Ministry of Health

Mpox Vaccine (Imvamune®) Guidance for Health Care Providers

Version 5.0 – June 26, 2024

Highlights of Changes:

- Revised high-risk criteria to align with the National Advisory Committee on Immunization (NACI) (page 3).
- Revised booster dose recommendations (page 2 and 5).
- Revised recommendations for special populations (page 5-7).
- Revised co-administration recommendation (page 9).
- Updated links in additional resources section (page 10).
- Removal of list of immunosuppressive medication list and clinical guide to verify immunosuppressive medications and eligibility.

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

Ontario continues to monitor for cases of mpox (formerly monkeypox) and is working collaboratively with health care providers, Public Health Ontario (PHO) and the Public Health Agency of Canada (PHAC) to address health risk(s). New guidance will continue to emerge as new information becomes available and epidemiology evolves.

Imvamune® Vaccine

Imvamune® is a live attenuated, non-replicating vaccine that is approved in Canada for protection against smallpox, mpox, and other orthopoxvirus related illness; it is a 3rd generation smallpox vaccine. It is produced from the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) strain of orthopoxvirus and was developed to provide an alternative for the vaccination of immunocompromised individuals and those with atopic dermatitis, who could not safely receive earlier generation (replicating) smallpox vaccines.

Health Canada first approved the use of this vaccine for active immunization against smallpox in a public health emergency in 2013. In 2020, Health Canada expanded approval of Imvamune® to include additional indications, specifically for mpox and related orthopoxvirus infections in adults 18 years of age and older at high risk of exposure. The use of Imvamune® has not been studied in individuals less than 18 years of age or in those who are pregnant or breastfeeding.

Evidence on Imvamune® vaccine effectiveness (VE) against mpox continues to accumulate. Numerous observational studies initiated during active mpox outbreaks since 2022 are reporting high VE against symptomatic mpox.

Individuals with signs or symptoms of mpox infection should not receive the vaccine as the vaccine is not indicated in the treatment of mpox infection.

Use of Imvamune® in Ontario

Imvamune® should be offered as a two-dose vaccine series, with at least 28 days between first and second doses for individuals currently eligible for pre-exposure or post-exposure vaccination.

A full dose, 0.5 mL of Imvamune®, should be given via the subcutaneous (SC) route for each dose.

This approach will continue to be evaluated with any changes in mpox epidemiology.and evidence surrounding the vaccine.

Individuals should continue to receive first and second dose vaccination to ensure optimal protection. As per the National Immunization Advisory Committee (NACI), booster doses are not recommended at this time.

Imvamune® should be considered for the following:

- **Pre-exposure vaccination** – when Imvamune® is administered before exposure to the virus for individuals at high risk of mpox exposure.
- **Post-exposure vaccination** – when Imvamune® is administered for individuals who have had a high-risk exposure to a probable or confirmed case of mpox, or within a setting where transmission is happening.

Pre-Exposure Vaccination for High Risk Individuals

The individuals listed below are considered at high risk for mpox exposure and are eligible for pre-exposure vaccination:

1. Two-Spirit, non-binary, transgender, cisgender, intersex, or gender-queer individuals who self-identify as belonging to the gay, bisexual, pansexual and other men who have sex with men (gbMSM) community **AND** who meet one or more of the following:
    a. Have more than one partner
    b. Are in a relationship where at least one of the partners has other sexual partners
    c. Have had a confirmed sexually transmitted infection within the last year
    d. Have attended venues for sexual contact (e.g., bath houses, sex clubs)
    e. Have had anonymous sex (e.g., using hookup apps) recently
2. Sexual partners of individuals who meet the criteria above
3. Sex workers (regardless of gender, sex assigned at birth, or sexual orientation) or who are a sexual contact of an individual who engages in sex work
4. Staff or volunteers in sex-on-premises venues where workers may have contact with fomites potentially contaminated with mpox
5. Individuals who engage in sex tourism[1] (regardless of gender, sex assigned at birth, or sexual orientation)
6. Individuals who anticipate experiencing any of the above scenarios

Household contacts of those identified for pre-exposure vaccination eligibility above AND who are moderately to severely immunocompromised (see Appendix A) or who are pregnant may be at higher risk for severe illness from mpox infection and may be considered for pre-exposure vaccine. Individuals who meet this criteria should contact their healthcare provider (or their local public health unit) for more information. Also see relevant sections under "Special Populations" for additional considerations.

