Whole Blood

This circular of information addresses:

- **Whole Blood, Leukocytes Reduced**

Composition and properties

Whole Blood Leukocytes Reduced is produced from approximately 480 mL of whole blood from male donors collected in 70 mL of citrate phosphate dextrose (CPD) anticoagulant. CPD anticoagulant contains citric acid 3.27 g/L, sodium citrate 26.3 g/L, sodium acid phosphate 2.51 g/L, and dextrose 25.5 g/L. The collected unit is leukocyte reduced using a platelet sparing filter.

A typical **Whole Blood Leukocytes Reduced** unit has an approximate volume of 496 mL, hematocrit of approximately 0.41 L/L, and contains approximately 234 mL of plasma, 62 g of hemoglobin and $0.2x10^6$ residual leukocytes. The iron content of a typical unit is approximately 210 mg/unit. (1) (2)

Manufacturing process quality criteria that must be met are volume ±10% labelled volume, Hb ≥40 g/unit in 90% of units tested, hemolysis ≤0.80 L/L in 90% of units tested, and residual leukocytes $<5x10^6$/unit in 95% of units tested.

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, RhD, and if present antibody identity, are indicated on the product label. Units determined to be Low Anti-A/B will be labeled as such.

Prior to making blood products 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

Red blood cell antigens tested and found to be negative are indicated on the eye readable portion of the label. Positive and negative antigen results are included in the barcode.

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

Whole Blood Leukocytes Reduced units are stored in di-ethyl hexyl phthalate (DEHP) plasticized polyvinyl chloride (PVC) bags. (3)

Storage and handling

Whole Blood Leukocytes Reduced should be stored at 1 - 6°C. The shelf life is 21 days, unless otherwise specified. Once the bag is breached, the unit should be transfused within 24 hours if maintained at 1 - 6°C or within 4 hours if stored above 6°C.

Whole Blood Leukocytes Reduced can be irradiated where indicated according to evidence-based guidelines. (8)

Visual inspection should be performed. A unit should be mixed thoroughly prior to transfusion.

Action

Transfused whole blood increases the oxygen-carrying capacity of the blood by increasing the circulating red blood cell mass and provides hemostatic support through provision of platelets and clotting factors present in the product.

Indications

Whole Blood Leukocytes Reduced is indicated for treatment of clinically significant bleeding recipients. (4)

Contraindications

The use of whole blood is not recommended as a treatment in the absence of active bleeding.

Relative contraindication: Data is lacking on use of whole blood in children with active bleeding under the age of 1. (5) Data on use of whole blood outside of active bleeding is limited.

Warnings and precautions

Pretransfusion recipient sample testing and recipient identification must be conducted as soon as possible in accordance with Canadian standard *CAN/CSA-Z902 Blood and Blood Components*.

DEHP plasticizer leaches gradually into the **Whole Blood Leukocytes Reduced** during storage. Currently, there is no scientific proof that DEHP, which is used in the composition of a large number of medical devices, may represent a toxicity risk for recipients exposed during a transfusion. However, a toxic effect on the development of the male reproductive system in rodents has been shown. Populations who may be most at risk include the following: fetuses, newborns, and pre-pubescent boys who receive massive transfusions. (6)

CAN/CSA-Z902 Blood and Blood Components requires that a policy be in place concerning group substitution when compatible blood group is not available. (7) Hemolysis can occur as a complication of ABO incompatibility with transfusions.

RhD positive blood given to an RhD negative recipient may cause sensitization.

Whole Blood Leukocytes Reduced should not be volume reduced.

Whole Blood Leukocytes Reduced should not be used in volume resuscitation unless indicated. Recipients being transfused with blood should be monitored for adverse events such as circulatory overload, allergic reaction, etc.

Careful donor selection and available laboratory tests do not eliminate the hazard of transmitting infectious disease agents for which testing is performed or for pathogens that are either not recognized or for which there is no donor screening test.

