

CIRCULAR of information

For the use of
Labile Blood
Products

DECEMBER 2015

Edition

WARNING: The risk of transmitting known and unknown infectious disease agents is present in the transfusion of labile blood products. Careful donor selection and available laboratory tests do not eliminate this hazard. Also, several other risks are associated with transfusion. The known risks are described in this Circular.



HÉMA-QUÉBEC

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NOTICE TO USERS

This Circular of information is intended to complement the information provided on labile blood product (LBP) bag labels.

Like many other medical acts, the transfusion of LBPs involves risks, as does deciding not to transfuse. LBPs are human biological products intended for use in the treatment of patients. Professional judgment based on clinical evaluation determines the selection of components, dosage, and the rate of administration. Attention to the specific indications for LBPs is needed to prevent inappropriate transfusions.

This Circular should not be considered or interpreted, in whole or in part, as an explicit or implicit guarantee of the safety of LBPs.

Given the risks associated with transfusion, physicians must be familiar with the known, common alternative procedures.

This Circular is being distributed to conform with applicable regulations issued by the Health Products and Food Branch of Health Canada, in accordance with the Food and Drugs Act. Additions to the Circular will be issued regularly to complete/update it between revisions.

An electronic version can be found on Héma-Québec's Internet site.

I. GENERAL INFORMATION

A GENERAL INFORMATION

A.1 Donor eligibility

The LBPs described in this Circular have been collected from eligible volunteer donors who have:

- been advised of high-risk behaviors exposing them to diseases potentially transmitted through blood;
- filled out a questionnaire intended to screen out high-risk donors;
- satisfied minimum physiological criteria set out in Héma-Québec's *Donor Selection Criteria Manual*;
- were informed that, if they think, for any reasons, that their blood should not be transfused to a patient, they should advise Héma-Québec immediately.

A.2 Preventive measures

The puncture site is disinfected with an antiseptic solution before the needle is inserted. The first milliliters of blood are shunted into a pouch to reduce the risk of bacterial contamination.

A.3 Testing of donor blood

Laboratory tests are done on each blood donation before the LBPs are placed in inventory.

Tableau I.1 Tests done on donor blood

Agents	Ab	Ag	NAT
HIV 1/2 and group O	√	N/A	N/A
HIV-1	N/A	N/A	√
HBV	√ ⁽¹⁾	√	√
HCV	√	N/A	√
HTLV I/II	√	N/A	N/A
Syphilis	√	N/A	N/A
CMV	√ ⁽²⁾	N/A	N/A
WNV	N/A	N/A	√ ⁽³⁾
Chagas or <i>Trypanosoma cruzi</i> ⁽⁴⁾	√	N/A	N/A
Parvovirus B19 ⁽⁵⁾	N/A	N/A	√

N/A Not applicable

(1) Anti-HBc

(2) Done on a portion of the inventory.

(3) Test performed on each donation during the WNV transmission season (generally from May 31st to November 30th). Outside this period, performed if travel outside of Canada in the last 56 days.

(4) Test perform if the donor present risk factors for Chagas disease (born in an endemic country, mother or maternal grandmother born in an endemic country, travelled to or resided in an endemic country for 30 consecutive days or more).

(5) Performed only on donation with a plasma for fractionation.

Tests are also done on each donation to determine the ABO and Rh groups (D and weak D antigens), and to screen for clinically significant irregular antibodies.

A.4 Labelling of LBPs

Labels contain the following information:

Table I.2 List of information on the label

Information	Bar code
1. Official name, including any qualifications and/or attributes Product code in ISBT format	N/A √
2. Donation identification number, including establishment code	√
3. Blood group; donor's ABO group and, where applicable, Rh group in ISBT format. When "Rh negative" is indicated, the blood has been found negative for both D and weak D antigens.	√
4. Date and time of collection (except for pooled platelets : date and time of preparation)	√
5. Expiration date and time	√
6. Method by which the LBP was prepared	N/A
7. Temperature range at which the LBP is to be stored	N/A
8. Preservatives and anticoagulants used	N/A
9. Real product volume	N/A
10. Type of donation (autologous, directed)	√
11. General statements regarding this Circular and infectious disease risks	N/A
12. Manufacturer's name and the establishment's license number	N/A
13. Sedimenting agent used during Granulocytes Apheresis	N/A
14. Red blood cell phenotypes	√
15. Platelets genotypes	√
16. T.E.N.D / H.T.N.D. : Titre Élevé Non Détecté / High Titer Not Detected	√
17. CMV related information	√
18. IgA deficient plasma related information	√

√ = Information encoded in an ISBT structure

A.5 General instructions concerning transfusion of LBPs

1. Compatibility

All blood samples from LBP recipients must be analyzed according to current medical practices to verify compatibility recipient-donor according to LBP to be transfused.

- **Red blood cells** must be ABO-compatible with recipient plasma ABO antibodies.
- **Platelets** should be ABO-compatible with recipient plasma ABO antibodies, when possible.
- Regarding **plasma**, compatibility tests before transfusion are not necessary. However, the plasma must be ABO-compatible with the recipient's red blood cells. Rh need not be considered when using this component.

- Because the **cryoprecipitate** contains ABO antibodies, an ABO-compatible material is preferred especially for large volume transfusion in relation to the red blood cell quantity of the recipient. Rh need not be considered when using this component.
- Compatibility tests before transfusion of **cryoprecipitate supernatant** are not necessary. However, cryoprecipitate supernatant must be ABO-compatible with the recipient's red blood cells. Rh need not be considered when using this component.

See table LABILE BLOOD PRODUCTS AVAILABLE FROM HÉMA-QUÉBEC at the end of this notice.