Post-Exposure Vaccination

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 <u>not</u> received both doses of pre-exposure vaccination.**

[1] Sex tourism is travel for the specific purpose of having sex, typically with commercial sex workers. It differs from having casual sex during travel with fellow travelers or locals (Centers for Disease Control and Prevention, 2022).

The provision of Imvamune® for post-exposure vaccination requires an assessment of the risk of exposure by the public health unit.

The first dose should be offered as soon as possible, ideally within 4 days (up to 14 days) from the date of the last exposure to individuals who are a high risk contact of a confirmed or probable case of mpox. A second dose should be offered 28 days after the first dose if mpox infection did not develop, regardless of ongoing exposure status. If the window for post-exposure is missed (i.e. more than 14 days after exposure) consider administration of Imvamune® as pre-exposure vaccination.

Anyone who self-identifies as a high risk contact of a confirmed or probable case of mpox should contact their local public health unit for further assessment to see if post-exposure vaccination would be recommended.

Intermediate risk contacts may also be offered post-exposure vaccination, following the public health unit's assessment of individual risks and benefits (i.e., to balance the risks from exposure, protection from vaccination and potential side effects from the vaccine).

Post-exposure vaccination is not recommended for low-risk contacts (see Table 1).

Table 1. Recommendations for Post-exposure Vaccination according to risk of infection

Risk of exposure[2]	**Post-exposure Vaccination**
High	Recommended
Intermediate	May be recommended based on the public health unit's assessment of risks and benefits
Low	Not recommended
No/very low	Not recommended

[2] Recommendations for the management of cases and contacts of mpox in Ontario

Special Populations

Individuals with History of Previous Smallpox Vaccination

Individuals eligible for Imvamune® as pre- or post-exposure vaccination and who have previously received smallpox vaccination (i.e. previous generation live-replicating vaccine) are recommended to receive a 2-dose series of Imvamune® with a minimum interval of 28 days between doses.

Individuals Who have had Previous Mpox Infection

Individuals who have been diagnosed with mpox are NOT recommended to receive the mpox vaccine as post-exposure or pre-exposure prophylaxis; this is based on the limited utility of the vaccine given that these persons are expected to have infection-mediated immunity due to recent infection.

Research Laboratory Employees

Research laboratory employees working directly with replicating orthopoxviruses, are eligible to receive two doses of Imvamune® at least 28 days apart. These individuals may be offered an additional dose after 2 years if they remain at risk of occupational exposure.

Healthcare Workers

At this time, Imvamune® is not routinely recommended for healthcare workers (HCWs), including those serving populations at high risk of mpox, with the exception of post-exposure vaccination.

HCWs are trained in appropriate infection prevention and control practices, including wearing of appropriate personal protective equipment (PPE) (e.g., eye protection, fit-tested and seal-checked N95 respirator or medical mask, gown and gloves). As such, if the HCW was following appropriate infection prevention and control practices, the risk of transmission is negligible.

If a HCW had contact with a patient who is diagnosed with mpox and did not follow appropriate infection prevention and control practices, an assessment of the risk to the HCW should be conducted (CIG, 2022).

Moderately to Severely Immunocompromised

Individuals who are moderately to severely immunocompromised and are currently eligible for pre-exposure vaccination should receive two doses Imvamune®. Please refer to Appendix A for the definition of moderate to severe immunocompromise.

Clinical trials of Imvamune® have included people living with human immunodeficiency virus (HIV) with a CD4 count of equal or greater than 100. There is less experience in individuals with severe immunosuppression. Additional risk/benefit discussion is indicated for those with severe immunosuppression prior to receiving vaccine as post-exposure vaccination.

Allergy/Hypersensitivity

Individuals who are hypersensitive to this vaccine or to any ingredient in the formulation or component of the container should not receive the vaccine. A list of ingredients can be found in the product monograph

Note: Imvamune® may contain trace amounts of antibiotics (gentamicin and ciprofloxacin) and egg products (egg cell DNA and protein) which are used during the vaccine production process. Individuals with known hypersensitivity to these products are still able to safely receive Imvamune® but should be monitored for an additional 15 minutes (30 minutes total) after vaccine administration.

Pregnancy and Breastfeeding

Although there are limited data regarding the use of Imvamune® in pregnancy or in individuals who are breastfeeding, these individuals should be offered Imvamune® if vaccination is recommended based on high-risk criteria.

No clinical trials have been conducted in pregnant individuals, although approximately 300 pregnancies have been reported to the manufacturer with no safety issues identified. There are no data on whether the vaccine is excreted in breastmilk, although this is unlikely as the vaccine is non-replicating.

