# BLOOD COMPONENT SUPPORT FOR INTRAUTERINE TRANSFUSION

## A NAC and CSNMT Collaborative Initiative

# INTRAUTERINE TRANSFUSION SUBCOMMITTEE


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## ACRONYMS

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|---|---|
| CSNMT | Comité stratégique national en médecine transfusionnelle (Québec transfusion medicine strategic committee) |
| CMV | Cytomegalovirus |
| FNAIT | Fetal Neonatal Alloimmune Thrombocytopenia |
| HDFN | Hemolytic Disease of the Fetus and Newborn |
| IUT | Intrauterine Transfusion |
| NAC | National Advisory Committee on Blood and Blood Products |
| PAS | Platelet Additive Solution |
| RBC | Red Blood Cell |

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## DEFINITIONS

**Extended Phenotype Matching** – selection of donor red cell units with a red cell antigen profile that is the same as the red cell antigen typing of the pregnant individual. A typical extended red cell phenotype match would include matching of donor and recipient that are the most common clinically significant antigens. This includes RhD, C/c, E/e, K, Fya/Fyb, Jka/Jkb and Ss.

## 1.0 BACKGROUND

Intrauterine transfusions (IUT) in Canada are infrequent, are performed at highly specialized sites, are typically scheduled in advance, require specific blood components, and require coordination with the transfusion service and/or blood supplier. Regardless of the indication for IUT or the type of component transfused, it is important to ensure ongoing monitoring post IUT as well as post delivery for efficacy of transfusion and evaluation of alloimmunization. The medical record and/or laboratory information system should also link the mother and neonate sufficiently to ensure inclusion of both transfused individuals for any recalls or withdrawals of blood components.

## 2.0 RED BLOOD CELLS

The following sections outline recommended characteristics for donor red blood cells (RBC) to be used for IUT. Table 1 ranks the priority of RBC characteristics to consider when selecting units.

### 2.1 Blood Group – ABO and Rh(D) Status

In most situations, blood group O units are typically provided but this is not an absolute requirement. In cases where multiple units are being transfused, or if specific phenotype requirements cannot be met with a group O donor, the ABO group of the RBCs for IUT can be matched to the maternal ABO.

The Rh(D) status of the unit for the IUT depends on the specificity of maternal antibodies and maternal Rh(D) status along with availability of cognate antigen negative donor RBCs.

Due to the immature immune status of the fetus/neonate, there is no strong biologic plausibility for fetal alloimmunization to either ABO or Rh(D) mismatched units.

### 2.2 Red Blood Cell Phenotype/Antigen Requirements

RBCs for IUT must be antigen negative for any current or historical clinically significant maternal antibodies as well as serologically crossmatch compatible with maternal plasma. Maternal antibodies that pose a risk for in vivo hemolytic transfusion reactions should be honored even if they are not implicated in hemolytic disease of the fetus and newborn (HDFN) since there is the possibility of the IUT RBCs crossing into the maternal circulation. In rare cases, a maternal autologous unit may be required but this should only be considered following consultation with the blood suppliers' Rare Blood Program.[1]

It is recommended that the maternal RBC extended phenotype should be determined before an IUT. If possible, units selected for IUT should be phenotype matched in the following order of preference: Rh(CE), Kell, Duffy* and Kidd with optional matching for Ss depending on availability of supply.[1]

* It is not necessary to provide Fyb negative for those with the GATA mutation.

The risk for maternal alloimmunization following IUT has been documented in a few retrospective studies[2-6] and has been reported to be approximately 14% per IUT when extended phenotype matching is not available.[2] Rh and Kell alloimmunization appears to be linked predominantly to exposure to paternal antigens but the suggestion of these retrospective studies is that Kidd, Duffy and S sensitization may be linked to non matched allogeneic RBC exposure. One study suggested that when Rh, Kell, Kidd, Duffy and S blood group matched units are provided, the alloimmunization risk can be reduced to 4.3% per IUT.[2] In Canada, IUTs are most often performed for HDFN secondary to non-ABO antibodies.[7] As these affected individuals have already demonstrated a propensity to alloimmunization with at least one antibody, any additional antibodies may further complicate the current or subsequent pregnancies as well as potentially limiting maternal treatment through transfusion. Hence, it is of paramount importance to prevent additional alloimmunization.[8,9]

### 2.3 Irradiation

Unless deglycerolized RBCs are being provided, RBCs for IUT should be irradiated as close as possible to the time of issue, and ideally no longer than 12 hours pre-transfusion to minimize the effect of potassium load. Postnatally, irradiated RBC transfusion support should be provided for a period of six months for any neonate who received an IUT. For additional information, please refer to the Neonatal Transfusions section of the *Recommendations for use of Irradiated Blood Components in Canada: A NAC and CSNMT Collaborative Initiative*.