2. The intended recipient and the LBP must be properly identified before the transfusion is started.
3. LBP containers must be intact.
4. LBPs must be transfused using a sterile, pyrogen-free transfusion set equipped with a filter designed to trap aggregates (170-260 µm in diameter) (see [Section A.6.4.4 Microaggregates](#)).
5. LBPs must be mixed thoroughly before use.
6. **No medications or solutions containing calcium or glucose should be added to or infused through the same tubing with the LBPs.** Depending on hospital policy, a 0.9% Sodium Chloride Injection (USP), ABO-compatible plasma or 5% albumin may be used.
7. Hemolysis may become evident during the storage of LBPs containing red blood cells. LBPs should be carefully inspected for signs of hemolysis before administration.
8. Microbial growth may become evident during the storage of LBPs. LBPs should be carefully inspected before administration for microbial growth.
9. If, upon visual inspection, the acceptability of a LBP is questionable (due, for example, to the presence of hemolysis, floccular material or a cloudy appearance), it should be returned to the hospital blood bank or Héma-Québec for further evaluation.
10. When thawing a LBP in a water bath, care must be taken to prevent contamination of ports. The use of watertight protective plastic over-wraps is required. Fibrin presence in a thawed product can be due to a partial thawing before transfusion.

11. If, for any reason, the pouch containing the LBP is opened (closed thus far), the LBP expires 4 hours after opening if maintained at 20-24 °C, or 24 hours after opening if refrigerated at 1-6 °C. The new date and time of expiration must be noted on the label and in production records. Opening the container for any reason increases the risk of contamination and reduces the valid storage period.
12. Unless otherwise indicated by the patient's clinical condition, the rate of infusion should be approximately 2 mL/min for the first 15 minutes of the transfusion. The patient should be observed during this period, since some life-threatening reactions may occur even after the infusion of a small amount of blood.
13. The transfusion should be completed within 4 hours of removing the unit from its controlled temperature location, and should never exceed the LBP expiration time and date. The expiration date is the last day on which a LBP may be used.
14. All serious adverse reactions to transfusion **must** be reported to Héma-Québec as soon as possible (see [section A.7 Reporting serious adverse reactions](#)).

A.6 Side effects and hazards of LBP transfusions

A.6.1 Infectious diseases

A.6.1.1 Transmission of infectious diseases

Transmission of infectious diseases may occur in spite of careful donor selection and testing of blood as described in Table I.1.

However, the tests listed above should prevent most, if not all, post-transfusion cases of hepatitis, HIV, HTLV I/II, and WNV. The table below describes the current residual risk.

Table I.3 Residual risk in Quebec

VIRUS	RESIDUAL RISK*
HCV	1/ 35 678 983
HIV	1/ 29 867 748
HBV	1/ 941 327
HTLV	< 1/ 5 382 150
WNV	Variable from year to year**

* Residual risks were calculated based on incident events that occurred at Héma-Québec during the period of August 1st 2006 until July 31st 2011. For HIV and HCV, only one case of seroconversion was observed in this period for each virus.

** Off season, the risk is considered negligible.

Cytomegalovirus (CMV) can cause complications in premature infants of CMV antibody-negative mothers (if the birth weight is less than 1,200 grams) and in other immuno-compromised recipients of cellular LBPs. Approximately 50% of donors are CMV antibody-positive, indicating a prior or current CMV infection. The virus can persist in leukocytes, leading to a carrier status, despite the presence of antibodies. Blood from antibody-negative donors is less likely to transmit CMV just like the use of cellular components leukoreduced also lessens the risk of CMV transmission. Indications for products from CMV antibody-negative donors, in a universal leukoreduced cellular product context at Héma-Québec (except for Granulocytes) are :

- 1- Granulocytes transfusion to CMV antibody-negative recipient or with unknown status;
- 2- Intra utérine transfusions;
- 3- Newborn Exchange transfusions ;
- 4- Transfusions to pregnant women before labour begins.

Babesiose is the most reported post transfusion infection in the United States. In the last 2 decades, more than 150 cases were described. Only one post transfusion Babesiose case was reported in Canada.

Other infectious agents transmitted by transfusion (although rarely in North America) include *Trypanosoma cruzi* (Chagas disease), *Plasmodium spp* (malaria agents), *Toxoplasma gondii*, *Coxiella burnettii* (Q-fever agent), *Rickettsia rickettsii* (Rocky Mountain spotted fever agent), *Borrelia spp*, *Treponema pallidum* (syphilis agent), parvovirus B19, leishmania, brucella, hepatitis A virus, Colorado tick fever, Epstein-Barr virus, Dengue fever virus and HHV-8. Although the possibility of transmission of TT and hepatitis G viruses by transfusion has been demonstrated, it was not documented that these viruses were associated with human pathologies.

A.6.1.2 Bacterial contamination

Bacterial contamination of LBPs may occur. Transfusion of contaminated LBPs can cause serious reactions, including shock and even death. Such reactions have been reported, mainly following the transfusion of platelets and, to a lesser extent, following the transfusion of red blood cells. Contaminations attributed to transfusion of plasma are extremely rare nowadays.

When a blood recipient experiences significant chills, high fever (> 39 °C), and/or hypotension during or immediately after transfusion, the possibility

that the transfused LBP may have been bacterially contaminated should be considered. Septic and toxic reactions may be life-threatening.

In addition to the first mL of blood shunted at the beginning of the donation, all platelet products are tested for bacterial contamination with 20 mL of product 48 hours post collection followed by a 12 hours waiting period post inoculation before distribution. The combination of these two measures decreases the residual risk of bacterial infection per transfusion of platelets to approximately 1/ 1 000 000.

Appropriate treatment should be initiated immediately after the collection of blood samples from the recipient and the LBP for culturing.

A Gram stain of the residual blood in the container should be examined promptly to identify the bacteria. Samples should be collected in a way so as to avoid external contamination during collection and storage. The blood bag should be refrigerated. The blood bag and the bacterial isolates should be saved until an investigation is completed. Such cases should be reported immediately to Héma-Québec, as per the instructions in [Section A.7, Reporting Serious Adverse Reactions](#).

A.6.2 Creutzfeldt-Jakob disease (vCJD)

There is also a theoretical risk of transmitting the classical form of Creutzfeldt-Jakob disease, although no cases have been documented to date. However, there are 4 reported cases of transmission by the variant Creutzfeldt-Jakob disease (vCJD) by transfusion, all in the United Kingdom, epicenter of the outbreak.

