

# CIRCULAR OF INFORMATION

## For the Use of Human Blood Components

### Platelets

This component information addresses:

- Pooled Platelets LR CPD
- Apheresis Platelets

### Composition and properties

**Pooled Platelets LR CPD** is a platelet concentrate prepared by separation of the buffy coat layer from approximately 480 mL of whole blood collected in 70 mL of CPD anticoagulant. Four ABO matched platelet concentrates are pooled in the residual plasma from one of the four donations. The pool is leukocyte reduced by filtration. The pooled platelet component is labelled as Rh negative, only when all units contained in the pool are from Rh negative donors.

**Apheresis Platelets** is a platelet concentrate collected into approximately 50 mL of ACD-A anticoagulant using automated apheresis techniques, which includes leukoreduction.

#### Notes:

CPD (citrate, phosphate, dextrose) anticoagulant contains citric acid 3.27 g/L, sodium citrate 26.3 g/L, sodium acid phosphate 2.51 g/L, dextrose 25.5 g/L.

ACD-A (acid citrate dextrose – formula A) anticoagulant contains sodium citrate 22.0 g/L, citric acid 7.3 g/L, dextrose 24.5 g/L.

**TABLE 1:** Typical unit content is based on the number of units (n) tested from May 2020 to October 2020, inclusive.

Platelet Component	Volume (mL) Mean $\pm$ 1 SD	Platelet Count ( $\times 10^9$ ) per unit Mean $\pm$ 1 SD	Residual Leukocytes ( $\times 10^6$ ) per unit Mean $\pm$ 1 SD
Pooled Platelets LR CPD	317 $\pm$ 16 n = 588	339 $\pm$ 44 n = 588	0.0427 $\pm$ 0.0877 n = 598
Apheresis Platelets	223 $\pm$ 9 n = 477	333 $\pm$ 34 n = 477	0.0966 $\pm$ 0.2206 n = 497

#### Quality criteria that must be met:

**Pooled Platelets CPD:** Volume:  $\pm 10\%$  labelled volume in all units tested; Platelet Count:  $\geq 240 \times 10^9$ /unit in  $\geq 75\%$  of units tested; Residual Leukocytes:  $< 5 \times 10^6$  in all units tested.

**Apheresis Platelets:** Platelet Count:  $\geq 240 \times 10^9$ /unit in  $\geq 75\%$  of units tested; Residual Leukocytes:  $< 5 \times 10^6$  in all units tested.

Trace amounts of red blood cells may be present in some units; refer to the *Visual Assessment Guide* for further information.<sup>1</sup>

The donor sample is tested for ABO group, RhD type, anti-A and anti-B titres and clinically significant antibodies against red cell antigens. ABO group and RhD is indicated on the component label. Units determined to be Low Anti-A/B will be labeled as such.

Prior to making blood components available for transfusion, a sample of each donor's blood must test non-reactive for:

- antibodies to human immunodeficiency virus (HIV-1 and HIV-2), hepatitis C virus (HCV), human T-cell lymphotropic virus, type I and II (HTLV-I/II), hepatitis B core antigen (HBcore)
- hepatitis B surface antigen (HBsAg)
- presence of viral RNA [HIV-1 and HCV]
- presence of viral DNA [hepatitis B virus (HBV)]
- syphilis

Platelets, LR components are cultured for bacteria 36 hours after collection and are issued to hospitals only if the culture is negative at the time of issue. If the component culture becomes positive after issue, the hospital is notified.

In some cases, a donor sample is also tested for cytomegalovirus (CMV) antibody and/or the presence of IgA; if CMV negative and IgA deficient, this is indicated on the label.

A donor sample is only tested for antibodies to *Trypanosoma cruzi* (*T. cruzi* or Chagas Disease) and the presence of viral RNA [West Nile Virus (WNV)] when increased risk is present.

In some emergency situations, with the approval of both Canadian Blood Services and recipient's physician, partially tested or untested blood may be released for transfusion.

### Packaging

**Pooled Platelets LR CPD** and **Apheresis Platelets** are stored in gas-permeable bags. Platelet component storage bags do not contain diethyl hexyl phthalate (DEHP) plasticizer; however platelets have been in contact with DEHP plasticizer during their manufacturing.<sup>2,3,4</sup>

**Apheresis Platelets** may be supplied in a single container or, in some instances, in two connected containers. If supplied in two connected containers, instructions for pooling the two containers are included on the transfusion instruction label that is adhered to the secondary container.

