An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)

Updated recommendations on measles post-exposure prophylaxis

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To obtain additional information, please contact:

Public Health Agency of Canada
Address Locator 0900C2
Ottawa, ON K1A 0K9
Tel.: 613-957-2991
Toll free: 1-866-225-0709
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications-publications@hc-sc.gc.ca

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On June 4, 2025, an Addendum to this NACI Statement was issued to provide clarity on immunoglobulin products for measles post-exposure prophylaxis. Please see the Addendum to NACI statement on Updated recommendations on measles post-exposure prophylaxis for additional information.

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.

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Introduction

Incidence of measles in Canada has been very low since the introduction of publicly funded measles vaccination programs in Canada in the 1970s. Canada has maintained measles elimination status since 1998. Routine immunization programs have been, and continue to be, essential for sustaining measles elimination in Canada. Achieving and maintaining vaccination coverage of at least 95% is necessary for herd immunity and to reduce the impact of isolated outbreaks. Since 1998, outbreaks have occurred periodically, often among those who are unvaccinated against measles. Measles post-exposure prophylaxis (PEP) is a critical component of measles exposure management, with the aim of minimizing severe outcomes and mortality due to measles for susceptible individuals who have had a confirmed exposure to measles.

Recent measles outbreaks in Canada and continued feasibility challenges of using human immunoglobulin products during measles outbreaks prompted NACI to revisit guidance on measles PEP. In 2018, NACI updated measles PEP guidance to include the use of intravenously administered human immunoglobulin (IVIg) for individuals weighing more than 30 kg or for those in whom large IM injection volumes or number of IM injections were a concern. However, the use of IVIg for measles PEP utilizes considerable healthcare resources, including infection prevention and control (IPC) measures and personnel requirements for product administration.

Guidance Objective

The objective of this advisory committee statement is to review the criteria for expected measles immunity in the context of recommendations for measles PEP, review recent evidence on the effectiveness of Ig products and vaccines for measles PEP and provide updated guidance on options for measles PEP.

Methods

In brief, the broad stages in the preparation of this NACI advisory committee statement were:

1. Analysis of burden of disease of measles in Canada
2. Knowledge synthesis (retrieval and summary of individual studies, assessment of the quality of the evidence from individual studies using GRADE methodology– summarized in Montroy et al.)[1]
3. Synthesis of the body of evidence of benefits and harms, considering the quality of the synthesized evidence and magnitude of effects observed across the studies
4. Jurisdictional scans of national and international measles PEP recommendations and strategies
5. Collaboration with subject matter experts on immunocompromised populations
6. Use of a published, peer-reviewed framework and evidence-informed tools to ensure that issues related to ethics, equity, feasibility, and acceptability (EEFA) were systematically assessed and integrated into the guidance[2]

7. Economic considerations: economic evidence for updated measles PEP recommendations was not considered in this guidance development
8. Translation of evidence and programmatic considerations into recommendations

For further information, please see NACI's evidence-based methods.

For this advisory committee statement, NACI reviewed the key questions for a literature review as proposed by the NACI Measles-Blood Products Working Group, including considerations such as the burden of the disease to be prevented, the target population(s), safety, immunogenicity, efficacy, effectiveness of products recommended for measles PEP, administration schedules, and other aspects of the overall immunization strategy. Knowledge synthesis was done by the NACI Secretariat and supervised by the NACI Measles-Blood Products Working Group, which included experts on human immunoglobulin products, public health and measles immunization policies.

NACI first met to discuss an update to measles PEP guidance on September 19, 2024. The evidence and proposed recommendations were presented to NACI on November 20, 2024 following critical appraisal of individual studies by the NACI Measles-Blood Products Working Group, engagement with the Canadian Immunization Committee (CIC), the Communicable and Infectious Disease Steering Committee (CIDSC), and collaboration with the Ontario Immunization Advisory Committee (OIAC) and additional subject matter experts from across Canada on the topic of measles PEP for immunocompromised populations. Following thorough review of the evidence and consultation, the committee voted on specific recommendations. The description of relevant considerations, rationale for specific decisions, and knowledge gaps are described in the text. In addition to consultation with OIAC and subject matter experts across Canada for measles PEP for immunocompromised populations, international guidance on this topic, such as the national measles guidelines from the UKHSA (United Kingdom Health Security Agency), informed the development of NACI's recommendations[3]. A systematic review of the efficacy, effectiveness and safety of measles post-exposure prophylaxis therapies was conducted, using GRADE methodology to assess the certainty of evidence. A summary of the systematic review methodology, results, and analyses are described in this statement. The full systematic review is available elsewhere[1].

A note on language

The writing in this statement uses a gender additive approach where the term 'woman' is used alongside gender-neutral language. This is intended to demonstrate a commitment to redress the historic exclusion of trans and non-binary people, whilst avoiding the risk of marginalising or erasing the experience of women within the healthcare environment. However, in line with best practice, it is recognized that when discussing or caring for individuals in a one-on-one capacity, language and documentation should reflect the gender identity of the individual.

Finally, NACI acknowledges the dynamic nature of language. It is likely that language deemed to be suitable or affirming in one context may not translate across others, and over the coming years will likely change and evolve with respect to appropriate representations.

Epidemiology/Background

Global measles activity

In late 2023, a global increase in measles activity was reported. On December 14, 2023, the World Health Organization issued an urgent warning about measles after an "alarming" 30-fold rise in cases across Europe since 2022[4].

Measles outbreaks in Canada

In 1998, Canada achieved elimination status for measles with endemic transmission no longer occurring. Measles elimination is a direct result of successful routine vaccination programs implemented between the 1970s and 1990s[5]. However, cases continue to occur in Canada due to exposure outside of Canada, which sometimes leads to outbreaks with limited spread in Canada. The risk of measles transmission is highest when unvaccinated or non-immune populations are clustered together in particular regions or communities. Vaccination rates in Canada, while high, are currently below the necessary threshold for herd immunity in some places[6-8].

National surveillance of measles cases is conducted through the Canadian Measles/Rubella Surveillance System (CMRSS)[9]. Among measles cases reported to CMRSS from January 2015 to September 2024, the majority of measles cases have occurred during the first four months of the calendar year[9]. The greatest proportion of cases have been in children 5 to 14 years of age and the highest rate of measles was in infants less than 1 year of age (0.8 cases per 100,000)[9]. Among measles cases reported during this time period for which vaccination status was known (387 out of 492 cases), the majority (72%) have been individuals not vaccinated with a measles-containing vaccine, the majority of whom were between 5 to 14 years of age. Eleven percent of measles cases (44 out of 387) had received 1 dose of a measles-containing vaccine (majority between 25 to 44 years of age); and 17% (66 out of 387) had received 2 doses of a measles-containing vaccine (majority between 15 to 44 years of age).

Immunization products for measles post-exposure prophylaxis

Preparations in Canada

Characteristics of the measles-containing vaccines currently authorized for use in Canada that may be used for measles PEP are summarized in Table 5 in the Appendix. For complete prescribing information for measles-containing vaccines and Ig, including contraindications and precautions, consult the product leaflet or information contained within the product monographs available through Health Canada's Drug

Product Database. The human Ig dosages recommended by NACI for measles PEP may differ from what is contained in product monographs as measles PEP is an off-label use for most of these products. For NACI recommended dosages, please refer to Tables 1 – 3 in this statement.

Efficacy/Effectiveness of Ig and vaccine products for measles PEP

NACI reviewed the available evidence on efficacy/effectiveness of products used for measles PEP, leveraging a systematic review on the effectiveness and safety of measles PEP (both Ig and measles-containing vaccines). A summary of this systematic review is provided below, with the entire review available elsewhere (Montroy et al.)[1].

Effectiveness against measles infection

Several studies reported on the effectiveness of measles PEP against measles infection, either using IVIg, intramuscularly administered Ig (IMIg) or a measles-containing vaccine. No studies included subcutaneously administered Ig (SCIg) products. After using GRADE to assess the certainty of available evidence, it was determined that when compared to those who did not receive PEP of any kind, the administration of measles PEP (either with Ig or measles-containing vaccine) is considered likely effective at preventing confirmed cases of measles infection (moderate certainty of evidence)[10-18].