A.6.3 Immunological reactions

A.6.3.1 Hemolytic transfusion reactions

Hemolytic transfusion reactions usually occur when the donor's red blood cells and the recipient's plasma are incompatible. Undetected serological incompatibilities can cause these reactions, but several immediate reactions occur when clerical or identification errors lead to an ABO mismatch. All personnel who draws samples from patients or who starts transfusions must know and follow procedures to ensure proper identification of the product and recipient. Delayed hemolytic reactions may occur a few days after transfusion in patients with antibodies undetectable at the time of compatibility testing.

The most severe transfusion reactions are characterized by shock, chills, fever, dyspnea, chest pain, back pain, headache, abnormal bleeding, or all

of these symptoms. These reactions can result in death. In anesthetized patients, hypotension and evidence of disseminated intravascular coagulation (DIC) may be the first indications of a transfusion reaction. Depending on the type and intensity of the hemolysis, hyperbilirubinemia, hemoglobinemia and hemoglobinuria can be detected. Renal failure may ensue if an immediate hemolytic reaction occurs. **The transfusion must be stopped immediately.** The procedure to follow must be outlined in a hospital procedure.

Some uncommon causes of acute, non-immune-mediated hemolysis in patients include:

- Administration of a hypotonic fluid;
- Overheating or freezing of red blood cells;
- Bacterial infection in the patient by a LBP (see [Section A.6.1.2 Bacterial contamination](#)).

A.6.3.2 Alloimmunization of the recipient

Alloimmunization of the recipient to red blood cell, leukocyte, platelet and protein antigens may be a consequence of transfusion. This complication is usually not life threatening, nor does it cause immediate symptoms. If erythrocyte alloimmunization is noted, LBP for subsequent transfusions may need to be negative for the specific antigens to which the recipient has become alloimmunized to avoid reactions.

Antibodies to red blood cells, which may have been stimulated by a previous pregnancy or transfusion, will usually be detected in an antibody-screening test before transfusion. See CAN/CSA–Z902 “Blood and Blood Components” (CSA) on this subject.

A.6.3.3 Post-transfusion purpura

Post-transfusion purpura (PTP) is a rare syndrome characterized by the sudden onset of thrombocytopenia, usually 7-10 days post-transfusion and lasting for a short period in a patient HPA-1b/1b (for example) previously sensitized to another platelet antigen, most of the time HPA -1a. PTP can be induced by transfusion from red blood cells, platelets or plasma. This reaction involves the destruction of transfused platelets and the patient's own platelets (mechanism still not well known). Available treatments for this serious complication include therapeutic plasmapheresis, immunosuppressant drugs and I.V. immunoglobulins.

A.6.3.4 Allergic reactions

Allergic reactions manifested by urticarial, dyspnea, sibilance or hypotension may occur in 1% or more of recipients depending on the type of transfused product.

This may be due to passive transfer of antibodies during the transfusion but the exact cause of these reactions is unknown for most cases. However, this may be prevented in patients with a prior history of such reactions by premedication of the patient with an antihistamine and/or a corticosteroid. If necessary, washed red blood cells can be used as an alternative.

For IgA deficient recipients, washed or deglycerolized red blood cells, or IgA deficient LBP may be used according to the medical assessment.

A.6.3.5 TRALI (Transfusion-related acute lung injury)

Respiratory failures without overload due to involvement of pulmonary microcirculation are, although rare, more common with plasma than red blood cells. These reactions can be caused by the presence of anti-leukocyte antibodies (anti-HLA and anti-HNA) in the blood donor.

Because these antibodies are more frequent in women with a history of pregnancy, the plasma and platelet products distributed to hospitals come from men or women without history of pregnancy. In rare cases, HLA and/or HPA compatible, rare or typed apheresis platelets from women with a history of pregnancy, may be distributed according to a medical assessment.

A.6.3.6 Febrile reactions without chills

Febrile reactions, with or without chills, may occur in more than 1% of transfusions depending on the type of transfused products. It is likely that the presence of inflammatory and pro-inflammatory products released by leukocytes in the labile blood product (LBP) can be the cause of these febrile reactions in the recipient.

The frequency of such reactions is reduced by using platelets and red blood cells leukoreduced before storage.

A.6.3.7 Graft-versus-host disease (GVHD)

Graft-versus-host disease may occur in patients with insufficient immune competence (e.g. premature babies and hematopoietic cell recipients). GVHD results from the presence of viable lymphocytes in transfused LBPs, which proliferate and attack host tissue. In rare cases, GVHD may occur in recipients of transfusions from first-degree family members (parents,

children and siblings) due to shared antigens of the major histocompatibility complex. Irradiation of LBPs before administration is useful in reducing the risk of GVHD.

Cellular products must be irradiated just before transfusion to newborns, in whom a significant portion (usually greater than 20%) of the total blood volume is being replaced. Removal of residual additive solution in transfusions to newborns is preferable to reduce the risk associated with high levels of potassium.

Irradiated red blood cells expire on their original expiration date or 28 days after irradiation, whichever comes first. See CAN/CSA–Z902 “Blood and Blood Components” (CSA) on this subject.

A.6.4 Physiological and metabolic complications

A.6.4.1 Circulatory overload reactions

Circulatory overload reactions manifested by pulmonary edema occur when excessive volumes of LBP are administered. It is necessary to take into account all the liquids administered and not only LBP volume.

This is a particular risk in the elderly, in women, in patients of small stature and in patients with chronic severe anemia. Immediate treatment for pulmonary edema should be instituted, as per hospital protocol. Careful monitoring of the transfusion volume (including all LBPs) will minimize the occurrence of these reactions.

A.6.4.2 Metabolic and thermal complications

Metabolic or thermal complications can occur when very large amounts of blood (equal to or greater than the patient’s blood volume) are infused quickly, or when the patient has severe liver or kidney disease. The following are examples of metabolic complications:

- a) *Hypothermia* with the risk of cardiac arrhythmia may occur in rapid, massive transfusion with cold blood or when cold blood is administered through a central venous line. Hypothermia may be accompanied by other metabolic changes and affect oxygen release from hemoglobin. Warming the blood can prevent this complication.
- b) *Citrate toxicity* due to the complexing of ionized calcium by the anticoagulant in the blood is very rare. The calcium stores in the body are large, and the citrate anticoagulant is usually rapidly metabolized. However, citrate toxicity may occur if a patient with severe liver disease undergoes exchange transfusion or rapid transfusion, where the rate of

infusion is greater than one unit every five minutes. Symptoms can range from tremors to cardiac arrhythmia, and even cardiac arrest. ECG monitoring can be helpful in detecting the effects of hypocalcemia.

