TRANSFUSION AND CYTOMEGALOVIRUS IN THE BLOOD SYSTEM SUPPORTED BY CANADIAN BLOOD SERVICES*

*This Document does not pertain to Granulocytes, which are produced by Héma-Québec.

CYTOMEGALOVIRUS SUBCOMMITTEE

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Publication Date: May 4, 2017

Date of Last Revision: July 17, 2025

Cite As:

Nahirniak S, Clarke G, Lieberman L, Wall D, Preiksaitis J. Transfusion and Cytomegalovirus in the Canadian Blood System Supported by Canadian Blood Services [Internet]. Ottawa: National Advisory Committee on Blood and Blood Products; May 4, 2017 [updated 2025 07 17, cited YYYY MM DD]. Available from: https://nacblood.ca/en/resource/transfusion-and-cytomegalovirus-canadian-blood-system-supported-canadian-blood-services

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ACRONYMS

CMV	Cytomegalovirus
IUT	Intrauterine Transfusion
IgG	Immunoglobulin G
NAC	National Advisory Committee on Blood and Blood Products
RBC	Red Blood Cell
TT-CMV	Transfusion Transmitted Cytomegalovirus

SUMMARY OF REVISIONS

2025

General	White paper and recommendations are now included in a single comprehensive document.
Title Pages	Change in title and disclaimer added to provide clarity regarding granulocytes. Subcommittee and authorship information added and/or updated. Citation, acronym list and summary of revisions added.
1.0 Introduction	Discussion regarding the considerations around pathogen reduction have been added. Addition of information on the balance of the risk for maternal alloimmunization over concerns for CMV transmission. Information deemed not relevant to the recommendation removed.
2.0 Recommendations	Order of recommendations have moved in the document. Request for CBS to explore feasibility of CMV NAT removed. Recommendation to CBS to develop a new process to maintain a small CMV seronegative inventory for intrauterine transfusion removed. Recommendation regarding CMV safe and CMV IgG seronegative products updated.

INTRODUCTION

Cytomegalovirus (CMV) is a herpes virus demonstrating seroprevalence ranges of 40-80% in the general population with variability due to age, geographic location, and socioeconomic status.[1-3] CMV is transmitted by direct contact with bodily secretions (blood, saliva, urine, or breast milk[4]) or tissues. CMV may remain latent in mononuclear cells and tissues for years, but healthy individuals are generally asymptomatic. In immunocompromised individuals, CMV infections can manifest as serious complications including interstitial pneumonia, hepatitis, retinitis, and encephalitis. Effective treatment and prophylaxis for CMV infection in most at-risk individuals is available.[5]

Unlike other transfusion transmissible viruses, the testing performed by blood suppliers has been reliant on serologic investigations as nucleic acid testing methods are not licensed for screening and can lead to unreliable or discordant results due to noninfectious cell free CMV DNA.[6,7] This means that historically, components provided when clinicians request CMV negative units in Canada are those where the donor does not have detectable Immunoglobulin G (IgG) antibody. A donor window period for infection can be up to eight weeks.[8] Despite this window period, the risk of transmission through transfusion remains very low since red blood cell (RBC) and platelet components that have been pre-storage leukoreduced have significantly reduced risk for CMV transmission and are considered CMV “safe” for most transfusion indications. For the purposes of prevention of transfusion transmitted CMV (TT-CMV) infection, and for almost all indications, CMV seronegative and pre-storage leukoreduced components are considered equivalent. Please note that these statements are not applicable to granulocytes which are produced by Héma-Québec. For guidance pertaining to granulocytes, readers are referred to Héma-Québec and Comité consultatif national de médecine transfusionnelle documents.

Components treated with psoralen and ultra violet irradiation for the purpose of pathogen reduction can also be considered CMV safe. Pooled platelets, psoralen treated, are available for transfusion in Canada and are CMV safe without requirement for CMV antibody testing or leukoreduction.[9]

Historically, there have been cases of TT-CMV infections demonstrating transmission rates as high as 60% with fresh warm whole blood.[7] In contrast, with current pre-storage leukoreduction techniques, the rate of TT-CMV has been dramatically reduced to 1 in 13,575,000.[10] In 2016, Mainou et al performed a systematic review and meta-analysis that evaluated component leukoreduction with or without donor serology testing in risk reduction of TT-CMV. Despite concerns with respect to quality of some studies, in the 11 studies evaluated there was no signal of increased risk demonstrated by clinical and/or laboratory evidence of TT-CMV infection when comparing leukoreduction to CMV untested units (n=5); leukoreduction to CMV seronegative units (n=3) or leukoreduction alone versus leukoreduction plus CMV seronegativity (n=2).[11] This was also supported by a 2020 publication by Mabilangan et al. demonstrating the safety of leukoreduced blood components without additional screening for CMV in immunocompromised recipients that may more closely mimic the fetal immune system than other recipients. [12]

At the time of the publication of the National Advisory Committee on Blood and Blood Products (NAC) *Education Document: Transfusion and Cytomegalovirus in the Canadian Blood System* (2017), recommendations regarding the continued preference for CMV seronegative as well as leukoreduced red cells and platelets for intrauterine transfusion (IUT) was included. Since that time, international surveys regarding blood components used for IUT have confirmed that in many countries, despite a higher CMV seroprevalence than that seen in Canada, leukoreduced components are considered CMV safe for all indications, including IUT.[13]

Further, the need for phenotype matched RBCs for IUT is sometimes in conflict with the need for CMV seronegative RBC components. For pregnancies treated with IUT, the risk of alloimmunization to RBC antigens that differ from those of the pregnant individual is up to 14% per IUT. This alloimmunization risk is reduced to 4.3% per IUT when Rh, Kell, Kidd, Duffy and S blood group matched units were provided.[14] General consensus by treaters in Canada has supported precedence of phenotype matched units over CMV seronegative testing status for patients undergoing IUT.

Given the safety profile of pre-storage leukoreduced RBCs, international practice and Canadian evidence that practitioners in Canada now consider pre-storage leukoreduced RBCs the norm for IUT with constraints in meeting both phenotype requirements and CMV seronegativity, the NAC CMV Subcommittee has modified their recommendations as written below.

RECOMMENDATION

Accordingly, the following updated (2025) recommendation has been provided by the NAC CMV Subcommittee:

NAC recommends that CMV safe (leukoreduced) and CMV IgG seronegative products be considered equivalent for blood components that are produced by Canadian Blood Services.

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