In studies where susceptible individuals received Ig as PEP following an exposure to measles, measles infection rates ranged from 0 to 30% (n=8 studies and 434 participants)[10-15,17,18]. The majority of data were among infants. Several large outbreak studies with control groups of individuals who did not receive PEP of any kind were able to provide estimates of PEP effectiveness. Estimates were high when available and ranged from 75% (95% CI 0 to 94%) to 100% (95% CI 56.2% to 99.8%)[11,15,17]. Similarly, measles infection rates in susceptible individuals receiving PEP in the form of a measles-containing vaccine ranged from 0 to 15% (n=6 studies and 226 participants), and estimates of effectiveness were again high when available, ranging from 83.4% (95% CI 34.4 to 95.8) to 100% (95% CI not estimable, as described by the study authors)[11,13,14,16-18]. The interpretation of results from individual studies warrants some caution, as most studies were determined to be at serious risk of bias, largely due to potential issues with confounding. Critical information such as the nature and intensity of measles exposure, the time from exposure to administration of prophylaxis, and the dose of Ig product received, was often not available.

This systematic review only included studies conducted after 1970. The decision to not include studies conducted prior to 1970 was made because after the introduction of routine immunization programs there has been a concomitant decrease in measles neutralizing antibody titres in donor derived plasma, and the dose of immunoglobulin appears to be correlated with the effectiveness of PEP[10,19-21]. There is potential that currently available immunoglobulin products may be less effective than observed in earlier studies[22]. Encouragingly, results from this systematic review demonstrate the

effectiveness of PEP and are in concordance with studies published prior to the introduction of routine immunization programs (i.e., prior to 1970)[22].

Effectiveness against death due to measles

There were no studies included in the systematic review which reported on the outcome of death due to measles. A previous systematic review of Ig measles PEP, which included studies prior to the introduction of routine measles vaccination programs (i.e., 1970), found that based on three studies (n=893 participants), Ig PEP was effective at preventing death due to measles, when compared to no PEP (RR 0.24, 95% CI 0.13 to 0.44)[22]. These results should be interpreted with caution, as the three studies were conducted between 1923 and 1930, and thus the donor-derived Ig products that were used have the potential to be considerably different than the products currently available. The studies also were of very low quality.

Effectiveness against complications due to measles

Data regarding the effectiveness of PEP against complications due to measles infection are very limited and the complications reported in the literature are very heterogeneous, resulting in an evidence base that is challenging to interpret.

In infants, one study from Japan administered IMIg at a dose of 0.33 mL/kg to young, susceptible infants (mean age 1.5 years). Nine of 33 IMIg recipients contracted measles. After 14 days of follow-up "no patient had complications of measles"[10]. A study from France, conducted during a measles outbreak on an obstetrics ward, administered IVIg (400 mg/kg) to neonates of exposed mothers or neonates who had a direct exposure to measles, and 2 of the 7 neonates subsequently developed measles[13]. The neonates who received PEP were followed for three years, and it was reported that for the 6 which had complete follow-up data, none (including the two who developed measles) experienced any neurodevelopmental issues.

In adults, following an outbreak in a military barracks in Japan, measles symptoms and severity in military recruits who had and had not been given MMR PEP were compared[16]. Among those who contracted measles, those who did not receive PEP had longer durations of hospital admission, longer durations of maximum fever temperature, and higher maximum fever temperatures, compared to those who did receive PEP.

Immunization product safety

A single study reported on adverse events following the administration of measles PEP. In this study, IVIg (400 mg/kg) was administered to susceptible infants less than 12 months of age (n=63)[15]. The IVIg was well tolerated, and there were no adverse reactions reported during the duration of hospital admission.

Adverse events following immunization (AEFIs) with MMR vaccine occur less frequently and are less severe than those associated with natural disease[23]. Injection site reactions following receipt of standard human Ig include tenderness, erythema,

and stiffness of local muscles, which may persist for several hours. Mild fever or malaise may occasionally occur.

The safety of measles-containing vaccines and Ig products used for measles PEP, including less common AEFIs, serious adverse events (SAEs), contraindications and precautions are further described in the product monographs available through Health Canada's Drug Product Database and the CIG, Part 4, Measles vaccines chapter[23]. Please consult guidance from your jurisdiction and/or institution on adverse events, precautions and administration procedures for Ig products, including guidance on informed consent.

Considerations on use of immunoglobulin products for measles PEP

Intramuscular immunoglobulin in individuals weighing more than 30 kg

In Canada, the recommended dosage of IMIg is 0.5 mg/kg, up to a maximum of 15 mL. Therefore, individuals weighing more than 30 kg will receive less than 0.5 mL/kg. The efficacy/effectiveness of IMIg in individuals weighing more than 30 kg (or given at a dose less than 0.5 mL/kg) is not known, nor is the serum concentration of anti-measles antibodies after a dose of IMIg is given. Information on the effective dose of IMIg can only be extrapolated from studies in infants and children. One international study on an IMIg product not currently available in Canada showed that lower doses of IMIg correlated with higher proportions of children who developed clinical measles following exposure[10]. While this study does demonstrate a possible dose-response relationship for IMIg, it cannot be used to predict the effectiveness of IMIg available in Canada (which meets a minimum titre of 25 IU/mL, relative to the 3rd International Standard for measles) due to the type of antibody titration method used in the study and lack of comparison to any international standards[5,20,24]. Another study reported on measles cases after administration of IMIg available in Canada, using dosages of 0.25 mL/kg or less than 0.25 mL/kg[12]. However, results from this study cannot be used to confidently infer a dose response relationship for IMIg, due to incomplete reporting of relevant data (e.g. weight of PEP recipients)[12].

While the stated maximum volume for IMIg is 15 mL[25], there are no data to inform on the maximum volumes for IM injections in general. Convention has been to limit volume per injection to 2 mL in children and 3 to 5 mL in adults (depending on site and muscle mass)[26]. In some circumstances, such as in remote communities, there may be a preference to give IMIg instead of IVIg, due to the healthcare facility and personnel resources required to administer IVIg. More than 15 mL of IMIg can be administered using clinical judgement.

Concentration of measles antibodies in IVIg products

The declining potency of measles antibodies in donor plasma used to manufacture immunoglobulin products used for measles PEP has implications for the recommended dosages of measles PEP. In 2018 the US Food and Drug Administration (FDA) lowered the minimum specification for measles neutralizing antibody in IVIg and SCIg products from 0.48 to 0.36 x Centre for Biologics Evaluation and Research (CBER)

Standard lot 176 (which has a titre of 42 IU/mL), citing declining titres of measles antibodies in plasma donors[20]. The specification for IMIg remains at 0.6 x CBER Standard lot 176. With these new specifications for IVIg products (which products used in Canada also meet), an IVIg dosage of 400 mg/kg is predicted to result in a serum measles antibody titre of approximately 270 mIU/mL two weeks post-infusion, according to pharmacokinetic (PK) modeling[20]. This dosage would meet the proposed minimum target of 240 mIU/mL for individuals with primary immunodeficiencies[20]. For individuals who are immunocompetent, the generally accepted correlate of protection for measles is 120 mIU/mL of measles neutralizing antibodies [20,27].

Considerations for measles PEP eligibility

Measles is a highly transmissible virus. After a known exposure, there is a high likelihood of infection in those who are unvaccinated. Breakthrough infections can occur among vaccinated individuals, especially in the context of exposures at close distance or for a prolonged period of time (e.g. household contact). These previously vaccinated individuals are much less likely to have severe disease or require hospitalization[28,29]. The goal of measles PEP is to prevent severe disease, including hospitalization, as well as to prevent mortality. If a case of measles is identified, it is important to contact trace, quickly identify contacts who are likely susceptible to measles infection and administer PEP as soon as possible. Previous vaccination status, history of measles infection, birth year, and in some cases, use of measles serological testing (IgG), can be considered to determine measles PEP eligibility. Specific populations (e.g., infants, pregnant women and pregnant individuals, or those who are immunocompromised) have additional considerations reflected in the guidance below.

Individuals who are immunocompetent

Previous measles infection, birth year and vaccination history should be considered when determining measles PEP eligibility among immunocompetent individuals. Those with a past infection or those who have completed recommended measles immunization are expected to maintain adequate protection against measles.

