Red Blood Cells, Leukocytes Reduced (LR)

This component information addresses:

- **Red Blood Cells LR SAGM added**

Composition and properties

Red Blood Cells LR SAGM added is a red cell concentrate prepared from approximately 480 mL of whole blood collected in 70 mL of CPD anticoagulant. The unit is plasma reduced by centrifugation, platelet reduced by either centrifugation or filtration and leukoreduced by filtration.

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.
SAGM (saline, adenine, glucose, mannitol) additive solution contains sodium chloride 8.77 g/L, dextrose 9.00 g/L, adenine 0.169 g/L, mannitol 5.25 g/L.

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

	Volume (mL) Mean ±1 SD	Hemoglobin (g) Mean ±1 SD	Hematocrit (L/L) Mean ±1 SD	Residual Leukocytes ($x10^6$) Mean ±1 SD
Red Blood Cells LR SAGM added	287 ± 20 n = 2916	55 ± 6 n = 2916	0.67 ± 0.03 n = 2916	0.0597 ± 0.1165 n = 3589

A typical unit contains less than 29 mL of plasma and approximately 110 mL of SAGM additive.
Note: The iron content of a typical unit is approximately 3.4 mg/g Hb[1,2] and may be calculated based on the Hb range provided in Table 1.

The donor sample is tested for ABO group, Rh type and unexpected antibodies against red cell antigens. ABO, Rh and, if present antibody identity, are indicated on the component label.

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

In some cases, a donor sample is also tested for cytomegalovirus (CMV) antibody and/or the presence of IgA; if CMV negative and/or IgA deficient the component will be labelled accordingly. Red 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

Red Blood Cells LR SAGM added, are stored in di-ethyl hexyl phthalate (DEHP) plasticized bags.[3,4,5] Segments containing red blood cells and plasma but no SAGM are yellow in colour; segments containing red blood cells, SAGM and residual plasma can vary in colour from pale yellow to a slight pink tinge (due to red blood cells settling out of SAGM).

Storage and handling

Red Blood Cells LR SAGM added must be stored at 1 - 6°C. The shelf life is 42 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.

Visual inspection should be performed; refer to the *Visual Assessment Guide* for further information.[6] A red blood cell unit should be mixed thoroughly prior to transfusion.

Action

Transfused red blood cells increase the oxygen-carrying capacity of the blood by increasing the circulating red blood cell mass.

Indications

Red Blood Cells LR SAGM added is indicated for supplementing oxygen-carrying capacity and for red blood cell replacement in exchange transfusions.

Alternatives to transfusion should be considered prior to the transfusion of red blood cells.

Contraindications

Red Blood Cells LR SAGM added is not suitable for clinical situations where limited oxygen-carrying capacity is not due to red blood cell deficiency or dysfunction.

Warnings and precautions

Red blood cells must be ABO-compatible. Pre-transfusion testing is required unless withholding blood might result in loss of life.[7] Except in special circumstances, Rh negative recipients should receive Rh negative red cells.

DEHP plasticizer leaches gradually into the red blood cells 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 patients 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. Exposure to DEHP may be minimized by using the freshest possible blood or by removing the supernatant.

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

Alloimmunization of the recipient may be a consequence of transfusion.

Red Blood Cells LR SAGM added less than 7 – 14 days old should be considered when large volumes are transfused rapidly to neonates and infants.[8] Theoretical calculations suggest that, in some settings of massive transfusion in the neonate, infusion of the quantities of constituents found in additive solutions should be avoided. In these settings it may be prudent to remove the supernatant additive solution and resuspend the red cells in the fluid that is most appropriate for the procedure. However, there are anecdotal reports of the use of additive solutions in large-volume transfusions in neonates without adverse effect.

Red blood cells should not be the only fluid used in volume resuscitation or massive transfusion.

Patients being transfused with large volumes of red blood cells should be monitored for circulatory overload and other complications of massive 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)[9] 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.†	
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 619 million

† 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.[7,10,20] For further information, refer to the Canadian Standards Association, *Blood and Blood Components* and *Transfusion Transmitted Injuries Surveillance System*.[7,12]

TABLE 3: The following adverse events have been described with transfusion of red blood cell components.[10,12,13,15,16,17]

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 500	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.
Transfusion related acute lung injury (TRALI)	1 in 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.
Delayed hemolytic transfusion reactions (HTR)	1 in 7,000	Hemoglobin levels fall 4 – 14 days post transfusion.	Direct antiglobulin test may be positive. Usually due to an anamnestic response.
Immediate hemolytic transfusion reactions (HTR)	1 in 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.
Septic reaction	1 in 500,000 (see explanation in Notes)	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and/or disseminated intravascular coagulation.	Approximate frequency per red 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[14]: • bacterial sepsis 1:500,000 • death from bacterial sepsis 1:10,000,000 For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference #10.
Isolated hypotensive reaction	Unknown	Hypotension, occasionally accompanied by urticaria, dyspnea or nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Non-immunologic hemolysis	Uncommon	Fever, chills, hemoglobinuria, chest pain, back pain, dyspnea, shock, disseminated intravascular coagulation and/or renal failure.	Due to simultaneous administration of a hypotonic fluid with transfusion, bacterial contamination or hemolysis from improper handling of the blood, e.g. freezing or overheating.
Anaphylaxis	Rare	Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea, 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.
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.
Graft-versus-host disease (GVHD)	Rare	Pancytopenia, rash, liver dysfunction, diarrhea.	Irradiated cellular blood components reduce this risk.
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.
Iron overload	Dependent on clinical situation	Early stages may be asymptomatic. Clinical signs relate to hepatic, pancreatic and/or cardiac organ damage.	Due to repeated red blood cell transfusions.
Hyperkalemia	Dependent on clinical situation	Cardiac arrhythmia, changes in ECG, and/or cardiac arrest.	Seen in massive, rapid transfusion; neonates and infants receiving red cells irradiated prior to storage are at particular risk.
Other complications of massive transfusion	Dependent on clinical situation	Complications may include hypothermia, citrate toxicity, acidosis, dilutional coagulopathy.	Appropriate monitoring may abrogate some complications.