### Storage and handling

**Pooled Platelets LR CPD** and **Apheresis Platelets** must be stored at 20 - 24°C with continuous gentle agitation. During transport cessation of agitation for 24 hours is acceptable.<sup>5</sup> The shelf life is 7 days.

Visual inspection should be performed; refer to the *Visual Assessment Guide* for further information.<sup>1</sup> A platelet unit should be mixed thoroughly prior to transfusion.

### Action

The primary role of transfused platelets is to participate in primary hemostasis through the provision of functionally normal platelets.

### Indications

The aim of transfusion is to prevent or treat bleeding due to platelet deficiency or dysfunction. Platelet transfusion is indicated for the treatment of patients with clinically significant bleeding and low platelet counts secondary to decreased production or dilutional thrombocytopenia.

On occasion, platelet transfusion may be indicated for the treatment of patients with platelet destructive conditions or functionally abnormal platelets in the setting of clinically significant bleeding or prior to an invasive procedure associated with high risk of bleeding.

Prophylactic platelet transfusions may be indicated for very low platelet counts ( $\leq 10 \times 10^9/L$ ) secondary to decreased production. Prophylactic transfusions at higher platelet count thresholds may be indicated for invasive procedures and/or in the presence of additional risk factors for bleeding.

For patients with alloimmune refractoriness, HLA and/or HPA matched **Apheresis Platelets** may be indicated. For platelet refractoriness due to disseminated intravascular coagulation, idiopathic thrombocytopenic purpura, hypersplenism, certain drugs, fever and sepsis, HLA and/or HPA matched **Apheresis Platelets** are no more effective than unmatched **Apheresis Platelets** or **Pooled Platelets LR CPD**.

## Contraindications

Do not use platelet components if bleeding is unrelated to decreased numbers of, or abnormally functioning, platelets.

Platelet components are not recommended for use in patients with destruction of endogenous and exogenous platelets, such as in thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura or heparin induced thrombocytopenia (HIT) unless the patient has a life-threatening hemorrhage.

Since platelet components contain donor plasma, recipients with known anti-IgA should receive IgA deficient platelets. Patients with known anaphylaxis to plasma should only receive platelet components under appropriate medical supervision.

## Warnings and precautions

The donor plasma in platelets should be ABO compatible with the recipient's red cells. Canadian Standards Association requires that a policy be in place concerning group substitution when platelets with compatible plasma are not available.<sup>6</sup> Hemolysis has been reported as an uncommon complication of plasma ABO incompatibility with platelet transfusions.

The intended recipient must be properly identified before the transfusion is started.

Rh positive platelets given to an Rh negative recipient may cause sensitization. If Rh positive platelets are transfused to an Rh negative recipient, RhlgG should be considered.

Alloimmunization of the recipient may be a consequence of transfusion.

Careful donor selection and available laboratory tests do not eliminate the hazard of transmitting infectious disease agents for which testing is performed (see Table 2)<sup>7</sup> or for pathogens that are either not recognized or for which there is no donor screening test.

**TABLE 2:** Estimated residual risk of transfusion-transmitted viral infections in Canada with incidence rates from observed donor seroconversions, 2015<sup>†</sup>

Virus	Estimated Residual Risk
	Per number of donations
HIV	1 in 21.4 million
HCV	1 in 12.6 million
HBV*	1 in 7.5 million
HTLV‡	1 in 619million

<sup>†</sup>Canadian Blood Services, National Epidemiology and Surveillance data (unpublished).

\*Adjusted for transient nature of HBsAg by the formula of Korelitz with further adjustment to account for the improved sensitivity of newer HBsAg assays.

‡The estimate includes the complimentary benefit of leukoreduction in further reducing the residual risk of transmission via red blood cell and platelet components.

For a fetus requiring an intrauterine transfusion [IUT], clinicians may choose, in addition to the use of LR components, to transfuse components from CMV-seronegative donors.

Some collection needles are in contact with latex. Canadian Blood Services cannot guarantee that this component is latex free.