In the absence of an underlying pathology contributing to hypocalcemia, most citrate reactions require no treatment other than slowing or discontinuing the transfusion.

- c) Hyperkalemia may occur during rapid or massive transfusions. Newborns and infants receiving red blood cells, irradiated before storage, are particularly at risk which could justify the washing of the product and in this case, the transfusion should occur within 48 hours. Other complications further to massive transfusion such as hypothermia, citrate toxicity, metabolic acidosis or coagulopathy by dilution may occur. Careful monitoring may prevent certain complications.

A.6.4.3 Clinically significant depletion of coagulation proteins and platelets

Clinically significant depletion of coagulation proteins and platelets is a potential complication associated with massive transfusion. To prevent or treat this complication, platelets or plasma, and, if needed, specific coagulation factors can be transfused.

A.6.4.4 Microaggregates

Microaggregates consisting of fibrin, white blood cells and platelets may develop during storage of blood. The smallest of these particles will not be trapped by the standard perfusion tubing filter. The use of microaggregate filters designed to trap these particles has been suggested during interventions requiring extracorporeal circulation, when pulmonary circulation is excluded from the vascular transfusion circuit.

A.6.4.5 Iron overload

Iron overload followed by hemosiderosis may occur in patients given numerous transfusions of red blood cells over the long term.

A.6.5 DEHP

DEHP [Di(2-ethylhexyl)phthalate] is a component of the plastic used in blood product bags and tubing allowing them to be flexible and malleable. However DEHP leaches gradually into the red blood cells during storage. DEHP integrates the red blood cells membrane favoring a prolonged

storage. Although DEHP does not accumulate during storage of frozen LBPs, DEHP concentration increases in thawed plasma stored 5 days between 1 and 6°C. It is also found in negligible quantity in platelets stored in bags manufactured with a plastic without DEHP.

There is actually no scientific proof that DEHP, which is use in the composition of a large number of medical devices, may represent a toxicity risk for patients exposed during a transfusion.

A toxic effect on the development of the male reproductive system in rodents has been shown. Recipient's populations most at risk are the following: Fetuses, newborns, and pre-pubescent boys who receive massive transfusions. Exposure to DEHP can be minimized by using the freshest possible blood.

World Health Organization considers DEHP like a possible carcinogen substance. Presently, alternative substances to DEHP for biomedical instruments are under investigation. Safety and biocompatibility levels of theses new plastics are still to be confirmed.

A.6.6 Latex

All types of bags used at Héma-Québec are latex free except for red blood cells pediatric bags.

A.7 Reporting serious adverse reactions

It is important to report serious transfusion reactions in order to:

- withdraw other LBPs produced from the blood of the donors in question;
- conduct the necessary investigations and, when appropriate, apply suitable corrective measures to prevent or reduce such reactions;
- ensure that all persons involved are notified so that preventive and/or therapeutic measures may be taken as soon as possible.

Any serious adverse reaction that appears to have been caused by a blood component must **immediately** be reported to Héma-Québec.

Héma-Québec must report the serious adverse reaction to Health Canada within 15 days of receiving the initial report from the hospital blood bank.

If a fatality occurs and an initial investigation by the hospital blood bank indicates the fatality is attributable to the blood transfusion, the hospital blood bank shall report **the fatality** to Héma-Québec within 24 hours.

Héma-Québec must report to Health Canada all fatalities related to the transfusion of a blood component within 24 hours following the notification by the hospital blood bank or the attending physician.

Benign adverse reactions such as minor febrile and allergic reactions need not normally be reported to Héma-Québec unless the attending physician feels that the nature of the reaction warrants investigation by Héma-Québec.

A.8 Traceback and lookback for HIV, HBV, HCV, HTLV, WNV, B19 and *Trypanosoma cruzi*

A.8.1 Traceback

Héma-Québec will conduct a traceback on donors whose blood was given to a patient who tested positive for one of these microorganisms post-transfusion.

Physicians must notify Héma-Québec as soon as possible of all HIV, HBV, HCV, HTLV, WNV, B19 and *Trypanosoma cruzi* infections diagnosed post-transfusion.

Héma-Québec must be notified even if there are other contamination risk factors for the patient in question.

To complete its traceback, Héma-Québec needs the list of blood products received by the infected person. For each transfusion, the hospital blood bank must provide the following information: Type of LBP, identification number, date of collection and date of transfusion.

A.8.2 Lookback

When Héma-Québec learns that a blood donor has tested positive for one of these microorganisms :

- it excludes the donor permanently (except for B19 and WNV);
- it draws up a list of the deferred donor's previous donations;
- it notifies hospitals that received LBPs prepared from these donations;
- it asks attending physicians to test their patients who were transfused with these products and to inform Héma-Québec of the results (except for B19 and WNV).

Thus, physicians should ask their patients infected with HIV, HBV, HCV, HTLV, WNV, B19 or *Trypanosoma cruzi* if they have ever donated blood. **If this is the case, Héma-Québec must be notified immediately.** The notification must include the donor's name, gender, address, date of birth

and donor number (if available) so that Héma-Québec can investigate the donor's previous donations and inform hospital blood banks that received LBPs prepared from these donations.

Physicians should only notify Héma-Québec after obtaining the patient's informed consent. They must always comply with public health regulations regarding certain infectious diseases. Donors can be assured that the information sent to Héma-Québec will be kept strictly confidential. When communicating with hospital blood banks, Héma-Québec only provides the unit identification number of the LBPs being investigated.

A.9 Reporting other transfusion-related infections

Suspected transfusion-related infections should be reported to Héma-Québec, which will then take measures similar to those described in [Section A.8, Traceback and lookback for HIV, HBV, HCV, HTLV, WNV, B19 and *Trypanosoma cruzi*.](#)

II. ALLOGENIC LABILE BLOOD PRODUCTS

Only allogenic red blood cells and platelets are leukoreduced.

These products respect the following standard: Less than 5×10^6 leukocytes per unit.