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

Adverse Events

Potential adverse events related to a blood transfusion range in severity from minor with no sequelae to life-threatening. Alloimmunization of the recipient may be a consequence of transfusion. 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 product), to Canadian Blood Services and the hospital/regional hemovigilance network. Federal Blood Regulations and Canadian standard *CAN/CSA-Z902 Blood and Blood Components* require reporting of adverse events associated with blood product quality to Canadian Blood Services. (7) (9) (10) For further information, refer to the *CAN/CSA-Z902 Blood and Blood Components* and *Transfusion Transmitted Injuries Surveillance System.* (9) (11)

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*, chapter 1: Vein to Vein: A Summary of Blood Collection and Transfusion in Canada. (4)

Dose and administration

Transfuse to recipients with clinically significant active bleeding. Consider degree of blood loss and risk of anemia, coagulopathy and platelet dysfunction when determining number of units and rate of administration. Pediatric dosing is up to 40 mL per kg body weight. (12)

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. A blood warmer licensed by Health Canada for that purpose may be used at the discretion of the recipient's physician.

No medications or solutions may be added to or infused through the same tubing simultaneously with blood products, 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 product involved is safe. (7) Co-administration of 0.9% sodium chloride injection, ABO-compatible blood products or 5% albumin can be performed at the discretion of the recipient's physician.

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

TABLE 1: The following adverse events have been described with transfusion of fresh blood components / products (4) (9) (13) (14) (15) (16) (17) (18) (19) (20)

Event	Approximate Frequency	Symptoms and Signs	Notes
Febrile non-hemolytic transfusion reactions (FNHTR)	0.5-2:100†	Fever, chills and/or rigor.	Diagnosis of exclusion. Rule out other causes.
Mild allergy	1:100	Urticaria, pruritis and/or erythema.	
Transfusion associated circulatory overload (TACO)	0.1-1:100†	Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.	
Delayed hemolytic transfusion reactions (HTR)	1:25,000	Hemolysis occurs 4 – 14 days post transfusion.	Direct antiglobulin test may be positive.
Acute hemolytic transfusion reactions (HTR)	1:40,000	Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain and/or back pain.	Often due to undetected serological incompatibility or sample misidentification.
Transfusion related acute lung injury (TRALI)	0.5-1:100,000†	New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.	Approximate frequency based on Canadian Blood Services hospital reported data: • 1:82,350 classified possible TRALI • 1:411,750 classified as TRALI
Septic reaction	Rare	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and/or disseminated intravascular coagulation.	Approximate frequency per red blood cell unit based on Canadian Blood Services data: • bacterial sepsis* 1 in 2,128,468 • death from bacterial sepsis* < 1 in 4,256,936 As reported by other international blood agencies (17): • bacterial sepsis 1:500,000 • death from bacterial sepsis 1:10,000,000 Approximate frequency per platelet concentrate based on Canadian Blood Service data: • bacterial sepsis** 1 in 125,000 • death from bacterial sepsis** 1 in 909,091 As reported by other international blood agencies (17): • estimated risk of bacterial sepsis 1 in 100,000 • estimated risk of death from bacterial sepsis 1 in 1,000,000 For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference #9. Products treated with pathogen inactivation technology reduce this risk.
Isolated hypotensive reaction	Rare	Hypotension, occasionally accompanied by dyspnea and nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Anaphylaxis	Rare	Severe multi-systemic reaction involving the skin, and/or respiratory, gastrointestinal, cardiovascular systems.	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.
Post transfusion purpura (PTP)	Very 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 / products.
Graft-versus-host disease (GVHD)	Very rare	Pancytopenia, rash, liver dysfunction, diarrhea.	Irradiated cellular blood components / products or products treated with pathogen inactivation technology reduce this risk.
Infectious disease	Very rare‡	Variable according to infectious disease.	Blood components / products have been described to transmit viruses other than HIV, HBV, HCV, HTLV I/II and WNV as well as parasites and prions. Products treated with pathogen inactivation technology reduce this risk.
Delayed serological	Varies by patient population	Presence of new or amnestic alloantibody.	
Iron overload	Varies by patient population	Early stages may be asymptomatic. Clinical signs relate to hepatic, pancreatic and/or cardiac organ damage.	Due to repeated red blood cell transfusions in certain patient populations.
Hyperkalemia	Varies by patient population	Cardiac arrhythmia, changes in ECG, and/or cardiac arrest.	Seen in massive, rapid transfusion; neonates and infants receiving red blood cells irradiated prior to storage are at particular risk.
Other complications of massive transfusion	Varies by patient population	Complications may include hypothermia, citrate toxicity, acidosis, dilutional coagulopathy.	Appropriate monitoring may abrogate some complications.