Year of birth

Individuals born prior to 1970 in Canada are likely to have been exposed to measles through natural infection. A significant decrease in the annual incidence of measles cases was observed in the 1970s (when measles-only vaccines were introduced) compared to between 1924 to 1958[30]. The average annual number of cases decreased further after the introduction of routine publicly funded immunization programs of one dose of MMR vaccine in infants one year of age in 1983, and even further after the introduction of two-dose MMR schedules across Canada in 1996 to 1997. Individuals born prior to 1970 comprised a very small proportion of measles cases identified in outbreaks in Canada between 2015 to 2024. Four percent of cases (19 out of 492) were among individuals born before 1970, although immunocompetent or immunocompromised status is unknown for these cases[9]. As routine measles vaccination programs were introduced at different times in different countries,

expected immunity to measles based on year of birth should consider the country of birth, if this information is readily available. Since measles elimination status was achieved after 1970 or has not yet been achieved in many countries, the birth year cut-off of 1970 for expected measles immunity through natural infection can be applied to the majority of measles contacts born outside of Canada, except for the United States where the birth year of 1957 should be used[31].

Previous vaccination status

Immunocompetent individuals who have received two doses of a measles-containing vaccine after 12 months of age (given at least 4 weeks apart) are expected to maintain long lasting protection against measles. However, breakthrough infections may occur. Breakthrough infections are generally milder and less likely to result in severe outcomes of measles including hospitalization and death.

Infants under 12 months of age are not currently recommended routine immunization with measles-containing vaccines in Canada. If they are travelling outside of Canada or to areas having outbreaks, they are recommended to receive a measles-containing vaccine if between 6 and 12 months of age. Infants under 6 months of age are not considered for vaccination because the effectiveness and safety of the MMR vaccine has not been established in this age group. While placental transfer of maternal measles antibodies occurs, protection wanes a few months after birth[32-35].

In rare instances, children 6 to under 12 months of age who have been vaccinated with a measles-containing vaccine may be identified as measles contacts and considered for post-exposure prophylaxis. For example, they may have been vaccinated prior to travel outside of Canada to areas where measles is circulating or to locations experiencing outbreaks, or they may have been vaccinated outside of Canada in a country where routine immunization for measles begins at less than 12 months of age. There is limited evidence on the vaccine effectiveness (VE) or durability of protection of measles-containing vaccines in children under 12 months of age who were vaccinated between 6 to under 12 months of age. In one retrospective study from Niger, the effectiveness of measles vaccination in children 6 to 11 months of age who received 1 dose of vaccine ranged from 19.8% to 82.8% depending on age at time of infection and age at vaccination[36]. There were no cases of measles in children 12 to 23 months of age who received 2 doses of a measles-containing vaccine before 12 months of age (0 out of 9 children) and 284 cases of measles in children from the same age group who were not vaccinated (284 out of 403 children)[36].

Previous measles infection

Immunocompetent individuals with a past measles infection are expected to maintain long lasting protective immunity against measles infection.

Individuals who are immunocompromised

Immunocompromising conditions and immunosuppressive therapies are heterogenous in the level of immunocompromise, leading to variability in both an individual's risk of contracting severe measles after an exposure, and the likelihood that past vaccination or infection will confer protective immunity against measles. Severely immunocompromised individuals who cannot mount adequate de novo immune responses or immunological memory responses (e.g., individuals with severe combined immunodeficiency, hematopoietic stem cell transplant recipients within the first 1-2 years) are considered susceptible to measles infection following exposure regardless of pre-transplant vaccination status. However, individuals who are immunocompromised and have detectable serum measles IgG meeting thresholds generally considered protective are unlikely to derive additional benefit from PEP with Ig[20].

Measles during pregnancy

Measles infection during pregnancy can lead to serious complications such as pneumonitis, hepatitis and premature labour, thus PEP should be considered for susceptible pregnant contacts[37]. Similar to immunocompetent adults, year of birth, past vaccination and/or infection history, and documented laboratory evidence of measles infection or immunity should be used to inform eligibility for PEP.

Measles and rubella-containing vaccines are generally contraindicated in pregnant women and pregnant individuals because there is a theoretical risk to the fetus. However, termination of pregnancy should not be recommended following inadvertent immunization with a measles and rubella-containing vaccine on the basis of fetal risks following maternal immunization.

Serological testing to inform expected measles immunity post-exposure

In specific circumstances, serological testing (e.g., serum anti-measles IgG assays) can help determine if certain individuals could benefit from PEP, and can be used to optimize the use of Ig products. The gold-standard assay to test for the presence of anti-measles neutralizing antibodies is the plaque reduction neutralization test (PRNT). PRNTs are labour-intensive and take several days to complete and are not feasible nor practical for routine assessments of immunity, or when results are needed rapidly. Enzyme-based immunoassays (EIAs) that detect the presence of anti-measles binding IgG antibodies are more suited to high throughput testing, rapid generation of results, and are available commercially and already in use in most Canadian provinces and territories. There is generally good agreement between EIAs and PRNTs, although EIAs may have lower sensitivity[38]. EIAs have high specificity and thus have a high positive predictive value[38].

Ethics, Equity, Feasibility and Acceptability Considerations

No significant ethical issues related to updating guidance on measles PEP were identified.

Measles infection can lead to severe outcomes among susceptible individuals. Rapid access to measles PEP products is critical across all Canadian regions to mitigate severe outcomes associated with measles infection, especially for vulnerable, high-risk populations such as susceptible individuals who are severely immunocompromised, pregnant women and pregnant individuals, and children less than 12 months of age. Updated guidance with clearly defined criteria for measles PEP would potentially increase equity, by increasing the likelihood of the most vulnerable individuals getting appropriate products for measles PEP.

A large-scale measles outbreak may pose significant resource and public health management constraints on jurisdictions. Remote regions may also have additional feasibility constraints as administration of IVIg may not be possible without trained personnel. Risk assessments, and in some circumstances, the use of serological testing, may be needed to inform public health actions for large measles outbreaks. Access to timely serology results may decrease the number of people who need PEP, allowing public health authorities to better allocate resources in outbreaks.

Economics

Although it is recommended that NACI guidance development should include a consideration of economic evidence, economic evidence was not identified as necessary for this policy question. Specifically, it was noted that PEP is already recommended following exposure to measles in individuals without expected measles immunity and that the updated guidance would not be expected to result in substantial increases in resource use associated with PEP.

Recommendations

1. NACI continues to strongly recommend completion of the routine childhood and adult recommended immunization schedule with a measles-containing vaccine.

- **High (e.g., >95%) routine measles immunization coverage provides herd immunity protecting people who live in Canada and ensuring Canada remains free of endemic measles.**
- **Routine immunization against measles is the best tool to mitigate the size of measles outbreaks and reduce the need for measles post-exposure prophylaxis.**
- **In the absence of contraindication to the vaccine, the measles-containing vaccine series is effective in protecting immunocompetent individuals and is the preferred strategy.**

(Strong NACI recommendation)

Further information on routine immunization with measles-containing vaccines can be found in the CIG, Part 4, Measles vaccines chapter[23].

2. NACI recommends that post-exposure prophylaxis (PEP) following exposure to measles should be offered to individuals not expected to have immunity to measles.

(Strong NACI recommendation)

Strategies for PEP for different populations

- **Tables 1-3 provide updated summaries of recommended measles PEP strategies by population.**
- These strategies for measles PEP are based on the available evidence, known and anticipated benefits and risks related to measles PEP, as well as expert opinion. They are a guide that jurisdictions can adapt to fit their specific public health needs.
- Any reference to measles serological testing below means measles IgG antibodies.

Table 1. Summary of recommended measles post-exposure prophylaxis strategies for infants and immunocompetent individuals

See additional guidance below Table 1 for a summary of updated measles PEP recommendations for pregnant women and pregnant individuals (Table 2), and for individuals 6 months of age and older who are immunocompromised (Table 3).