Additional risk/benefit discussion is indicated for those who are pregnant or breastfeeding prior to receiving vaccine as pre- or post-exposure vaccination.

Children and Youth

Imvamune® is not authorized for use in persons under 18 years of age, however, off-label use in pediatric populations may be considered for those that meet criteria for pre- or post-exposure vaccination. Imvamune® may be given on a case-by-case basis at the health care provider's discretion, after a risk/benefit discussion. Although the use of Imvamune® has not been studied in this age group, it has been offered to children as PEP in previous United Kingdom mpox incidents as cited in UK PEP guidance. Clinical trials have studied other vaccines (TB and malaria) using Modified Vaccinia Ankara (MVA) as a vector in children with a reassuring safety profile.

For the process of setting up infectious disease consults for mpox post-exposure vaccination in pediatric populations, please refer to Appendix B.

Persons with Atopic Dermatitis

Persons with atopic dermatitis may have more frequent and more intense reactions after vaccination. This population was specifically studied in clinical trials as those with a history or presence of atopic dermatitis are contraindicated to receive the previous generation of smallpox vaccine (ACAM, 2000).

Potential Side Effects of Imvamune®

The most common side effects include reactions at the injection site like pain, erythema, induration and swelling. The most common systemic reactions observed after vaccination are fatigue, headache, myalgia, and nausea. Most of the reported adverse drug reactions observed in clinical trials were of mild to moderate intensity and resolved within the first seven days following vaccination.

Older generation (i.e., replicating) smallpox vaccines have been associated with myocarditis. No trends have been identified which suggest the occurrence of any particular unexpected adverse reaction or classes of adverse reactions following vaccination with Imvamune®. To date, myocarditis has not been determined to be causally associated with Imvamune, but monitoring is ongoing (CIG, 2024). Individuals should be counselled to seek medical attention if cardiac symptoms (i.e., chest pain, shortness of breath, palpitations) develop following vaccination with Imvamune®.

Informed Consent

The *Health Care Consent Act, 1996* provides specific information as to the consent required for treatment. According to the HCCA, and the College of Nurses of Ontario (CNO) and College of Physicians and Surgeons of Ontario (CPSO) standards, nurses and physicians are accountable for obtaining consent when providing treatment. It is therefore the responsibility of the health practitioner who is proposing the treatment to take reasonable steps to ensure that informed consent for that treatment is obtained.

According to the HCCA, consent to treatment for a capable person is informed if, before giving the consent:

a. the person received the information about the treatment that a reasonable person in the same circumstances would require to make a decision; and

b. the person received responses to his/her requests for additional information about the treatment.

This information must include:

- The nature of the treatment
- The expected benefits of the treatment
- The material risks of the treatment
- The material side effects of the treatment
- Alternative courses of action
- The likely consequences of not having the treatment.

The elements required for consent to treatment include:

- The client must have the capacity to consent
- The consent must relate to the treatment
- The consent must be informed
- The consent must be given voluntarily
- The consent must not be obtained through misrepresentation or fraud.

Evidence of Consent:

Although the HCCA states that consent to treatment may be expressed or implied (i.e., written or verbal), the CNO and CPSO strongly advise nurses and physicians to document that consent was obtained from the client. Examples include: 1) a signed consent form and/or 2) documented consent in the client's health records.

How to order Imvamune®

To order the vaccine, the local public health unit must complete this electronic form. Please contact the Vaccine Policy & Programs Branch at vaccinesupplyandlogistics@ontario.ca for any questions.

Clinicians who think they have a patient (i.e., a contact of a case) who might be recommended to receive post-exposure vaccination using the criteria above should contact their local public health unit.

Co-Administration of Imvamune®

As per NACI, Imvamune® can be given concurrently (i.e., same day) or at any time before or after other live or non-live vaccines.

Storage Conditions

Please see Mpox (monkeypox) resources for health care professionals for information on storing and handling Imvamune®.

Reporting Adverse Events Following Immunization

Reports of any Adverse Event Following Immunization (AEFI) following Imvamune® vaccine should be made using the Ontario AEFI form and sent to the local public health unit. Please see Public Health Ontario's vaccine safety webpage and Fact Sheet – Adverse Event Following Immunization Reporting for Health Care Providers in Ontario for additional guidance.

