associated risks (i.e., sex tourism) presents feasibility and equity challenges. Travel-associated risks are difficult to identify through public health clinics in some jurisdictions, and this impacts feasibility of operationalizing recommendations relating to travel risk. It has also been identified that vaccine programs administered in travel clinics based on travel risk assessment can incur individual costs, which can create inequities. However, despite feasibility and potential equity challenges, NACI and CATMAT considered it important to support vaccine access to travelers who may be at increased risk of mpox due to the evolving global situation.

III.5 Economics

While vaccine supply has been purchased and is currently managed federally, provinces and territories continue to bear the costs associated with administering the Imvamune[®] vaccination program. Cost-effectiveness analyses have not been conducted at this time, but may be considered in the future.

IV. RECOMMENDATIONS

Please see Table 1 for an explanation of strong versus discretionary NACI recommendations.

Recommendations

1. NACI continues to recommend that individuals at high risk of mpox should receive two doses of Imvamune® administered at least 28 days (4 weeks) apart.

- At this time, individuals considered at high risk of mpox in Canada include:
 1. Men who have sex with men (MSM) who:
 - i. have more than one partner; or
 - ii. are in a relationship where at least one of the partners has other sexual partners; or
 - iii. have had a confirmed sexually transmitted infection acquired in the last year; or
 - iv. have engaged in sexual contact in sex-on-premises venues.
 2. Sexual partners of individuals who meet the criteria above.
 3. Sex workers regardless of gender, sex assigned at birth, or sexual orientation.
 4. Staff or volunteers in sex-on-premises venues where workers may have contact with fomites potentially contaminated with mpox.
 5. Individuals who anticipate experiencing any of the above scenarios, including during travel outside of Canada.
- Also at high risk are individuals who are travelling to an area with ongoing community transmission of MPXV clade I* and anticipate either of the following:
 - i. Prolonged close contact (e.g., sharing accommodation), with people who reside in the area of active transmission; or
 - ii. Sexual contact with people who reside in, or spend extended time in, the area of active transmission.

*See [Mpox: Advice for travellers](#) for a list of countries meeting this criteria. Note: NACI guidance related to international travel has been updated above, in collaboration with CATMAT, to reflect current mpox epidemiology worldwide.

- Doses should be administered via subcutaneous injection. Dose sparing strategies involving intradermal administration are not recommended in the context of routine immunization.
- Those who have started a primary series with Imvamune®, in whom more than 28 days has passed without receipt of the second dose, should receive the second dose regardless of time since the first dose.

- Those who have previously received smallpox vaccination (e.g., first- or second-generation live-replicating smallpox vaccine) and are recommended to receive Imvamune® based on risk factors for mpox should also receive a 2-dose series with a minimum interval of 28 days.
- Imvamune® vaccination can be given concurrently (i.e., same day) or at any time before or after other live or non-live vaccines.

(Strong NACI Recommendation)

Additional considerations and summary of evidence

- Vaccine recommendations based on increased risk for mpox should be informed by available clinical evidence and ongoing epidemiology. Risk factors may change over time and should be assessed by local and/or provincial/territorial public health.
 - Individuals with uncontrolled HIV infection (e.g., CD4 count $<200 \times 10^6$ cells/L) are considered at higher risk of severe mpox based on available evidence. However, numerous studies are reporting that two doses of Imvamune® are effective at preventing mpox and associated outcomes including among individuals living with HIV infection. Clinicians should discuss Imvamune® and risks for mpox exposure with individuals who are living with HIV.
 - Evidence remains limited in pediatric populations <18 years, and the current indication of Imvamune® is for individuals 18 years of age and older. Off-label use in pediatric populations may be considered for pre-exposure vaccination for those meeting the high-risk criteria, with their clinician's discretion.
 - Vaccination is not recommended for individuals who have had mpox. Healthcare professionals should use clinical judgement when considering vaccinating individuals who have a history of mpox infection.
 - Although there are limited data regarding Imvamune® use among specific populations (e.g., immunocompromised due to disease or treatment; pregnancy or breastfeeding), these individuals should be offered Imvamune® if vaccination is recommended based on risk criteria.
 - Currently, in MPXV endemic countries, there is considerable transmission of MPXV clade I (both clade Ia and clade Ib) outside of gbMSM sexual networks, including in children. Evidence regarding transmission dynamics of MPXV clade I subclades are still emerging, and may be different than MPXV clade IIb. Therefore, travellers to areas with ongoing community transmission of MPXV clade I should take appropriate precautions when travelling.
- 2. At this time, Imvamune® is not routinely recommended for healthcare workers, with the exception of post-exposure vaccination. However, it may be considered on an individual basis based on a high risk of frequent exposure (e.g., healthcare workers who work at clinics that are frequently involved in the diagnosis and management of mpox).**

(Discretionary NACI recommendation)

3. **NACI recommends that healthcare workers who are travelling internationally to support mpox outbreaks should be vaccinated with Imvamune® ahead of deployment.**

(Strong NACI recommendation)

4. **A) NACI continues to recommend that personnel who work in research laboratory settings and who are at high risk of occupational exposure to replicating orthopoxviruses that pose a risk to human health should receive two doses of Imvamune® administered at least 28 days (4 weeks) apart.**

(Strong NACI recommendation)

- For those who are immunocompetent and have previously received a first- or second-generation live-replicating smallpox vaccine within the last 10 years, a single dose of Imvamune® may be offered. This single Imvamune® dose should be given at least two years after the latest first- or second-generation live-replicating smallpox vaccine. Although the duration of clinical protection is not currently known, epidemiological studies have demonstrated that protection conferred from first- or second- generation live-replicating smallpox vaccines can persist for up to, and perhaps beyond, 10 years.