Populations	**Time since exposure to measles**	
	≤ 72 hours	**73 hours to 6 days**
Infants less than 6 months of age	**IMIg 0.5 mL/kg**[a,b] as soon as possible and within 6 days of exposure.	
Immunocompetent, unvaccinated infants 6 to under 12 months of age[c] (see Rationale and Additional Considerations below for further advice for vaccinated infants in this age group)	**MMR vaccine**[d,e] as soon as possible and within 72 hours of exposure.	**IMIg 0.5 mL/kg**[a,b] as soon as possible and within 6 days of exposure.
Immunocompetent individuals 12 months of age and older	Consider **criteria for expected measles immunity**: • Year of birth before 1970 • History of laboratory-confirmed measles infection • Receipt of two doses of a measles-containing vaccine (given at least 4	

	weeks apart) administered after 12 months of age • Documented evidence of previous positive measles serology[f] If none of the listed criteria for expected measles immunity are met or vaccination history is unknown, administer **measles-containing vaccine** as soon as possible[g], If any of the listed criteria for expected measles immunity are met, measles PEP is not recommended.

a. Unless contraindicated, individuals who receive Ig should receive routine immunization with measles-containing vaccines after the specified interval. For more information, refer to the CIG, Part 1, Blood Products, Human Immunoglobulin and Timing of Immunization[39].
b. IMIg should be administered at a concentration of 0.5 mL/kg, to a maximum of 15 mL administered over multiple injection sites. If injection volume is a major concern, or if recipients weigh >30 kg, or if access to IVIg is more feasible than access to IMIg, IVIg can be administered at a concentration of 400 mg/kg.
c. For immunocompetent children 6 months to under 12 months of age who have previously received a dose of MMR, options include a dose of MMR within 72 hours of exposure or IMIg within 6 days of exposure if seronegative for measles**;** clinical judgement should be used. Two doses of a measles-containing vaccine (given at least 4 weeks apart) would still be required after 12 months of age for long term protection. Please see Rationale and Additional Considerations for more information.
d. Two additional doses of measles-containing vaccine administered after 12 months of age (given at least 4 weeks apart) are required for long-term protection.
e. NACI has not reviewed the use of MMRV in infants less than 12 months of age. MMR is recommended for PEP for infants 6 to under 12 months of age.
f. Routine testing for laboratory evidence of measles immunity is not recommended for the general population.
g. A measles-containing vaccine is not known to provide protection after 72 hours of exposure, however, starting or completing a two-dose series should not be delayed as it provides long term protection.

Table 2. Summary of updated recommended measles post-exposure prophylaxis strategies for pregnant women and pregnant individuals by risk level

Immune Status	Recommended measles PEP strategy for pregnant women and pregnant individuals
Unvaccinated/known measles IgG negative (known status)	IVIg (400 mg/kg)[a] as soon as possible and within 6 days of exposure. Serological testing is not required Administer measles-containing vaccine series postpartum for future protection
One previous dose of measles-containing vaccine or uncertain vaccination status	Consider serological testing if results are expected within 24h of sampling time IVIg (400 mg/kg)[a] as soon as possible and within 6 days of exposure if serology is negative or timely measles serology testing is not available (i.e., results not expected within 24 hours of sampling) Administer measles-containing vaccine postpartum for future protection
Meets criteria for expected measles immunity (Table 1, row 3)	Measles PEP is not recommended

a. IMIg is no longer recommended for individuals weighing more than 30 kg due to the lack of evidence of the efficacy/effectiveness of IMIg administered at dosages below 0.5 mL/kg. In some circumstances, such as in remote communities, there may be a preference to give IMIg instead of IVIg. More than 15 mL of IMIg can be administered using clinical judgement.

Table 3. Summary of updated recommended measles post-exposure prophylaxis strategies for individuals 6 months of age and older who are immunocompromised.

Note: Recommended measles PEP strategies are stratified by extent of immunocompromise, the likelihood of maintaining measles-antibody mediated protection from past vaccination or infection, and the ability to safely receive a measles-containing vaccine. Additional considerations are given below Table 3. This table does not provide a comprehensive list of immunocompromising medical conditions, and therapies that result in immunosuppression. Assessment of severity of immunocompromising condition is best determined by consulting with the treating physician, infectious disease expert/immunologist, or special immunization clinic.

Group	**Examples of immunocompromising conditions**	**Recommended measles PEP strategy**
Group 1: Individuals with an **absent/ near absent immune system** and therefore are **not expected to have sufficient natural/acquired measles antibody-mediated protection** and are known to have a high risk of severe disease	**1. Transplant** • Within 12 months of receiving autologous hematopoietic stem cell transplant (HSCT) or 24 months of receiving allogeneic HSCT, and HSCT recipients with chronic graft-versus-host disease (GVHD) • Within 12 months of a solid organ transplant **2. Chimeric antigen receptor T-cell (CAR T) therapy** • Within 12 months of receiving CAR T therapy for malignancy **3. Acute lymphoblastic leukemia (ALL)** • ALL within and up to 3 months after completion of chemotherapy or 6 months after completion of B cell-depleting therapy	• Offer PEP as soon as possible and within 6 days of exposure; previous vaccination status/serological testing is not relevant • If >30 kg, IVIg[b,e] (400 mg/kg) • If ≤ 30 kg, IMIg[b,f] (0.5 mL/kg)

	4. Human immunodeficiency virus (HIV) infection • HIV infection with a current CD4 T cell count <200 cells/mm^3 (age ≥14 years) or <15% for children aged 1 to 13 years **5. Primary immunodeficiency** • Significant primary immunodeficiency or inborn error of immunity (e.g., X-linked agammaglobulinemia, severe combined immunodeficiency) for which live vaccines are contraindicated[a,b] **6. Therapies/medications**[c] • Receiving cyclophosphamide or anti-thymocyte globulin[d] • Receiving or completed alemtuzumab or B cell-depleting (e.g., anti-CD20, etc.) treatment within the past 12 months	
Group 2: Individuals who are immunocompromised who **may have measles antibody-mediated protection** from known previous vaccination or infection	**1. Transplant** • More than 12 months but less than 24 months post autologous HSCT without evidence of GVHD requiring immunosuppression and received measles vaccine after transplant • >12 months post solid organ transplant without evidence of rejection requiring augmented immunosuppression	• Measles immunity and need for measles PEP should be examined regardless of year of birth, or measles vaccination status • Ideally, consult the specialist responsible for the clinical care of the individual or an

	2. CAR T-cell therapy
	• >12 months after CAR T-cell therapy[g]
	
	3. Malignancy
	• Lymphoproliferative diseases including hematologic cancers (e.g., indolent lymphoma, lymphocytic leukemia or plasma cell lymphoma not included above) not receiving B cell-targeting therapy
	• Immunotherapy/chemotherapy/ radiotherapy for malignancy other than ALL (solid tumour or hematologic) that is ongoing or completed within the last 3 months
	
	4. Secondary immunodeficiency
	• Secondary hypogammaglobulinemia due to disease or therapy[b]
	
	5. Therapies/medications[c]
	• Targeted immunosuppressive biologic and small molecule therapies not mentioned above (e.g., tumour necrosis factor inhibitors, costimulation modulators, cytokine inhibitors, tyrosine kinase inhibitors) that are ongoing or received <6 months prior to exposure, alone or in combination with: 1) steroids or 2) disease-modifying antirheumatic drugs (DMARDs)[h]
	• Ongoing or <4 weeks since completion of daily corticosteroid therapy at a prednisone or equivalent dose of ≥20 mg/day for adults or ≥1 mg/kg/day for children for ≥14 days, or undergoing dose
		infectious disease expert/ immunologist
		
		• Consider rapid measles serological testing
		
		• If serology is negative or measles serology testing is not available within 24 hours of sampling, administer PEP as soon as possible and within 6 days of exposure
		  • If >30 kg, administer IVIg[b,e] (400 mg/kg)
		