### 2.4 Cytomegalovirus

The risk for alloimmunization by RBCs far exceeds the risk for cytomegalovirus (CMV) transmission when pre-storage leukoreduced units are provided. Since the need for phenotype matched RBCs for IUT was often in conflict with the request for CMV seronegative RBC components, the National Advisory Committee on Blood and Blood Products (NAC) and the Comité stratégique national en médecine transfusionnelle (CSNMT) revised their CMV recommendations in 2025 and 2026 respectively to reflect that phenotype matching for maternal RBC antigens should take precedence over any requests for CMV seronegativity.[10] Leukoreduced components are now considered CMV safe for all indications, including IUT.[11]

### 2.5 Hemoglobin S

Due to rare case reports of sickling crisis in utero due to the low oxygen environment, selection of RBCs screened to be negative for hemoglobin S is often recommended or preferred in clinical practice for IUT.[12, 13] Data supporting this practice is limited. Studies in both adults and children have reported transfusion of sickle cell trait units to patients without harm.[14, 15] Therefore hemoglobin S negativity is low priority. Practices continue to vary among institutions, and this specification is no longer a regulatory requirement.

### 2.6 Collection Time

Many recommend that the ideal unit for IUT is one collected within 5-7 days prior to transfusion. However, if antigen requirements/RBC phenotype selection necessitates use of an

older unit, this is clinically acceptable. The approach of as fresh as possible while meeting phenotype requirements is recommended. However, frozen RBC inventory that has been deglycerolized prior to IUT is a safe and effective alternative to recently collected donor units and may be required in cases with rare RBC phenotype requirements.[16-18]

### 2.7 Hematocrit

The RBC unit is washed or concentrated to a hematocrit of 70-85%, as requested by the clinical team.

### 2.8 Warming

Some institutions warm RBC units prior to or during the IUT, but the processes for how this is accomplished are variable. Some may use a blood warmer while others consider the unit to be naturally warmed during a slow infusion process. Other centres do not actively warm the blood prior to IUT, but surveys indicate some practitioners may hold the product at room temperature at the bedside for a 30 to 60 minute period prior to transfusion.[19]

**Table 1: Recommended Priority of RBC Characteristics for IUT**

| Highest Priority | | | Lowest Priority |
|---|---|---|---|
| Antigen/phenotype requirements | ABO group/Rh(D) status | Age of unit | Sickle status |

## 3.0 PLATELETS

Platelets are also a component that may be administered as an IUT. Intrauterine platelet transfusion for the management of fetal neonatal alloimmune thrombocytopenia (FNAIT) is not routinely recommended at inexperienced centres. At inexperienced centres, the morbidity and mortality risk has been reported to be as high as 11%, indicating that the risk from the procedure could be greater than or equal to the risk of severe bleeding in the fetus secondary to the thrombocytopenia.[20]

If there is a decision to proceed with an IUT for FNAIT or for other causes of fetal thrombocytopenia (such as viral infection) the ideal platelet component characteristics include:

1) Human platelet antigens compatible with the maternal alloantibody if administered for FNAIT;
2) Irradiated;**
3) CMV reduced risk (leukoreduced);
4) Low isohemagglutinin titre if the platelets are suspended in plasma; and,
5) Further concentrated.

** If apheresis platelets, psoralen treated are administered, irradiation of the unit would not be required as the psoralen treatment removes the proliferation capacity of lymphocytes and therefore this component poses no risk for transfusion-associated graft-versus-host disease.

Similar to RBCs, there is no concern for Rh(D) alloimmunization of the fetus and the platelet unit should be ABO/Rh(D) compatible with the mother.

The introduction of pathogen reduced apheresis platelet components (apheresis platelets, psoralen treated) by Canadian Blood Services has resulted in a platelet component that will not transmit CMV and requires no donor CMV testing. The use of these components in neonates is safe, however use in the setting of IUT has not been studied and is not currently recommended as the preferred product. Instead, an alternative product, apheresis platelets in platelet additive solution (PAS),[21] that has not undergone pathogen reduction, is also available upon request from Canadian Blood Services. While available, these PAS apheresis platelets may require up to a three-day turnaround for donor recruitment, collection, testing and processing. Given that intrauterine platelet transfusions, when performed, are typically urgent, this preferred component may not be a feasible alternative to pathogen reduced/psoralen treated platelets.[1]

## 4.0 RECOMMENDATIONS

NAC and CSNMT recommend that for IUT, RBCs that are appropriately selected for maternal alloantibodies and prophylactically phenotype matched to the maternal RBC antigen profile as well as crossmatch compatible with maternal plasma, should be provided.

NAC and CSNMT recommend that for IUT, platelets that are suspended in plasma or PAS and are not psoralen treated/pathogen reduced should, ideally, be provided.

NAC and CSNMT recommend that the medical record and/or laboratory information system should link the mother and neonate sufficiently to ensure inclusion of both transfused individuals for any recalls or withdrawals of blood components.

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