† Range of frequency varies based on blood component / product type.
‡ Transmissible blood-borne infection surveillance is carried out by Canadian Blood Services on a continuous basis, and reported annually. (18)
* Canadian Blood Services Red Blood Cell units transfused between April 1, 2011, and October 31, 2016 (n=4,256,936); frequencies are likely to have quite wide confidence intervals due to quality of reporting.
** Unpublished Canadian Blood Services Surveillance data 2006-2016.

Transformed and additional information

TABLE 2: Modified Products

Modification	Description	Indication	Storage	Benefits	Adverse events
None currently available from Canadian Blood Services					

References

1. **Angelucci, E. Brittenham, GM. McLaren, CE. Ripalti, M. Baronciani, D. Giardini, C. et al.** Hepatic iron concentration and total body iron stores in thalassemia major. *New England Journal of Medicine.* 2000. Vol. 343, 23, pp. 327-31.
2. **Garry, PJ. Saiki, JH.** Idiopathic hemochromatosis: serum ferritin concentrations during therapy by phlebotomy. *Clinical Chemistry.* 1982. Vol. 28, 8, pp. 1806-8.
3. **Prowse, CV, et al.** Commercially available blood storage containers for the Biomedical Excellence for Safer Transfusion (BEST). *Vox Sanguinis.* 2014. Vol. 106, pp. 1-13.
4. **Canadian Blood Services.** Clinical Guide to Transfusion. 4th [ed.] G Clarke and M Blajchman. Toronto, ON : s.n., 2007.
5. **Yazer, MH. Seheult, JN. Beckett, A. Triulzi, DJ. Spinella, PC.** Rebirth of the cool: the modern renaissance of low titer group O whole blood for treating massively bleeding civilian patients. *Annals of Blood.* 2021.
6. **Walker, R.** *di(2-ethylhexyl) phthalate (DEHP) health Canada expert advisory panel on DEHP in medical devices, final report.* Ottawa (ON) : Health Canada, 2002.
7. **Canadian Standards Association.** Blood and blood components. CAN/CSA-Z902:20 March 2020.
8. **National Advisory Committee on Blood and Blood Products.** Guidelines and Recommendations. 2018.
9. **Public Health Agency of Canada.** Supplement guideline for investigation of suspected transfusion transmitted bacterial contamination. *Canada Communicable Disease Report.* 2008. pp. 1-8. 34S1.
10. **Health Canada.** Blood Regulations. *CAN.* in force October 23, 2014. SOR/2013-178.
11. **Public Health Agency of Canada.** Transfusion transmitted injuries surveillance system.
12. **Morgan, KM. Yazer, MH. Triulzi, DJ. Strotmeyer, S. Gaines, BA. Leeper, CM.** Safety profile of low-titer group O whole blood in pediatric patients with massive hemorrhage. *Transfusion.* 2021. Vol. 61, S1, pp. S8-S14.
13. **Popovsky, MA, [ed.].** Transfusion Reactions. 3rd *AABB.* 2007.
14. **Callum, JL, et al.** bloody easy 4, Blood Transfusions, Blood Alternatives and Transfusion Reactions, A Guide to Transfusion Medicine. *Ontario Regional Blood Coordinating Network.* 2016.
15. **Yazer, M, et al.** The effect of prestorage WBC reduction on the rates of febrile nonhemolytic transfusion reactions to platelet concentrates and RBC. *Transfusion.* 2004. Vol. 44, pp. 10-5.
16. **Pavenski, K, Webert, KE and Goldman, M.** Consequences of transfusion of platelet antibody: a case report and literature review. *Transfusion.* 2008. Vol. 48, pp. 1981-9.
17. **Popovsky, MA, [ed.].** Transfusion Reactions. 4th *AABB.* 2012.
18. **Canadian Blood Services.** Surveillance Reports. [ed.] Sheila O'Brien. 2019.
19. **Delaney, M, et al.** Transfusion reactions: prevention, diagnosis, and treatment. *Lancet.* 2016. Vol. 388, pp. 2825-36.
20. **Kleinman, S, Chan, P and Robillard, P.** Risks associated with transfusion of cellular blood components in Canada. *Transfusion medicine reviews.* April 2003. Vol. 17, 2, pp. 120-62.

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This *Circular* is an extension of the product label and conforms to the applicable Regulations issued by the Health Products and Food Branch, Health Canada. (10)