		  • If ≤ 30 kg, administer IMIg[b,f] (0.5 mL/kg)

	tapering following treatment with a prednisone or equivalent dose of ≥20 mg/day for adults or ≥1 mg/kg/day for children for ≥14 days[i] • Ongoing or within 3 months of completing treatment with immunosuppressive drugs for immune-mediated diseases (e.g., methotrexate >0.4 mg/kg/week [children: >10 mg/m^2/week; adults: >15 mg/m^2/week], azathioprine >3 mg/kg/day, 6-mercaptopurine >1.5 mg/kg/day, cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil, and small molecule inhibitors)[h]	
Group 3: Individuals who have low-level immunocompromise who are expected to have measles antibody-mediated protection from known previous infection or vaccination, for whom measles-containing vaccine is not contraindicated	**1. Transplant** • >24 months following HSCT with no chronic GVHD and received measles-containing vaccine after transplant	If no documented evidence of positive measles IgG post-transplant, provide **measles-containing vaccine** as soon as possible. See Table 1 for more details[j].
	2. HIV infection • Asymptomatic HIV-infected patients with CD4 T cell counts of >200 cells/mm^3 (age ≥14 years) or >15% for children aged 1 to 13 years **3. Primary immunodeficiencies** • Minor B cell deficiency with intact T cell function not requiring Ig therapy, partial T cell defects, and other primary immune deficiencies or inborn error of immunity **4. Therapies/medications**[c] • Prednisone or equivalent doses <20 mg/day for adults or <1 mg/kg/day for children taken for ≥14 days or receiving	Consider criteria for expected measles immunity: • Year of birth before 1970 • History of laboratory-confirmed measles infection • Receipt of two doses of a measles-containing vaccine (given at least 4 weeks apart) administered after 12 months of age • Documented evidence of

	alternate day corticosteroid therapy[h] • ≥4 weeks after discontinuation of long-term (≥14 days) high-dose systemic steroids, or immediately after discontinuation of high-dose steroids taken for <14 days[i] • Therapies that target immune system components, but are unlikely to have significant effects on humoral immunity pathways (e.g., IgE blockers, IL-5 inhibitors, IL-5 receptor blockers, IL-4 inhibitors, IL-13 inhibitors and other cytokine inhibitors) • Methotrexate ≤0.4 mg/kg/week (children: ≤10 mg/m^2 /week; adults: ≤15 mg/m^2/week) • Azathioprine ≤3 mg/kg/day[k] • 6-mercaptopurine ≤1.5 mg/kg/day • Hydroxychloroquine (any dose)	positive measles serology If none of the listed criteria for expected measles immunity is met or patient history is unknown, provide **measles-containing vaccine** as soon as possible. See **Table 1** for more details[j]. If any of the listed criteria for expected measles immunity is met, measles PEP is not recommended.

a. There may be other forms of combined immunodeficiencies with a severe phenotype that may impact the ability to maintain measles antibody-mediated protection from past infection or vaccination. Healthcare providers should use clinical judgement when assessing whether Ig PEP should be administered as soon as possible or if serology should be considered.
b. For individuals who are already receiving Ig replacement therapy (as IVIg or SCIg), Ig for measles PEP is not required if the last dose of IVIg (at least 400 mg/kg) was received within three weeks prior to measles exposure, or if SCIg (at least 200 mg/kg) was received for 2 consecutive weeks prior to measles exposure. If outside of these parameters, administer the patient's usual dose as soon as possible.
c. As new immunomodulatory drugs become authorized or if various combinations of immunomodulatory drugs are used, advice from clinical experts should be sought as to the degree of immunosuppression likely to be induced and the effect on immunity from past measles infection and/or vaccination.
d. The period for which an individual remains immunocompromised and at high risk of severe disease after cessation of these medications can vary. Consultation with the specialist responsible for the clinical care of the individual is recommended.
e. IMIg is no longer recommended for individuals weighing more than 30 kg due to the lack of evidence of the efficacy/effectiveness of IMIg administered at dosages below 0.5 mL/kg. In some circumstances, such as in remote communities, there may be a preference to give IMIg instead of IVIg. More than 15 mL of IMIg can be administered using clinical judgement.
f. IMIg should be administered at a concentration of 0.5 mL/kg, to a maximum of 15 mL administered over multiple injection sites. If injection volume is a major

concern, or if recipients weigh >30 kg, or if access to IVIg is more feasible than access to IMIg, IVIg can be administered at a concentration of 400 mg/kg.

g. The timeframe for immune reconstitution following CAR T-cell therapy is variable. Consultation with the specialist responsible for the clinical care of the individual is recommended.
h. Interval may vary with the type and intensity of treatment. Period may be shortened for biologics/treatments with a shorter duration of effect.
i. For children, a dose of 20 mg/day is often equivalent to doses below 2 mg/kg/day. There is no consensus regarding the lowest prednisone dose that would be considered immunosuppressive in children; thresholds vary across various guidelines from ≥0.5 mg/kg/day to ≥2 mg/kg/day[40-42].
j. A measles-containing vaccine is not known to provide protection after 72 hours of exposure, however, starting or completing a two-dose series should not be delayed as it provides long term protection.
k. Individuals on azathioprine exhibiting signs of myelosuppression/myelotoxicity should be assessed for susceptibility and need for Ig PEP. Please refer to Group 2: Individuals who are immunocompromised who may have measles antibody-mediated protection from known previous vaccination or infection in Table 3.

Rationale and additional considerations

- Routine immunization, including completing immunization prior to pregnancy or beginning immunosuppressive therapy, continues to be essential to protect individuals in Canada. Achieving and maintaining vaccination coverage of at least 95% is necessary to develop herd immunity, reduce the impact of importations and maintain measles elimination in Canada.
- With increasing measles activity globally, reduced vaccination rates, and increased international travel measles cases in Canada will continue to occur. This will also result in the need for measles PEP and other public health measures in response to imported measles cases and outbreaks.
- Vaccination is anticipated to provide long-lasting protection against measles however breakthrough infection can occur. Breakthrough infections are generally milder and less likely to result in severe outcomes of measles including hospitalization and death[28,29].
- IMIg is no longer recommended for individuals weighing more than 30 kg due to the lack of evidence of the efficacy/effectiveness of IMIg administered at dosages below 0.5 mL/kg. In some circumstances, such as in remote communities, there may be a preference to give IMIg instead of IVIg. More than 15 mL of IMIg can be administered using clinical judgement.
- To facilitate administration of IMIg in children, injection volumes of up to 3 mL could be considered to reduce the number of injections, using clinical judgement. For high volume injections, the anterolateral thigh is generally preferred due to the greater muscle mass. Clinical judgement should be used when selecting the most appropriate site for IMIg administration.
- A measles-containing vaccine is expected to provide effective protection as post-exposure prophylaxis when administered within 72 hours of exposure to individuals able to mount a humoral response to primary vaccination. However, it is important, particularly during an ongoing measles outbreak, to continue to

offer measles-containing vaccine, even if >72h since exposure, to provide long-term protection.

- In some situations where the risk of transmission from a close contact is high (i.e., household contacts of a confirmed case), IMIg no later than 6 days after exposure could be considered, using clinical discretion, for unvaccinated, immunocompetent children 12 months of age or older weighing 30 kg or less, considering factors such as acceptability and feasibility of timely administration. IMIg is a form of passive immunity and will not provide long-term protection. For long-term protection, vaccination with two doses of a measles-containing vaccine given at least 4 weeks apart after 12 months of age is recommended.
- Rarely, immunocompetent children 6 months to under 12 months of age who have previously received a dose of MMR may be exposed to measles. In this situation, clinical judgement should be used, considering factors such as the nature and intensity of exposure, limited evidence on the VE of 1 dose of MMR in this age group, and timing of previous dose. Providing MMR within 72 hours of exposure could be considered, however an additional 2 doses after 12 months of age, given at least 4 weeks apart, are required for long-term protection. Serological testing (with results expected within 24 hours of sampling time) can be done, and if negative, IMIg should be administered (within 6 days of exposure). If considering administration of IMIg after receipt of MMR, refer to the CIG, Part 1, Blood Products, human Immunoglobulin and timing of Immunization[39].
- SCIg products were considered but ultimately not recommended for measles PEP at this time. SCIg administration requires specialized training, presenting feasibility hurdles for implementation. Additionally, data on the safety and efficacy/effectiveness of a single dose of SCIg for measles PEP are not available.