Henceforth, to lighten the text, the term “leukoreduced” will be omitted.

Table II.1

Summary of anticoagulants					
Anticoagulant solution	Sodium citrate	Citric acide	Monobasic sodium phosphate	Dextrose	Adenine
Citrate phosphate dextrose (CP2D) (63 mL)	26,3 g/L	3,27 g/L	2,22 g/L	51,1 g/L	N/A
CPD (63 mL)	26,3 g/L	3,27 g/L	2,22 g/L	25,6 g/L	N/A
ACD-A	22,0 g/L	7,3 g/L	N/A	24,5 g/L	N/A
Sodium citrate	40 g/L	To adjust pH	N/A	N/A	N/A

Table II.2

Summary of additives		
In water for injection (USP)	AS-3 additive (100 mL)	SAGM additive (100 mL)
Glucose	11 g/L	9 g/L
Adénine	0,3 g/L	0,169 g/L
Citric acid	0,42 g/L	N/A
Sodium citrate	5,88 g/L	N/A
Phosphate	2,76 g/L	N/A
Sodium chloride	4,1 g/L	8,77 g/L
Mannitol	N/A	5,25 g/L

Table II.3

Summary of Red Blood Cells characteristics				
QC data* 2013, May 27 to 2015, March 31	Hb mean (g/bag)	Ht mean (L/L)	Volume mean (mL)	RBC Volume mean (mL)
RBC CP2D/AS-3 (n=3335)	56 ±6	0.55 ±0.03	304 ±17	166 ± 17
RBC CPD/SAGM (n=1184)	53 ±5	0.56 ±0.02	277±19	156 ±15
Apheresis RBC ACD-A/AS-3 (n=806)	59 ±3	0.55 ±0.02	321 ±11	176 ±9
Washed RBC 24 h expiration (n=59)	55 ±5	0.70 ±0.04	230 ±20	162 ±15
Washed RBC 7 days expiration (n=36)	51 ±6	0,53 ±0.04	285 ±15	150 ±14
Deglycerolyzed RBC (n=88)	52 ±5	0.70 ±0.04	203 ±26	155 ± 19

* ± 1 Standard Deviation

B RED BLOOD CELLS

B.1 Description

a) AS-3 red blood cells from whole blood

AS-3 red blood cells are prepared from whole blood collected into CP2D anticoagulant. A typical unit of red blood cells has a hemoglobin superior or equal to 35 g / bag, a hematocrit less or equal to 0.80 L/L and complies with the following table:

If red blood cells volume	State
> 390 mL	washed red blood cells
between 370 and 390 mL with a corresponding plasma < 200 mL	washed red blood cells
between 370 and 390 mL with a history of pregnancy	washed red blood cells

After removal of most of the plasma, the additive solution AS-3 is mixed with the red blood cells (the residual quantity of plasma is evaluated at 29 ± 9 mL).

b) AS-3 red blood cells from apheresis

AS-3 red blood cells are collected by apheresis into ACD-A anticoagulant solution. Units of AS-3 red blood cells have a hemoglobin superior or equal to 35 g / bag and a hematocrit less or equal to 0,80 L/L. This product contains red blood cells with an AS-3 additive solution. The residual quantity of plasma in a unit of AS-3 red blood cells from apheresis is evaluated at 29 ± 5 mL.

c) SAGM red blood cells from whole blood

SAGM red blood cells are prepared from whole blood collected into CPD anticoagulant. A typical unit of red blood cells has a hemoglobin superior or equal to 35 g / bag, a hematocrit less or equal to 0.80 L/L and complies with the following table:

If red blood cells volume	State
> 390 mL	washed red blood cells
between 370 and 390 mL with a corresponding plasma < 200 mL	washed red blood cells
between 370 and 390 mL with a history of pregnancy	washed red blood cells

After removal of most of the plasma, the additive solution SAGM is mixed with the red blood cells (the residual quantity of plasma is evaluated at 17 ± 5 mL).

B.2 Actions

These components improve the oxygen-carrying capacity of the blood by increasing the circulating red blood cell mass.

B.3 Indications

Red blood cells are indicated for treating patients with a symptomatic deficit of oxygen-carrying capacity, including treating newborns with the use of small transfusions. In this case, washed red blood cells or blood from young donors whose level of lead is usually lower, could be used for large volume transfusion.

B.4 Contraindications

Do not use red blood cells when anemia can be treated with specific medications.

Hypovolemia without significant red cell mass deficit is best treated with colloid solutions, crystalloid solutions or albumin.

B.5 Side effects and hazards

The side effects and hazards of transfusion of red blood cells are described in [Section A.6, Side effects and hazards of LBP transfusions](#).

Information on cautions concerning Graft-versus-host disease and indications on the use of irradiated red blood cells can be found in [Section A.6.3.7, Graft-versus-host disease](#).

B.6 Dosage and administration

In an adult, one unit of blood will increase the recipient's hemoglobin by approximately 10 g/L or the hematocrit by 0.03 L/L to 0.04 L/L. The dosage depends on the patient's clinical condition, as well as his/her weight and height.

Transfusion should be completed within 4 hours of removing the unit from its controlled temperature location.

If it is indicated to decrease the volume of LBP transfused, the unit of blood can be centrifuged to remove all or part of the additive solution. This must be done **immediately** before transfusion.

If it is indicated to decrease the additive solution content, it may be desirable to remove it through washing or centrifugation and to resuspend the red blood cells in albumin, 0.9% sodium chloride injection (USP) or plasma to facilitate administration.

B.7 Storage

AS-3 or SAGM red blood cells collected in a hermetically sealed container must be stored at a temperature between 1 to 6 °C. Under these conditions, there is no significant loss of viability or function of red blood cells stored for 42 days.

Validity of these conditions and storage duration applies to units that are intact.

C RED BLOOD CELLS, DEGLYCEROLIZED

C.1 Description

Red blood cells can be prepared for cryopreservation by adding glycerol as a protective agent.

Red blood cells frozen at -80 °C can be stored for up to ten (10) years. With a medical assessment, the storage period can be extended to more than 10 years.