Additional Resources

Bavarian Nordic – Imvamune Product Monograph

European Centre for Disease Prevention and Control - Factsheet for health professionals on mpox (monkeypox)

Ontario Ministry of Health - Mpox (monkeypox)

Ontario Ministry of Health - Mpox (monkeypox) resources for health care professionals

Ontario Ministry of Health - Recommendations for the management of cases and contacts of mpox in Ontario

Public Health Agency of Canada - Mpox (monkeypox)

Public Health Ontario – Mpox (formerly known as monkeypox)

United States Centers for Disease Control - Mpox

World Health Organization – Mpox (monkeypox) Key Facts

World Health Organization - Mpox (monkeypox) Questions and Answers

Appendix A

Moderately to severely immunocompromised is defined as:

- Individuals receiving dialysis (hemodialysis or peritoneal dialysis)
- Individuals receiving active treatment[3] (e.g., chemotherapy, targeted therapies, immunotherapy) for solid tumour or hematologic malignancies
- Recipients of solid-organ transplant and taking immunosuppressive therapy
- Recipients of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Individuals with moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Individuals with HIV with current CD4 count ≤ 200/mm3 **or** CD4 fraction ≤ 15% or detectable viral load (i.e., not suppressed)
- Individuals receiving active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies[4] (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (refer to the Canadian Immunization Guide for suggested definition of high dose steroids), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive (See Table 2).
- For guidance on the timing of vaccine administration for transplant recipients and those requiring immunosuppressive therapies, a more comprehensive list of conditions leading to primary immunodeficiency, and for further information on immunosuppressive therapies, refer to Immunization of Immunocompromised Persons in the Canadian Immunization Guide (CIG), Part 3 – Vaccination of Specific Populations.

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[3] Active treatment includes patients who have completed treatment within 3 months. Active treatment is defined as chemotherapy, targeted therapies, immunotherapy, and excludes individuals receiving therapy that does not suppress the immune system (e.g., solely hormonal therapy or radiation therapy). See Ontario Health/Cancer Care Ontario's Frequently Asked Questions for more information.

[4] Active treatment for patients receiving B-cell depleting therapy includes patients who have completed treatment within 12 months.