- **Role of Measles serology testing considering extensive resource requirements for IVIg**
    - IVIg requires administration in a specialized health care setting and active patient monitoring over several hours of infusion, performed by appropriately trained staff. In remote settings, need for IVIg administration can require evacuation by air to a larger medical centre.
    - Given the diversity across Canadian regions and varying access to healthcare services, serology may not be routinely available with a rapid (e.g., within 24 hours of sampling) turnaround time in all jurisdictions. However, in the event of a large, ongoing measles outbreak, jurisdictions should consider increasing capacity for serologic testing for measles.
    - Large-scale use of IVIg in vulnerable populations would require extensive healthcare resources that could be mitigated by the use of serological testing to inform who is most at risk and should be prioritized for PEP.
    - The use of serology should be considered only if results are available with turnaround time of 24-48 hours of sampling that allows for Ig PEP administration within 6 days of exposure.

- Routine testing for laboratory evidence of measles immunity is not recommended for the general population.

- **Guidance for measles PEP for individuals who are immunocompromised is based on their level of immunocompromise (summarized in Table 3).**
  - Immunocompromising conditions and immunosuppressive therapies are heterogenous in the level of immunocompromise, leading to variability in both an individual's risk of contracting severe measles after an exposure, and the likelihood that past vaccination or infection will confer protective immunity against measles after the onset of immunocompromise.
  - Individuals receiving chronic IVIg or SCIg therapy may already have sufficient serum measles antibodies to prevent infection. For individuals who are already receiving Ig replacement therapy, Ig for measles PEP is not required if the last dose of IVIg (at least 400 mg/kg) was received within three weeks prior to measles exposure, or if two consecutive weeks of SCIg (at least 200 mg/kg) was received prior to measles exposure. If outside of these parameters, administer the patient's usual dose as soon as possible.
  - Public health units should consider having established relationships with clinical experts who can assist in evaluating immunocompromised individuals who have been exposed to measles (e.g., nature of immunocompromise, use of serology vs immediate Ig PEP); such expert consultation will be particularly important during larger/ongoing outbreaks where administering IVIg to large numbers of people is challenging.
- As measles epidemiology evolves both globally and within Canada, NACI will continue to monitor emerging evidence and update guidance on measles post-exposure prophylaxis and other recommendations on measles vaccination as needed.

Table 4. NACI recommendations: Strength of recommendation

Strength of Recommendation	**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.

Research Priorities

1. Further evaluation of the effectiveness and safety of products for measles PEP, including studies that control for and/or compare different routes of administration for Ig products (IM, IV and SC), intervals between measles exposure and PEP administration, type and duration of measles exposure, previous vaccination and/or infection status, and studies that include or compare special populations (e.g., individuals who are immunocompromised, pregnant women and pregnant individuals, and infants) and studies that assess duration of effectiveness and effectiveness against re-infection.
2. Evaluation of the pharmacokinetics (e.g., half-life, bioavailability) of Ig products for measles PEP, including comparisons between IV, IM and SC delivery.
3. Evaluation and comparison of different dosages of immunoglobulin products marketed in Canada and/or products titred against US or WHO (World Health Organization) standards, in both infant and adult populations
4. Assessment of the long-term durability of measles-containing vaccine effectiveness through the lifespan.
5. Evaluation of the safety and effectiveness of measles-containing vaccines in various immunocompromised populations for pre-exposure and post-exposure use.

List of Abbreviations

AEFI	Adverse event following immunization
ALL	Acute lymphoblastic leukemia
CAR T	Chimeric antigen receptor T-cell
CBER	Center for Biologics Evaluation and Research
CI	Confidence interval
CIC	Canadian Immunization Committee
CIG	Canadian Immunization Guide
CIDSC	Canadian Infectious Disease Steering Committee
CMRSS	Canadian Measles/Rubella Surveillance System
DMARD	Disease-modifying antirheumatic drug
EEFA	Ethics, equity, feasibility and acceptability
EIA	Enzyme-based immunoassay
FDA	Food and Drug Administration
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
GVHD	Graft versus host disease
HIV	Human immunodeficiency virus
HSCT	Hematopoietic stem cell transplantation
IDSA	Infectious Diseases Society of America
Ig	Immunoglobulin
IL	Interleukin
IM	Intramuscular
IU	International Units
IV	Intravenous
IMIg	Intramuscular immunoglobulin
IVIg	Intravenous immunoglobulin
mIU	Milli International Units
mL	Millilitres
MMR	Measles, Mumps, and Rubella
MMRV	Measles, Mumps, Rubella, and Varicella
NACI	National Advisory Committee on Immunization
PEP	Post-exposure prophylaxis
PHAC	Public Health Agency of Canada
PK	Pharmacokinetic(s)
PRNT	Plaque reduction neutralization test
RR	Risk ratio
SAE	Serious adverse event

SC	Subcutaneous
SCIg	Subcutaneous immunoglobulin
SOT	Solid organ transplant
UKHSA	United Kingdom Health Security Agency
US	United States
VE	Vaccine effectiveness
WHO	World Health Organization

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NACI Measles-Blood Products Working Group

Members: M O'Driscoll (Chair), V Arsenault, A Chan, V Dubey, T Filardo, J Hiebert, M Houle, D Moore, A Pham-Huy, V Price, O Prokopchuk-Gauk, C Renaud, K Webert and S Wilson.

NACI

NACI Members: R Harrison (Chair), V Dubey (Vice-Chair), M Andrew, J Bettinger, N Brousseau, A Buchan, H Decaluwe, P De Wals, E Dubé, K Hildebrand, K Klein, M O'Driscoll, J Papenburg, A Pham-Huy, B Sander, and S Wilson.

Liaison Representatives: L Bill/ M Nowgesic (Canadian Indigenous Nurses Association), S Buchan (Canadian Association for Immunization Research, Evaluation and Education) E Castillo (Society of Obstetricians and Gynaecologists of Canada), J Comeau (Association of Medical Microbiology and Infectious Disease Control), M Lavoie (Council of Chief Medical Officers of Health), J MacNeil (Center for Disease control and Prevention), M McIntyre (Canadian Nurses Association), D Moore (Canadian Paediatric Society), M Osmack (Indigenous Physicians Association of Canada), J Potter (College of Family Physicians of Canada), A Pucci (Canadian Public Health Association), D Singh (Canadian Immunization Committee), and A Ung (Canadian Pharmacists Association).

Ex-Officio Representatives: E Ebert (National Defence and the Canadian Armed Forces), P Fandja (Marketed Health Products Directorate, Health Canada), E Henry (Centre for Immunization Surveillance and Programs (CISP), PHAC), M Lacroix (Public Health Ethics Consultative Group, PHAC), T Stothart (Centre for Immunization Surveillance, PHAC), J Kosche (Centre for Vaccines and Therapeutics Readiness (CVTR), PHAC), C Pham (Biologic and Radiopharmaceutical Drugs Directorate, Health Canada), M Routledge (National Microbiology Laboratory, PHAC), M Su (COVID-19 Epidemiology and Surveillance, PHAC), and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada).

References

1. Montroy J, Yan C, Khan F, et al. Post-exposure prophylaxis for the prevention of measles: A systematic review. *Vaccine.* Jan 2025;47(126706)http://doi.org/10.1016/j.vaccine.2025.126706.

2. Ismail SJ, Hardy K, Tunis MC, et al. A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations. *Vaccine.* 2020 Aug 10;38(36):5861-5876. http://doi.org/10.1016/j.vaccine.2020.05.051.

3. UK Health Security Agency. National measles guidelines [Internet]. United Kingdom. 2024 Jul 25 [cited 2024 Dec 23]. Available from: https://www.gov.uk/government/publications/national-measles-guidelines

4. World Health Organization. A 30-fold rise of measles cases in 2023 in the WHO European Region warrants urgent action. [Internet]. 2023 Dec 14 [cited 2024 Nov 14]. Available from: https://www.who.int/europe/news/item/14-12-2023-a-30-fold-rise-of-measles-cases-in-2023-in-the-who-european-region-warrants-urgent-action

5. Tunis M, Salvadori M, Dubey V, Baclic O. Updated NACI recommendations for measles post-exposure prophylaxis Ottawa. 2018 Sep 06 [cited 2025 Jan 09]. Available from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2018-44/issue-9-september-6-2018/article-7-naci-recommendation-pep.html

6. Osman S, Crowcroft N, McLachlan E, et al. Population immunity to measles in Canada using Canadian Health Measures survey data – A Canadian Immunization Research Network (CIRN) study. *Vaccine.* 2022 May 20;40(23)http://doi.org/10.1016/j.vaccine.2022.04.011.