## Adverse events

Potential adverse events related to a blood transfusion range in severity from minor with no sequelae to life-threatening. All adverse events occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted. All adverse events suspected to be related to a transfusion (whether during or after a transfusion) should be reported to your local transfusion service and when required (i.e. when the adverse event could be attributed to the quality of a blood component), to Canadian Blood Services and the hospital/regional hemovigilance network. Health Canada, Health Products & Food Branch, Blood Regulations and Canadian Standards Association require reporting of adverse events associated with blood component quality (e.g. bacterial contamination) to Canadian Blood Services.<sup>6,8,17</sup> For further information, refer to the Canadian Standards Association, *Blood and Blood Components* and *Transfusion Transmitted Injuries Surveillance System*.<sup>8,9</sup>

**TABLE 3:** The following adverse events have been described with transfusion of platelet components.<sup>8,10,11,13,14,15</sup>

Event	Approximate Frequency	Symptoms and Signs	Notes
Mild allergy	1 in 100	Urticaria, pruritis and/or erythema.	Transfusion can be restarted after assessment and necessary intervention.
Febrile non-hemolytic transfusion reactions (FNHTR)	1 in 200	Fever, chills and/or rigor.	Diagnosis of exclusion. A patient with fever should be evaluated for other more serious transfusion reactions.
Transfusion associated circulatory overload (TACO)	1 in 700	Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.	Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI.
Septic reaction	1 in 100,000 (see reference #12 and Notes)	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and disseminated intravascular coagulation and/or renal failure.	Approximate frequency per platelet concentrate based on Canadian Blood Service data*: <ul style="list-style-type: none"> <li>bacterial sepsis 1 in 125,000</li> <li>death from bacterial sepsis 1 in 909,091</li> </ul> As reported by other international blood agencies <sup>12</sup> : <ul style="list-style-type: none"> <li>estimated risk of bacterial sepsis 1 in 100,000</li> <li>estimated risk of death from bacterial sepsis 1 in 1,000,000</li> </ul> For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference #8.
Transfusion related acute lung injury (TRALI)	1 in 1,200-5,000	New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.	Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.
Post transfusion purpura (PTP)	Rare	Abrupt onset of severe thrombocytopenia 1 – 24 days post transfusion.	Most cases of PTP occur in recipients who are HPA-1b homozygous receiving HPA-1a positive blood components.
Transfusion-related alloimmune thrombocytopenia	Rare	Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.	Passive transfer of platelet antibodies leading to thrombocytopenia.
Immediate hemolytic transfusion reactions (HTR)	Rare	Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain and/or back pain.	May be associated with ABO plasma incompatibility.
Anaphylaxis	Rare	Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea and vomiting.	Resuscitation according to institutional guidelines. IgA deficient patients who have formed anti-IgA antibodies may experience anaphylactic reactions. However, in most cases of anaphylactic reactions, no specific antibodies are found in the patient.
Graft-versus-host disease (GVHD)	Rare	Pancytopenia, rash, liver dysfunction, diarrhea.	Irradiated cellular blood components reduce this risk.
Isolated hypotensive reaction	Unknown	Hypotension, occasionally accompanied by urticaria, dyspnea and nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Infectious disease	See Table 2, Residual risk of tested viruses	Variable according to infectious disease.	Blood components have been described to transmit viruses other than HIV, HBV, HCV, HTLV I/II and WNV as well as parasites and prions.

\*Unpublished Canadian Blood Services Surveillance data 2006-2016

Reporting of suspected cases of transfusion-related infections such as HIV, HCV, HTLV, HBV, WNV and other transfusion-related infections is described in the *Clinical Guide to Transfusion*, section 1: Vein to Vein: A Summary of Blood Collection and Transfusion in Canada.

## Dose and administration

The number of units of Platelets, LR to be administered depends on the clinical situation of each patient. The response to platelet transfusions is best assessed by observing whether bleeding stops and by measuring post transfusion platelet counts. Standard doses are:

- adults:** one unit of **Apheresis Platelets** or one dose of **Pooled CPD Platelets LR CPD**.
- children:** 25% of an adult standard dose per 10 kg body weight up to one standard adult dose.
- neonates:** 10 mL/kg of Platelets.

Each dose of platelets should increase the patient's platelet count by at least  $15 \times 10^9/L$ .<sup>13</sup> In some instances more than one standard dose may be required.