** 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

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

Clinical signs and symptoms of hypoxia, ongoing blood loss and risk of anemia to the patient need to be considered when determining dose. Each unit should raise the hemoglobin concentration in an average size, non-bleeding adult by approximately 10 g/L.[12] Common pediatric dosing is 10-15 mL per kg body weight. Alternatively, the following formula could be used:[18]

Volume to transfuse = 0.5 x (desired Hb – current Hb) x patient weight
Volume in mL; Hb in g/L; weight in kg

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 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.[7] 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.

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. Patients should be under clinical observation, in accordance with institutional guidelines, during transfusion with close observation during the first 15 minutes.

Modification and additional information

TABLE 4: Modified Components

Modification	Description	Indication	Storage	Benefits	Adverse events
Washed	Most of the plasma is removed; unit contains ≥75% of red blood cells from original unit after washing. Washed red blood cells are resuspended in 100 mL **SAGM**.	Recipient with a history of severe or repeated reactions to blood components (unresponsive to pre-medication).	1 - 6°C: transfuse within 7 days. 20 - 24°C: transfuse within 4 hours.	Less frequent febrile non-hemolytic and allergic reactions.	As per Table 3.
Extra Wash (IgA deficient)	Most of the plasma is removed; unit contains ≥75% of red blood cells from original unit after washing. Washed red blood cells are resuspended in 100 mL **SAGM**.	IgA-deficient recipient with anti-IgA	1 - 6°C: transfuse within 7 days. 20 - 24°C: transfuse within 4 hours.	Less frequent febrile non-hemolytic and allergic reactions.	As per Table 3.
Deglycerolized (frozen/thawed)	Glycerol added and unit frozen within 21 days of collection. Once thawed, washing removes glycerol and supernatant fluid in a process known to retain an average of ≥80% of red blood cells from original cryopreserved unit and a hematocrit ≤0.80 L/L. The suspension medium is either AS-3 or 0.9% sodium chloride injection, with 0.2% dextrose as indicated on the label. A pink-tinged supernatant after washing is acceptable for transfusion, otherwise return unit to the blood bank.	Red blood cells for patients requiring specific or rare phenotypes not available in liquid inventory.	Frozen: up to 10 years. 1 - 6°C: In AS-3, transfuse within 24 hours or 14 days, as indicated on the product label. 1-6°C: in 0.9% sodium chloride injection with 0.2% dextrose, transfuse within 24 hours. If stored above 6°C: In either suspension medium transfuse within 4 hours.	Permits prolonged storage of rare blood types.	As per Table 3. Intravascular hemolysis due to residual glycerol; slightly increased risk for bacterial contamination.
Irradiation[19]	Cells are exposed to ionizing radiation (i.e., gamma or x-ray).	Recipients who are immunocompromised or who receive units from closely matched HLA or related/directed donor.	1 - 6°C: 14 days post-irradiation or 28 days post collection, which ever comes first[21]. **Washed, Extra Washed & Irradiated** 1 - 6°C: 48 hours post-irradiation or original expiry date, which ever comes first.	Reduces risk of GVHD.	As per Table 3. The risk of hyperkalemia following irradiation increases with time in storage.
Divided	An integral satellite pack is attached to the unit to facilitate transfusion of aliquots.	Neonates.	1 - 6°C: 42 days, unless otherwise specified.	Reduced donor exposure.	As per Table 3.
Pooled Component for neonate exchange transfusion	Units meeting the following criteria: ≤ 5 days old, ABO group O, Rhesus negative, CMV seronegative, Kell antigen negative, antigen negative to maternal antibody and ideally negative for hemoglobin S are irradiated and the SAGM additive volume is reduced. Compatible thawed plasma is then added to a final hematocrit of 0.45 to 0.60 L/L.	Exchange transfusion for the treatment of neonates with severe hemolytic disease of the newborn (HDN).	1 - 6°C: transfuse within 24 hours.	Antigen negative to maternal antibody	As per Table 3.

Autologous Donations

Autologous donor samples are typically tested as described previously. Syphilis and anti-HBcore are not mandatory tests for autologous donations.[7] Autologous units found to be repeat reactive, but negative/indeterminate on confirmatory/supplemental testing for any of the transmissible disease markers will be labelled as "Biohazard" and providing all other requirements have been met, may be released with the approval of both Canadian Blood Services and recipient's physician.

In addition, syphilis confirmatory positive units may also be released with "Biohazard" labelling.

Directed Donations

Directed donations are donations made by a donor chosen for or by the recipient. This type of donation is offered in specific and limited cases and may be given only by parents or legal guardians to their minor children. A directed red blood cell unit must meet all the standards required for **Red Blood Cells LR SAGM added**.

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Canadian Blood Services
1800 Alta Vista Drive
Ottawa, Ontario, Canada
K1G 4J5

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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.[20]