7. Public Health Agency of Canada. Adult National Immunization Coverage Survey (aNICS): 2023 results [Internet]. Ottawa (ON). 2024 Jan 17 [cited 2024 Nov 18]. Available from: https://www.canada.ca/en/public-health/services/immunization-vaccines/vaccination-coverage/adult-national-immunization-coverage-survey-2023-results.html

8. Public Health Agency of Canada. Highlights from the 2021 childhood National Immunization Coverage Survey (cNICS) [Internet]. Ottawa (ON). 2024 Jun 18 [cited 2024 Nov 18]. Available from: https://www.canada.ca/en/public-health/services/immunization-vaccines/vaccination-coverage/2021-highlights-childhood-national-immunization-coverage-survey.html

9. Public Health Agency of Canada. Canadian Measles and Rubella Surveillance System [CMRSS]. Data cut-off 2024 Sep 03. Ottawa (ON):

10. Endo A, Izumi H, Miyashita, M, et al. Current efficacy of postexposure prophylaxis against measles with immunoglobulin. *The Journal of pediatrics.* 2001 Jun;138(6)http://doi.org/10.1067/mpd.2001.113710.

11. Arciuolo R, Jablonski R, Zucker J, Rosen J. Effectiveness of Measles Vaccination and Immune Globulin Post-Exposure Prophylaxis in an Outbreak Setting-New York City, 2013. *Clinical infectious diseases.* 2017 Nov 13;65(11)http://doi.org/10.1093/cid/cix639.

12. Bigham M, Murti M, Fung C, et al. Estimated protective effectiveness of intramuscular immune serum globulin post-exposure prophylaxis during a measles outbreak in British Columbia, Canada, 2014. *Vaccine.* 2017 May 09;35(20)http://doi.org/10.1016/j.vaccine.2017.03.069.

13. Charlier C, Hourrier S, Leruez-Ville M, et al. Polyvalent immunoglobulins in neonates after perinatal exposure to measles: Benefits and long-term tolerance of immunoglobulins. *Journal of Infection.* 2015;71(1)http://doi.org/10.1016/j.jinf.2015.01.010.

14. Kaman A, Oğuz M. Prevention of Health Care–Associated Measles Transmission in a Pediatric Clinic. *Journal of Pediatric Infectious Diseases.* 2022 Nov;17(06)http://doi.org/10.1055/s-0042-1758054.

15. Kohlmaier B, Holzmann H, Stiasny K, et al. Effectiveness and Safety of an Intravenous Immune Globulin (IVIG) Preparation in Post-exposure Prophylaxis (PEP) Against Measles in Infants. *Frontiers in Pediatrics.* 2021 Dec 02;9http://doi.org/10.3389/fped.2021.762793.

16. Sakuta H, Sawada S, Kuroki Y. Severity of Measles among Patients with Incidental Postexposure Vaccination. *Japanese Journal of Infectious Diseases.* 2008 Jul 28;61(4)http://doi.org/10.7883/yoken.JJID.2008.304.

17. Sheppeard V, Forssman B, Ferson M, et al. The effectiveness of prophylaxis for measles contacts in NSW. *New South Wales public health bulletin.* 2009 May;20(5-6)http://doi.org/10.1071/NB08014.

18. Tapisiz A, Polat M, Kara S, et al. Prevention of measles spread on a paediatric ward. *Epidemiology and infection.* 2015 Mar;143(4)http://doi.org/10.1017/S0950268814001344.

19. Williamson K, Faddy H, Nicholson S, et al. A Cross-Sectional Study of Measles-Specific Antibody Levels in Australian Blood Donors—Implications for Measles Post-Elimination Countries. *Vaccines 2024.* 2024 Jul 22;12(7):818. http://doi.org/10.3390/vaccines12070818

20. U.S. Food and Drug Administration (FDA). Letter to Immune Globulin (Human) Licensed Manufacturers: Option to Lower Lot Release Specification for Required Measles Antibody Potency Testing [Internet]. 2018 Nov 05 [cited 2024 Nov 18]. Available from: https://www.fda.gov/media/118428/download

21. Stokes J, Maris E, Gellis S. Chemical, Clinical, and Immunological Studies on the Products of Human Plasma Fractionation. Xi. The Use of Concentrated Normal Human Serum Gamma Globulin (Human Immune Serum Globulin) in

the Prophylaxis and Treatment of Measles. *The Journal of clinical investigation.* 1944 Jul;23(4)http://doi.org/10.1172/JCI101518.

22. Young M, Nimmo G, AW C, MA J. Post-exposure passive immunisation for preventing measles. *Cochrane Database of Systematic Reviews.* 2014;2014(4)http://doi.org/10.1002/14651858.CD010056.pub2.

23. Public Health Agency of Canada. Measles vaccines: Canadian Immunization Guide [Internet]. Ottawa. 2023 Sep 08 [cited 2024 Nov 18]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-12-measles-vaccine.html

24. National Institute for Biological Standards and Control. 3rd International Standard for Anti-Measles NIBSC code: 97/648 Instructions for use Version 2.0 [Internet]. Potters Bar (UK). 2008 Feb 26 [cited 2025 Jan 16]. Available from: https://nibsc.org/documents/ifu/97-648.pdf

25. Grifols Therapeutics LLC. Product monograph: GamaSTAN (Immunoglobulin [Human]) [Internet]. Ontario. Grifols Canada Ltd; 2019 Mar 13 [cited 2024 Nov 18]. Available from: https://pdf.hres.ca/dpd_pm/00050163.PDF

26. Public Health Agency of Canada. Vaccine administration practices: Canadian Immunization Guide [Internet]. 2024 Sep 05 [cited 2024 Nov 18]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-8-vaccine-administration-practices.html#p1c7a3c

27. Chen R, Markowitz L, Albrecht P, et al. Measles antibody: reevaluation of protective titers. *The Journal of infectious diseases.* 1990 Nov;162(5)http://doi.org/10.1093/infdis/162.5.1036.

28. Leung J, Munir N, Mathis A, et al. The Effects of Vaccination Status and Age on Clinical Characteristics and Severity of Measles Cases in the United States in the Post-Elimination Era, 2001-2022. *Clinical infectious diseases.* 2024 Sep 13;http://doi.org/10.1093/cid/ciae470.

29. Sundell N, Dotevall L, Sansone M, et al. Measles outbreak in Gothenburg urban area, Sweden, 2017 to 2018: low viral load in breakthrough infections. *Eurosurveillance.* 2019 Apr 25;24(17)http://doi.org/10.2807/1560-7917.ES.2019.24.17.1900114.

30. Public Health Agency of Canada. Guidelines for the Prevention and Control of Measles Outbreaks in Canada Ottawa (ON). Government of Canada; 2013 [cited Available from: https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/publicat/ccdr-rmtc/13vol39/acs-dcc-3/assets/pdf/meas-roug-eng.pdf

31. Watson J, Hadler S, Dykewicz C, et al. Measles, Mumps, and Rubella -- Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports.* 1998;47:1-57.

32. Science M, Savage R, Severini A, et al. Measles Antibody Levels in Young Infants. *Pediatrics.* 2019 Dec;144(6)http://doi.org/10.1542/peds.2019-0630.

33. Guerra F, Crowcroft N, Friedman L, et al. Waning of measles maternal antibody in infants in measles elimination settings - A systematic literature review. *Vaccine.* 2018 Feb 28;36(10)http://doi.org/10.1016/j.vaccine.2018.01.002.

34. Leuridan E, Hens N, Hutse V, et al. Early waning of maternal measles antibodies in era of measles elimination: longitudinal study. *BMJ.* 2010 May 18;340http://doi.org/10.1136/bmj.c1626.

35. Waaijenborg S, Hahné SJM, Mollema L, et al. Waning of Maternal Antibodies Against Measles, Mumps, Rubella, and Varicella in Communities With Contrasting Vaccination Coverage. *The Journal of Infectious Diseases.* 2013 May 8;208(1)http://doi.org/10.1093/infdis/jit143.

36. Kaninda A, Legros D, Jataou I, et al. Measles vaccine effectiveness in standard and early immunization strategies, Niger, 1995 - PubMed. *The Pediatric infectious disease journal.* 1998 Nov;17(11)http://doi.org/10.1097/00006454-199811000-00014.