## Modification and additional information

**TABLE 4:** Modified Components

Modification	Description	Indication	Storage	Benefits	Adverse events
Irradiation <sup>16</sup>	Cells are exposed to ionizing radiation (i.e., gamma or x-ray).	Recipients who are immunocompromised or who receive cellular components from closely matched HLA or related/directed donor.	Unchanged.	Reduces the risk of GVHD.	As per Table 3.

A standard blood administration set containing a 170 – 260 micron filter or a filter of equivalent efficacy, approved by Health Canada, must be used for infusion. Transfusion may proceed as fast as tolerated but must be completed in less than four hours.

No medications or solutions may be added to or infused through the same tubing simultaneously with blood or blood components, unless the solution has been approved for this use by Health Canada or there is documentation available to show that addition of the solution to the blood component involved is safe.<sup>6</sup> Co-administration of 0.9% sodium chloride injection, ABO-compatible plasma or 5% albumin can be performed at the discretion of the recipient's physician.

All transfusions should be complete within 4 hours of removal from storage. For more information, refer to the *Clinical Guide to Transfusion*. Patients should be under clinical observation, in accordance with institutional guidelines, during transfusion with close observation during the first 15 minutes.

## References

1. Canadian Blood Services. Visual Assessment Guide T05 021. Canadian Blood Services, 2009.
2. MacoPharma. MacoPharma Thromboflex TXP Filter-TDV & TRV Systems NOTUNIPLT\_2017-06-02. 2017.
3. Fresenius Kabi AG. CompoStop CS and CompoStop Flex 33720-1 04-2015; CompoStop Flex 33722-1 04-2020.
4. Prowse CV, de Korte, D, Hess JR, van der Meer PF, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Commercially available blood storage containers. *Vox Sanguinis* 2014; 106: 1-13.
5. Price TH, chair. Standards for blood banks and transfusion services. 26th ed. Bethesda (MD): AABB; 2009: 51-2.
6. Canadian Standards Association. Blood and blood components Z902-15. Canadian Standards Association December 2015.
7. Kleinman S, Chan P, and Robillard P. Risks associated with transfusion of cellular blood components in Canada. *Transfus Med Rev* 2003; 17:120–62.
8. Public Health Agency of Canada. Supplement guideline for investigation of suspected transfusion transmitted bacterial contamination. *Canada Communicable Disease Report* 2008; 34S1: 1-8.
9. Public Health Agency of Canada. Transfusion transmitted injuries surveillance system.
10. Clarke G, Blajchman M, editors. *Clinical guide to transfusion*. 4<sup>th</sup> ed. Toronto (ON): Canadian Blood Services; 2007.
11. Popovsky, MA. *Transfusion reactions*. 3<sup>rd</sup> ed. Bethesda (MD): AABB; 2007.
12. Popovsky, MA. *Transfusion reactions* 4<sup>th</sup> ed. Bethesda (MD): AABB; 2012.
13. Callum JL, Lin Y, Pinkerton PH, Karkouti K, Pendergrast JM, Robitaille N, Tinmouth AT, Webert KE. *Bloody easy 3, blood transfusions, blood alternatives and transfusion reactions, a guide to transfusion medicine*. 3<sup>rd</sup>. Toronto (ON): Sunnybrook and Women's College Health Sciences Centre; 2011.
14. Yazer M, Podlosky L, Clarke G, Nahirniak S. The effect of prestorage WBC reduction on the rates of febrile nonhemolytic transfusion reactions to platelet concentrates and RBC. *Transfusion* 2004; 44:10-5.
15. Pavenski K, Webert KE, Goldman M. Consequences of transfusion of platelet antibody: a case report and literature review. *Transfusion* 2008; 48:1981-9.
16. Voak D, chairman. BCSH Blood Transfusion Task Force. Guidelines on gamma irradiation of blood components for the prevention of transfusion-associated graft-versus-host disease. *Transfus Med* 1996; 6:261-71.
17. CAN, Health Canada, Health Products & Food Branch, Blood Regulations, SOR/2013-178, in force October 23, 2014.

The *Circular* as a whole or in part cannot be considered or interpreted as an expressed or implied warranty of the safety or fitness of the described blood or blood components when used for their intended purpose. Attention to the specific indications for blood components is needed to prevent inappropriate transfusion.

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This *Circular* is an extension of the component label and conforms to the applicable Regulations issued by the Health Products and Food Branch, Health Canada.<sup>17</sup>