This component is deglycerolised by a method known to retain a mean recovery of at least 80% of the red cells that were in the original red blood cells. The hematocrit is inferior or equal to 0,8 L/L. The hemoglobin is 35 g/bag or more. In LBPs not leukoreduced before storage (prior to June 1999), virtually all the plasma, anticoagulant, residual platelets and leukocytes are removed in the washing procedure. Trace amounts of the cryoprotective agent may still be present in the product. The suspension medium is 0.9% sodium chloride injection (USP), with small amounts of dextrose (0.2%).

After thawing, the free hemoglobin in the supernatant from the last washing is no greater than 150 mg/dL. A pink-tinged supernatant is acceptable for transfusion; however, if the supernatant appears dark red and/or cloudy, the unit should be returned to the blood bank or Héma-Québec for evaluation.

An autologous transfusion from frozen product may be necessary for rare blood types or for individuals with multiple red cell alloantibodies.

C.2 Actions

Red blood cells, deglycerolized are similar in function and post-transfusion survival to AS-3/SAGM red blood cells.

C.3 Indications

Indications for transfusion of this component are the same as for AS-3/SAGM red blood cells. However, their use should be limited to special situations, including:

- Transfusion to individuals with rare blood types;
- Individuals with an alloantibody to a high-incidence antigen.

C.4 Contraindications

Contraindications are the same as for AS-3/SAGM red blood cells.

C.5 Side effects and hazards

Side effects are similar to those for red blood cells, except for reduced risk of febrile non-hemolytic reactions and allergic reactions.

There is a greater risk of bacterial contamination for deglycerolised products prepared with an open system process (24 hours expiration time).

C.6 Dosage and administration

Dosage and administration are the same as for AS-3/SAGM red blood cells.

Transfusion should be completed within 4 hours of removing the unit from its controlled temperature location.

C.7 Storage

Red blood cells, deglycerolized must be administered within 24 hours or 7 days depending on the deglycerolization process used, when stored between 1 to 6 °C and must be transfused before the expiration time or date indicated on the label.

D RED BLOOD CELLS, WASHED

D.1 Description

Red blood cells are washed to reduce considerably the quantity of various plasma proteins and other substances that may cause adverse reactions.

This component contains more than 75% of the red blood cells from the original component. Almost all other substances (anticoagulant, platelets, leukocytes and potassium) are removed in the washing procedure.

Héma-Québec uses two washing procedures. In the open system, the suspension medium is 0.9% sodium chloride injection (USP) and in the closed system, the suspension medium is AS-3 (additive solution).

D.2 Actions

Red blood cells, washed are similar in function and post-transfusion survival to AS-3/SAGM red blood cells.

D.3 Indications

Red blood cells, washed are indicated for patients who are IgA-deficient as well as those with major allergic reactions to other plasma proteins or those with repeat febrile non hemolytic transfusion reaction - FNHTR (as a last resort).

D.4 Contraindications

The contraindications are the same as for AS-3/SAGM red blood cells.

D.5 Side effects and hazards

The side effects are the same as for AS-3/SAGM red blood cells except for the reduced risk of febrile non-hemolytic reactions and allergic reactions.

When using the open system procedure, the risk of bacterial contamination is theoretically increased.

D.6 Dosage and administration

Dosage and administration are the same as for AS-3/SAGM red blood cells.

The transfusion should be completed within 4 hours of removing the unit from its controlled temperature location.

D.7 Storage

When using the open system procedure, RBCs washed have an expiration time of 24 hours when stored between 1 and 6° C and must be administered before the expiration time indicated on the label.

When using the closed system procedure, RBCs washed have an expiration time of 7 days when stored between 1 and 6° C, except when irradiated, see product label.

E RED BLOOD CELLS PEDIATRIC PACKS (NON DIVIDED)

E.1 Description

A sterile connection is used to enable the distribution by the hospital, of the contents of a single pack into four smaller bags as required and the use of the entire product. Pediatric packs enable multiple transfusions of red blood cells from the same unit.

E.2 Actions

Function and post-transfusion survival of the red blood cells in the pediatric packs are similar to those of AS-3/SAGM red blood cells.

E.3 Indications

For neonates requiring multiple transfusions, the advantage of pediatric packs is that the patient is only exposed to the blood of a single donor. Pediatric packs can be used for more than one neonate and also for people with a tiny frame.

E.4 Contraindications

Contraindications are the same as for AS-3/SAGM red blood cells.

E.5 Side effects and hazards

Side effects and hazards are the same as for AS-3/SAGM red blood cells.

E.6 Dosage and administration

Dosage and administration of pediatric packs is essentially the same as for AS-3/SAGM red blood cells.

In the following situations, it may be desirable to remove the preservative medium (AS-3 or SAGM) by washing or centrifugation and to resuspend the red blood cells in albumin or 0.9% sodium chloride injection (USP), as appropriate to prevent hyperkalemia:

- a) Extremely premature neonates or those with hepatic and/or renal insufficiency.
- b) Massive transfusion, e.g. two-volume exchange transfusion, surgery involving a heart-lung machine, and extra-corporeal membrane oxygenation (ECMO) in infants and small children.

E.7 Storage

Pediatric packs have the same expiration time as AS-3/SAGM red blood cells.

F PLATELETS

F.1 Pooled platelets

F.1.1 Description

Five (5) buffy coats from whole blood collected onto a CPD anticoagulant solution and leukoreduced to decrease the leukocytes are used to prepare pooled platelets. This LBP contains at least 2.4×10^{11} platelets/unit suspended in plasma. The plasma used in the pool is from one of the 5 buffy coat donors. Trace amounts of red blood cells may also be present (approximately $11 \pm 5 \mu\text{L}$) and the color of the unit of pooled platelets is yellowish; but may vary from pink to reddish. Pooled platelets contain less than 5×10^6 leukocytes per unit. Moreover, each unit of pooled platelets is cultured for bacterial contamination. See section A.6.1.2.

F.1.2 Actions

The primary role of platelets is to participate in blood coagulation by forming an aggregate that blocks injured blood vessel walls to prevent any bleeding. Platelets also play a role in blood coagulation, inflammatory reactions and the healing of wounds.

F.1.3 Indications

Transfusion of pooled platelets to patients with thrombocytopenia, thrombasthenia and hemorrhaging can stop the bleeding, correct bleeding time and increase platelet count.