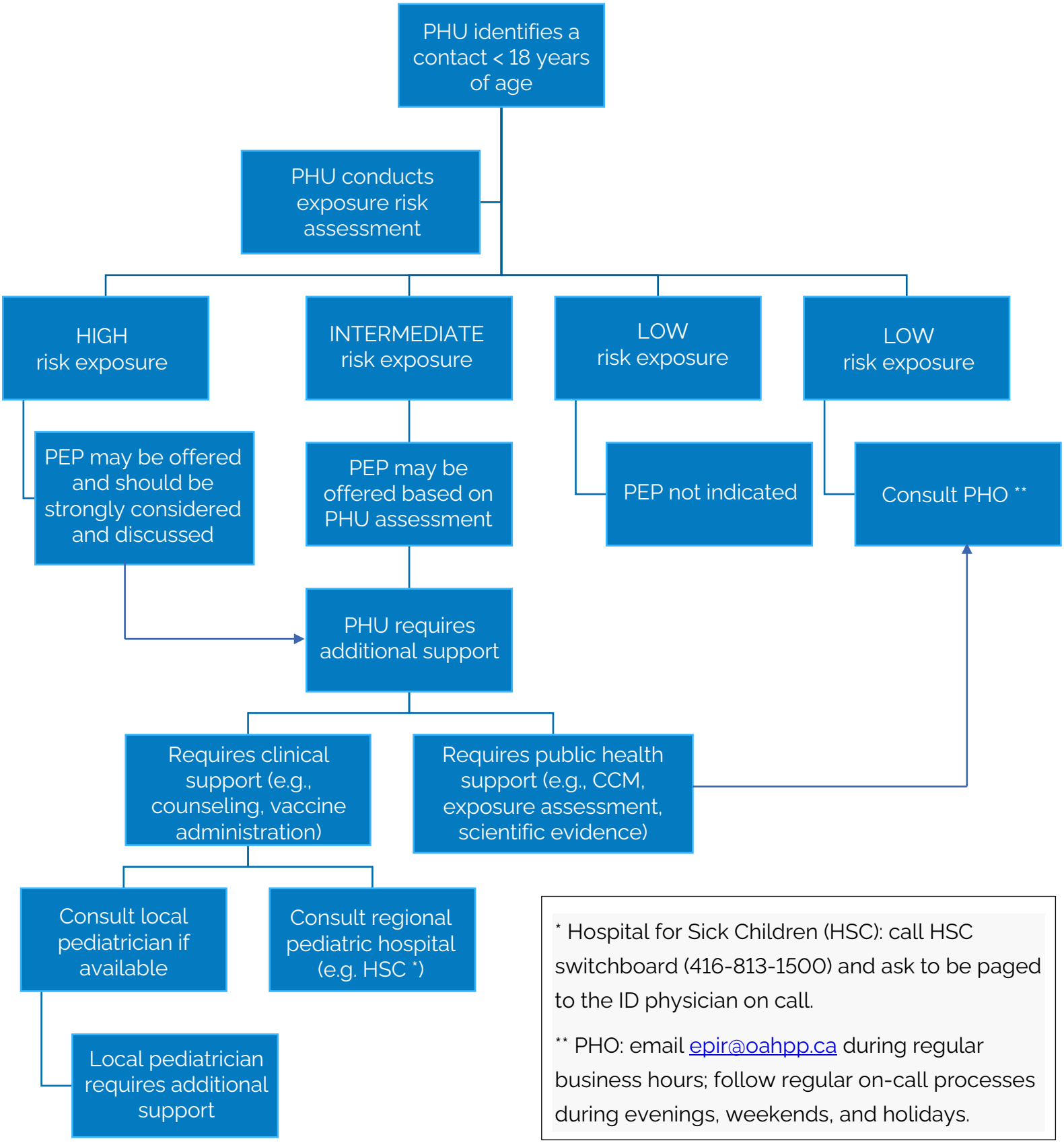
Appendix B

Process for Pediatric ID Consultations for mpox PEP Vaccination in Pediatric Populations

Objectives

- To develop a clear and systematic referral process for Public Health Units (PHUs) to consult pediatric infectious disease clinicians for consideration of post-exposure prophylaxis (PEP) vaccination with the Imvamune® vaccine in pediatric contacts (i.e., under 18 years of age), when needed.
- To ensure timely referral, counseling, informed consent, discussion of the risks and benefits of PEP vaccination, and the administration of Imvamune® in children under 18 years of age where indicated.

Process



* Hospital for Sick Children (HSC): call HSC switchboard (416-813-1500) and ask to be paged to the ID physician on call.

** PHO: email epir@oahpp.ca during regular business hours; follow regular on-call processes during evenings, weekends, and holidays.

Roles and Responsibilities

1. **PHUs**

- Proactively develop internal processes and resources as part of their local mpox response. This includes:
    - Resources for staff to provide appropriate counseling to individuals identified as contacts of a known mpox case and/or their guardians about PEP with Imvamune® (e.g., risks and benefits of receiving PEP).
    - Identifying local pediatric specialist(s) as well as determining the threshold or indications for triggering a pediatric consult for clinical advice and/or support in vaccine administration.
    - Where pediatric specialists are not available locally, PHUs should reach out to their regional tertiary pediatric hospital and consult ID (e.g., HSC).
    - A process to ensure timely transportation of Imvamune® if requesting an external provider (e.g., a local pediatrician) to support vaccine administration.
- Conduct exposure risk assessment of all contacts of a known/confirmed or suspected case of mpox.
- Obtain and provide the following information when consulting a pediatric specialist:
    - Age of child
    - History and nature of exposure to a mpox (e.g., date(s) of exposure, type of exposure, etc.);
    - Relevant medical risk factors for severe disease (e.g., immunocompromised);
    - PHU's risk assessment of exposure (i.e., high, intermediate, or low risk exposure) of the child and recommendations for PEP if available;
    - Clinical question/request (e.g., provide guidance to PHU on counseling, provide direct counseling to parents, request for vaccine administration etc.); and
    - Contact information for parent/guardian.

2. Ministry of Health

- Provide and communicate provincial level guidance on mpox related policies to PHUs, including the establishment of an eligibility criteria for Imvamune® for use of mpox PEP.

3. Public Health Ontario (PHO)

- Provide technical and scientific support to PHUs on public health aspects of mpox case and contact management, including questions on:
    - Exposure risk assessment
    - Scientific evidence for Imvamune®

4. Pediatric specialist(s)

- Provide guidance/support to PHU when consulted on clinical questions relating to mpox including the administration of Imvamune®, in pediatric populations.
- When requested by PHU, provide direct counseling to the contact and/or their parents/guardians about the risks and benefits of Imvamune® PEP.
- When requested by PHU, support Imvamune® administration in a child as indicated.