B) NACI recommends that additional doses of Imvamune® may be offered for personnel who work in a research laboratory setting and who remain at high risk of occupational exposure to replicating orthopoxviruses that pose a risk to human health, with a minimum interval of 2 years.

(Discretionary NACI Recommendation)

Additional considerations and summary of evidence

- The exposure risk for personnel working with replicating orthopoxviruses in research laboratory settings is inherently different from those who may be exposed to MPXV in community settings. Personnel who work in research laboratory settings may be exposed to high concentrations of orthopoxviruses (some of which may be more virulent than MPXV), are potentially introduced to uncommon routes of viral exposure (i.e., needlestick injuries), and are at a consistent, ongoing risk of exposure, regardless of levels of community transmission.
- Data regarding the duration of protection provided by Imvamune® are currently limited. However, to date, there is no evidence to suggest that additional doses of

Imvamune® are needed for individuals at high risk in community settings, including immunocompromised populations. Evidence will continue to be reviewed on this topic as it becomes available.

- Available evidence suggests that while the antibody response to a primary series of Imvamune® may wane over time, it is quickly restored within days following a booster dose, even five years after the initial primary series. This suggests a strong persistent memory response from the primary series, which is expected to continue to provide protection in the event of exposure or infection, even without a third dose.
- Evidence continues to suggest that breakthrough infections are less severe among individuals who received one or two doses of vaccine, and there have not yet been any indications globally of a decline in vaccine effectiveness, several years after completion of the primary series.
- NACI will continue to monitor emerging evidence and update guidance on Imvamune® for pre-exposure vaccination against mpox as warranted. This will include monitoring the duration of protection following two doses of Imvamune® or MPXV infection, to inform the need for booster doses for individuals at high risk in community settings or vaccination of those previously infected, respectively.

5. NACI continues to recommend the use of Imvamune® as post-exposure vaccination (also known and referred to as post-exposure prophylaxis) to individuals who have had high risk exposure(s) to a probable or confirmed case of mpox, or within a setting where transmission is happening, if they have not received both doses of pre-exposure vaccination.

- A post-exposure vaccine dose should be offered as soon as possible, preferably within 4 days of last exposure, but can be considered up to 14 days of last exposure.
- After 28 days, a second dose of Imvamune® should be offered if MPXV infection did not develop, regardless of ongoing exposure status.
- Individuals with previous or active MPXV infection should not be offered Imvamune®.
- Off-label use in pediatric populations is recommended for those meeting the criteria for post-exposure vaccination, and may be offered.
- Imvamune® vaccination can be given concurrently (i.e., same day) or at any time before or after other live or non-live vaccines.

(Strong NACI Recommendation)

For additional information, please refer to the [CIG, Part 4, Smallpox and mpox vaccines chapter](#).

Table 1. Strength of NACI recommendations

Strength of NACI Recommendation based on factors not isolated to strength of evidence (e.g., public health need)	STRONG	DISCRETIONARY
Wording	"should/should not be offered"	"may/may not be offered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), OR Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

V. RESEARCH PRIORITIES

1. Further study of the durability of protection offered by Imvamune[®] vaccine against mpox infection, disease and transmission (in pre-exposure and post-exposure vaccination scenarios), including:
 1. Understanding which immune responses are protective against infection and disease and defining protective thresholds, including the duration of protection
 2. Understanding how the impact of previous orthopox infection or vaccination impacts the protection offered by Imvamune[®]
 3. Real-world evidence on the vaccine effectiveness of Imvamune[®] against mpox when used as a single SC dose, with extended intervals, and/or in combination with fractional intradermal dosing.
2. Additional studies to further inform on the safety of Imvamune[®] vaccine including both clinical trials and post-market safety surveillance.
3. Further studies to assess vaccine efficacy/effectiveness and safety of Imvamune[®] in priority populations, including people who are pregnant or breastfeeding, children <18 years of age, and people who are immunocompromised.
4. Further study into the epidemiology of the disease to better understand the modes of transmission and the disease presentation, and to identify the populations at

highest risk for severe disease in order to inform and optimize disease prevention strategies.

5. Further study into the optimal immunization strategies for outbreak control (e.g., ring vaccinations, population groups at medium/low risk of infection).
6. Further study into the optimal immunization strategies to reach and enhance vaccine acceptance and uptake in populations at highest risk of infection.