It may also be useful in treating some patients with dilutional thrombocytopenia or platelet consumption (see [Section A.6.4.3, Clinically significant depletion of coagulation proteins and platelets](#)).

Pooled platelets may be useful if given prophylactically to patients with thrombopenia (less than $10 \times 10^9/\text{L}$) who are not bleeding. In most instances of dilutional thrombocytopenia, bleeding stops without transfusion.

F.1.4 Contraindications

Do not use this component if bleeding is unrelated to decreased numbers of / or abnormally functioning platelets.

Platelet transfusion is not usually effective or indicated in patients with idiopathic thrombocytopenic purpura (ITP).

Platelets are generally contraindicated in patients with thrombotic thrombocytopenic purpura (TTP), unless the patient has a life-threatening hemorrhage.

F.1.5 Side effects and hazards

Given that the pooled platelets are leukoreduced before storage, the risk of febrile reactions and alloimmunization to HLA and leukocyte antigens is reduced. Moreover, demonstration was made that leukoreduction reduces the risk of transmission of intraleukocyte infectious agents, such as CMV.

As described for LBPs in general (see [Section A.6, Side effects and hazards of LBP transfusions](#)), the side effects of a transfusion of platelets may include fever, circulatory overload and allergic reactions, as well as the transmission of infectious diseases, alloimmunization and GVHD. Information on the use of irradiated blood products can be found in [Section A.6.3.7, Graft-versus-host disease](#).

Special attention must be given to patients who have had a major allergic reaction to platelet transfusion. Of all LBPs, platelets are the ones most likely to cause side effects in the event of bacterial contamination of the product (see [Section A.6.1.2, Bacterial contamination](#)). The recorded risk approximately 1 in 1 000 000 transfusions of platelets.

Platelets carry a variety of antigens, including HLA. When transfused to a patient with a specific antibody for an expressed antigen, the survival time of the transfused platelets may be markedly shortened. The patient may become refractory to all but HLA-matched platelets (see [Section F.2, Platelets, apheresis](#)).

Immunization to red blood cell antigens may rarely occur because of the presence of trace amounts of red blood cells in the platelets unit (see F.1.1 for quantity). When the platelets from Rh-positive donors are transfused to an Rh-negative female of childbearing age, prevention of antigen D immunization by use of Rh immunoglobulin should be considered. In the presence of ABO incompatibility, a direct antiglobulin test may be positive with or without hemolysis.

F.1.6 Dosage and administration

The number of units of pooled platelets to be administered depends on the clinical situation of each patient. One unit of pooled platelets should increase the platelet count of a 70-kg adult by 30 to 60 x 10⁹/L (30 000 - 60 000 / μ L) when measured 20-60 minutes post-transfusion. The expected response will not occur in the following cases: sepsis, fever, ITP, anti-platelet alloimmunization, DIC (disseminated intravascular coagulation) or splenomegaly. Failure to obtain a change in hemostasis, or an increase in platelet count of less than 15 x 10⁹/L/m² (15 000 / μ L/m²), 1-2 hours post-transfusion, in at least 2 consecutive events, may signify that the patient is refractory to the transfused platelets.

Because of the short life span of the transfused platelets, the dose may need to be repeated 1-3 days later.

For pediatric needs, a sterile connection is used to enable the transfer, by the hospital, of the contents of a single unit of pooled platelets into four smaller bags as required. The platelets part transferred in the pediatric bag should be administrated in the 24 hours of the transfer. A residual quantity of 100 mL is necessary in the mother bag to maintain an adequate storage.

Pooled platelets may be transfused as fast as tolerated by the patient, but the transfusion should not take more than 4 hours.

Certain microaggregate filters **should not be used** (see the filter manufacturer's package insert for instructions).

F.1.7 Storage

Pooled platelets may be stored for up to 7 days, as indicated on the label.

Pooled platelets must be stored between 20 to 24 °C and agitated gently and continuously during storage.

F.2 Platelets, apheresis

F.2.1 Description

Apheresis is an effective way to harvest a therapeutic adult dose of platelets from one individual donor. A typical unit of platelets, apheresis collected into ACD-A contains at least 3×10^{11} platelets. If necessary, this dose may be obtained from a donor who is HLA or HPA-matched with the patient.

The component contains less than 5×10^6 leukocytes. Trace amounts of red blood cells may also be present (approximately $3 \pm 2 \mu\text{L}$). Moreover, each unit of platelets is cultured for bacterial contamination. See section A.6.1.2.

F.2.2 Actions

The action of this component is the same as for pooled platelets prepared from whole blood.

F.2.3 Indications

Platelets, apheresis indications are similar to those for pooled platelets prepared from whole blood. Platelets, apheresis from an HLA-compatible donor are primarily indicated for patients refractory to platelets further to anti-HLA alloimmunization. Other causes of refractoriness to platelets include DIC, ITP, hypersplenism, fever and sepsis. For the latter conditions platelets, apheresis from an HLA-compatible donor are just as effective.

Platelets from donors with rare platelet antigens are collected only by apheresis.

F.2.4 Contraindications

The contraindications of this component are the same as for pooled platelets.

F.2.5 Side effects and hazards

The side effects and hazards of this component are similar to those for pooled platelets.

The administration of type O platelets, apheresis to a type A, B or AB recipient may be suitable as long as the hemolysins anti-A / anti-B titer is not considered high (H.T.N.D.).

Note : T.E.N.D / H.T.N.D indicates *Titre Élevé Non Détecté / High Titer Not Detected*.

Without this information, it is best to avoid the transfusion of non isogroup type O platelets, apheresis especially for infant, so that the risk of hemolysis is lower for the recipient.

F.2.6 Dosage and administration

Dosage and administration are similar to those for pooled platelets, because one unit of platelets, apheresis may replace 1 unit of pooled platelets. One unit of platelets, apheresis should increase the platelet count of a 70-kg adult by 30 to 60 x 10⁹/L (30,000 to 60,000/μL) when measured 20-60 minutes post-transfusion. A transfusion of platelets may be required every one (1) to three (3) days during a period of severe bone marrow aplasia.