37. Atmar RL, Englund JA, Hammill H. Complications of Measles during Pregnancy. *Clinical Infectious Diseases.* 14(1)http://doi.org/10.1093/clinids/14.1.217.

38. Latner D, Sowers S, Anthony K, et al. Qualitative Variation among Commercial Immunoassays for Detection of Measles-Specific IgG. *Journal of clinical microbiology.* 2020 May 26;58(6)http://doi.org/10.1128/JCM.00265-20.

39. Public Health Agency of Canada. Blood products, human immunoglobulin and timing of immunization: Canadian Immunization Guide [Internet]. 2024 Jun 27 [cited 2024 Nov 18]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html

40. Rubin L, Levin M, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical infectious diseases.* 2014 Feb;58(3)http://doi.org/10.1093/cid/cit684.

41. Public Health Agency of Canada. Immunization of immunocompromised persons: Canadian Immunization Guide [Internet]. 2024 Nov [cited 2024 Nov 18]. Available from: 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

42. Jansen M, Rondaan C, Legger G, et al. EULAR/PRES recommendations for vaccination of paediatric patients with autoimmune inflammatory rheumatic diseases: update 2021. *Annals of the rheumatic diseases.* 2023 Jan;82(1)http://doi.org/10.1136/annrheumdis-2022-222574.

43. Merck Canada Inc. Product monograph: M-M-R II (measles, mumps and rubella virus vaccine, live, attenuated, Merck Std.) [Internet]. Quebec. Merck Canada Inc.; 2024 Dec 03 [cited 2025 Jan 09]. Available from: https://pdf.hres.ca/dpd_pm/00077954.PDF

44. GlaxoSmithKline Inc. Product monograph: PRIORIX (Combined measles, mumps and rubella vaccine, live, attenuated) [Internet]. Ontario. GlaxoSmithKline Inc.; 2019 Aug 14 [cited 2024 Nov 18]. Available from: https://pdf.hres.ca/dpd_pm/00052672.PDF

45. GlaxoSmithKline Inc. Product monograph: PRIORIX-TETRA (Combined measles, mumps, rubella and varicella vaccine, live, attenuated) [Internet]. Ontario. GlaxoSmithKline Inc.; 2019 Aug 14 [cited 2024 Nov 18]. Available from: https://pdf.hres.ca/dpd_pm/00052673.PDF

46. Merck Canada Inc. Product monograph: ProQuad (Measles, Mumps, Rubella and Varicella Virus Vaccine Live) [Internet]. Quebec. Merck Canada Inc.; 2024 Oct 2 [cited 2024 Nov 18]. Available from: https://www.merck.ca/en/wp-content/uploads/sites/20/2021/04/PROQUAD-PM_E.pdf

Appendix

Characteristics of the measles-containing vaccines currently authorized for use in Canada that may be used for measles PEP are summarized in Table 5 below. For complete prescribing information for the measles-containing vaccines and human immunoglobulin including contraindications, warnings and precautions, drug interactions, and intervals between Ig products and measles-containing vaccines, consult the product leaflet or information contained within the product monographs available through Health Canada's Drug Product Database as well as the CIG, Part 4, Measles vaccines chapter[23].

Table 5. Comparison of measles-containing vaccines that may be used for measles PEP

	Live attenuated combined measles, mumps and rubella vaccine (MMR)		Live attenuated combined measles, mumps, rubella vaccine and varicella vaccine (MMRV)	
Trade Name	M-M-R® II[43]	PRIORIX[44]	PRIORIX-TETRA[45]	ProQuad®[46]
Manufacturer	Merck Canada Inc.	GlaxoSmithKline Inc.	GlaxoSmithKline Inc.	Merck Canada Inc.
Composition of Each Dose After Reconstitution	Measles: ≥ 1000 $CCID_{50}$ Mumps: ≥ 5000 $CCID_{50}$ Rubella: ≥ 1000 $CCID_{50}$ 50% Cell Culture Infectious Dose	Live attenuated measles virus[a] (Schwarz strain) - not less than $10^{3.0}$ $CCID_{50}$[b] Live attenuated mumps virus[a] (RIT 4385 strain, derived from Jeryl Lynn strain) - not less than $10^{3.7}$ $CCID_{50}$[b] Live attenuated rubella virus[c] (Wistar RA 27/3 strain) - not less than $10^{3.0}$ $CCID_{50}$[b]	Live, attenuated measles virus[a] (Schwarz strain) not less than $10^{3.0}$ $CCID_{50}$ [b] Live, attenuated mumps virus[a] (RIT 4385 strain, derived from Jeryl Lynn strain) not less than$10^{4.4}$ $CCID_{50}$[b] Live, attenuated rubella virus[c] (Wistar RA 27/3 strain) not less than $10^{3.0}$ $CCID_{50}$ [b] Live, attenuated varicella virus[c] (OKA	Measles ≥ 3.00 $\log_{10}$ $TCID_{50}$ (50% tissue culture infectious dose) Mumps ≥ 4.30 $\log_{10}$ $TCID_{50}$ Rubella ≥ 3.00 $\log_{10}$ $TCID_{50}$ Varicella ≥ 3.99 $\log_{10}$ PFU

			strain) not less than $10^{3.3}$ PFU	
Dose	~ 0.5 mL	~ 0.5mL	~ 0.5 mL	~ 0.5 mL
Minimum interval[d]	4 weeks	4 weeks	4 weeks	4 weeks
Route of administration	SC or IM	SC[e] or IM[f]	SC or IM[f]	SC
Recommended age for measles PEP	6 months[g] of age and older	6 months[g] of age and older	12 months[h] up to 12 years of age	12 months up to 12 years of age
Storage Requirements	**Before Reconstitution**			
	<u>Vial of powder:</u> Store[i] at 2°C to 8°C **OR** Store in a freezer above -50°C; if subsequently transferred to a refrigerator, the vaccine may be placed back in the freezer. Cumulative time between 8°C and 25°C must not exceed 6 hours. Protect from light. <u>Diluent:</u> Store at 2°C to 27°C (e.g., with vial of powder	<u>Vial of powder:</u> Store[i] at 2 to 8°C Protect from light. Do not freeze. <u>Diluent:</u> Store with vial of powder in the refrigerator or separately at room temperature.	<u>Vial of powder:</u> Store[i] at 2 to 8°C Protect from light. Do not freeze.	<u>Vial of powder:</u> Store[i] at 2°C to 8°C **OR** Store in a freezer above -50°C; if subsequently transferred to a refrigerator, the vaccine may be placed back in the freezer. Cumulative time between 8°C and 25°C must not exceed 14 hours. Protect from light. <u>Diluent:</u> Store at 2°C to 27°C (e.g., with vial of powder

	in the refrigerator or separately at room temperature). Do not freeze.			in the refrigerator or separately at room temperature) Do not freeze.
	After Reconstitution			
	Use as soon as possible Store[i] at 2°C to 8°C Protect from light. Do not freeze. Discard if not used within 8 hours	Use as soon as possible Store[i] at 2°C to 8°C Protect from light Discard if not used within 8 hours.	Use as soon as possible Store[i] at 2°C to 8°C Discard if not used within 8 hours.	Use as soon as possible Store at room temperature Protect from light Do not freeze Discard if not used within 30 minutes.

a. Produced in chick embryo cells
b. Cell Culture Infective Dose 50%
c. Produced in human diploid (MRC-5) cells
d. Minimum interval between measles-containing and or varicella containing vaccines
e. recommended route by product monograph
f. The vaccine should be administered SC in subjects with bleeding disorders (e.g. thrombocytopenia or any coagulation disorders)
g. If administered at less than 12 months of age, two additional doses of measles-containing vaccine administered after 12 months of age (given at least 4 weeks apart) are required for long-term protection
h. While the MMRV vaccine PRIORIX-TETRA is indicated for active immunization against measles, mumps, rubella and varicella in individuals from 9 months to up to 12 years of age, NACI has not yet reviewed the use of MMRV in infants less than 12 months of age. MMR is recommended for PEP for infants 6 to under 12 months of age
i. Storage at 2 to 8°C in a refrigerator