LIST OF ABBREVIATIONS

AE	Adverse event
AEFI	Adverse event following immunization
CANVAS	Canadian National Vaccine Safety Network
CATMAT	Canadian Committee to Advise on Tropical Medicine and Travel
CDC	Centers for Disease Control and Prevention
CFR	Case Fatality Rate
CI	Confidence Interval
CIC	Canadian Immunization Committee
CIG	Canadian Immunization Guide
DRC	Democratic Republic of the Congo
EUNDS	Extraordinary Use New Drug Submission
HIV	Human immunodeficiency virus
ICU	Intensive care unit
gbMSM	Individuals who self-identified as gay, bisexual, and men who have sex with men
MPXV	Monkeypox virus
MSM	Man or Two-Spirit identifying individual who has sex with another person who identifies as a man, including but not limited to individuals who self-identify as trans-gender, cis-gender, Two-Spirit, gender-queer, intersex, and non-binary.
MVA-BN	Modified vaccinia Ankara - Bavarian Nordic; Imvamune®
NACI	National Advisory Committee on Immunization
NESS	National Emergency Strategic Stockpile
OR	Odds Ratio
PHAC	Public Health Agency of Canada

PHEIC	Public Health Emergency of International Concern
USA	United States of America
UK	United Kingdom
VE	Vaccine effectiveness
WG	Working Group
WHO	World Health Organization

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APPENDIX A: VACCINE EFFECTIVENESS STUDIES

Table 1: Summaries of recently published mpox vaccine effectiveness studies (N=5)

Author, date, country	Study design, period, data sources	Study population, sample size	Vaccine	Outcome	VE results	Overall risk of bias
Back, et al. (2024) USA ⁵⁸	Retrospective cohort April 1 2021 – December 31 2022 HealthVerity's administrative US healthcare data	Male sex assigned at birth and ≥18 years of age and one of: (1) Presence of a diagnosis code related to High-Risk Sexual Behaviour; (2) presence of a diagnosis code indicating HIV infection; or (3) presence of a drug or procedure code indicating HIV pre-exposure prophylaxis (PrEP) among those without a diagnosis code indicating history of substance use disorder within the study period. N=163 vaccinated N=815 unvaccinated	1 or 2 doses of MVA-BN	Laboratory-confirmed symptomatic mpox infection	1-dose VE: 70% (95% CI: 44% to 84%) 2-dose VE: 89% (95% CI: 12% to 99%)	Moderate
Charles, et al. (2024) UK ³⁷	Case-coverage January 1 – December 31 2023 UK Health Security Agency (UKHSA) Second Generation Surveillance System (SGSS)	Vaccine-eligible gbMSM N=137 cases of mpox	1 or 2 doses of MVA-BN	Confirmed and highly probable mpox infection	1-dose VE: 84% (95% CI: 74% to 91%) 2-dose VE: 80% (69% to 83%) No vaccinated individuals were hospitalized.	Serious
Guagliardo, et al. (2024) USA ³³	Retrospective cohort May 11 2022 – May 1 2024	Individuals eligible for Jynneos® N=271 vaccinated N=24,507 unvaccinated	2 doses of MVA-BN	Moderate-to-severe mpox disease (i.e., mpox-related hospitalization)	Odds of hospitalization in persons with mpox who were vaccinated vs unvaccinated OR: 0.2 (95% CI: 0.0 to 0.5)	Serious

CDC National Notifiable Diseases Surveillance System						
Haverkate, et al. (2024) Netherlands ⁵⁹	Retrospective cohort May 2022 – December 2024 National surveillance database (SOAP) of the RIVM	gbMSM and transgender persons who are: using HIV- PrEP via sexual health centres (SHC); on the waiting list for the HIV-PrEP-pilot via SHC; using HIV-PrEP via their general practitioner; living with HIV at high risk of mpox infection; or are at high risk of mpox infection N=162 cases of mpox	2 doses of MVA-BN	Laboratory-confirmed symptomatic mpox infection	2-dose VE: 68.2% (95% CI: 4.3% to 89.5%)	Moderate
Yeganeh, et al. (2024) USA ³⁵	Retrospective cohort August 29 2022 – January 1 2023 REDCap (Research Electronic Data Capture hosted at LACDPH, Vanderbilt University, Nashville TN) and My Turn (California Department of Public Health vaccine and clinic management system)	Men aged 18 years or older who were at risk for mpox, eligible for Jynneos®, and residing in Los Angeles County N=152 vaccinated (N=114 partially vaccinated, N=38 fully vaccinated) N=2,019 unvaccinated	1 or 2 doses of MVA-BN	Laboratory-confirmed symptomatic mpox infection and moderate-to-severe mpox disease (i.e., mpox-related hospitalization, complication)	<u>Full population</u> 1-dose VE: 69% (95% CI: 59% to 77%) 2-dose VE: 84% (95% CI: 80% to 87%) <u>People living with HIV</u> 1-dose VE: 28% (95% CI: -96% to 73%) 2-dose VE: 72% (95% CI: 57% to 82%) 0 fully vaccinated hospitalisations and 1 (<1%) partially vaccinated hospitalization	Moderate

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