For pediatric needs, a sterile connection is used to enable the transfer, by the hospital, of the contents of a single unit apheresis platelets into four smaller bags as required. The platelets part transferred in the pediatric bag should be administrated in the 24 hours of the transfer. A residual quantity of 100 mL is necessary in the mother bag to maintain an adequate storage.

For pediatric cases requiring specific HPA platelets, Héma-Québec can collect one single bag of apheresis platelets and split it in two.

F.2.7 Storage

Platelets, apheresis may be stored for up to 7 days when stored between 20 to 24 °C.

Platelets, apheresis must be gently and continuously agitated during storage.

G GRANULOCYTES

G.1 Description

A preparation of granulocytes can be obtained by apheresis from a single donor. The donor is stimulated with a corticosteroid*. Each unit of granulocytes contains at least 1×10^{10} granulocytes, 44 mL (23–76) of red blood cells and a variable number of lymphocytes and platelets in plasma.

Hespan* 6% is used to facilitate the collection of granulocytes.

Approximately 35 ± 10 mL of Hespan 6% can be found in the final product. A 500 mL solution of 6% sodium citrate solution in Hespan 6% is used to collect granulocytes. (Average volume: 32 mL).

* These products are not approved for this use in Canada.

G.2 Actions

Granulocytes phagocytize bacteria. There is an inverse quantitative relationship between the amount of circulating granulocytes and the prevalence of bacterial infection.

A transfusion of granulocytes in itself is rarely associated with an increased amount of granulocytes in the patient. This may be attributable to the sequestering of granulocytes resulting from a prior immunization against leukocytic antigens or the consumption of granulocytes during the infectious process.

G.3 Indications

Granulocytes are primarily indicated as maintenance therapy in patients with significant neutropenia (generally less than $0.5 \times 10^9/L$) and severe, documented bacterial or fungal infection not responding to antimicrobials or antifungals. The efficacy of granulocyte transfusions in various clinical settings has not been proven.

Granulocytes for CMV-seronegative and immunodeficient recipients must come from CMV-seronegative donors.

To prevent GVHD, granulocytes must be irradiated for patients with immune deficiencies.

G.4 Contraindications

This product is not recommended for the prophylactic treatment of infection.

G.5 Side effects and hazards

See [Section A.6, Side effects and hazards of LBP transfusions](#). Chills, fever and pulmonary insufficiency in patients receiving granulocytes can be prevented or reduced by slowing the rate of transfusion and administering meperidine hydrochloride.

Although the amount of Hespan 6 % in the product is approximately 35 mL, side effects, especially allergic reactions, are still possible.

G.6 Dosage and administration

Granulocytes contain a large number of red blood cells, and compatibility tests must be conducted.

Transfusions must be administered at least daily until the infection is cured, fever diminishes or disappears, the absolute number of granulocytes returns to at least $0.5 \times 10^9/L$ (500/ μL), or the attending physician decides to stop the therapy.

Granulocytes should be administered as close to the time of collection as possible using a standard transfusion set. **Microaggregate and leukocyte depletion filters trap granulocytes and must not be used in the transfusion of this component.**

G.7 Storage

The product may be stored between 20 to 24 °C for no longer than 24 hours **without agitation**.

H FROZEN PLASMA

H.1 Description

Plasma is placed and maintained at -18 °C or colder within 24 hours of collection. These products contain proteins, including albumin, stable coagulation factors, such as Factor IX and fibrinogen in concentrations similar to those in fresh frozen plasma, apheresis, although they contain less of Factors V and VIII and of von Willebrand.

Frozen plasma :

- a) is prepared from whole blood collected in a closed system into CP2D or CPD.
- b) is harvested by apheresis in a closed system, in ACD-A.

H.2 Actions

Frozen plasma is a source of multiple plasma proteins of therapeutic value, including albumin and stable coagulation factors in variable quantities. Amongst those that can be administered to treat patients with plasma protein deficiencies, there is the fibrinogen (2–4 mg per mL) and other coagulation factors with a concentration that reaches one unit per mL. Factors V, VIII and von Willebrand are excluded because of their low concentration in this type of plasma.

H.3 Indications

Legend – Levels of evidence

- I Evidence obtained from at least one properly randomized controlled trial.
- II Evidence obtained from well-designed controlled trials without randomization, cohort or case-control analytic studies, preferably from more than one centre, or evidence obtained from comparisons between times or places with or without the intervention.
- III Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

Referring to this table, the [Guidelines for red blood cell and plasma transfusion for adults and children](#) of the *Canadian Medical Association Journal*, recommend that plasma be transfused to patients with acquired deficiencies of several coagulation factors in the following circumstances:

- a. Serious bleeding has occurred or when preparing for an emergency surgical or invasive procedure in patients with vitamin K deficiency (or on warfarin therapy) with significantly increased PT, INR or aPTT. (Level of evidence: III)
- b. Actual bleeding in patients with liver disease and increased PT, INR or aPTT. Plasma may also be administered to prepare for surgery or liver biopsy when the results of PT, INR, aPTT or other appropriate coagulation assay are deemed sufficiently abnormal. (Level of evidence: II)
- c. Plasma can be administered in patients with acute disseminated intravascular coagulation (DIC) with active bleeding associated with increased PT, INR or aPTT. This decision is at the discretion of the attending physician who can evaluate the risk inherent to DIC. (Level of evidence: II)

d. Plasma should be administered in the context of massive transfusion (more than 1 blood volume) if there is microvascular bleeding associated with a significantly increased PT, INR or aPTT. If PT, INR or aPTT cannot be measured quickly, plasma may be transfused in accordance with a massive transfusion protocol.
(Level of evidence: II)

Plasma should be used in the treatment of TTP or adult HUS, followed as soon as possible by daily plasmapheresis with either cryosupernatant or plasma. Plasma transfusion or exchange is not recommended in the classic form of pediatric HUS.
(Level of evidence: I)

Plasma should be used in patients with acquired deficiencies of a single coagulation factor only when DDAVP (desmopressin) or appropriate factor concentrates are ineffective or unavailable. Plasma should be used in these patients only when bleeding has occurred or is reasonably expected to occur from surgery or other invasive procedures.
(Level of evidence: III)

H.4 Contraindications

Several concentrated coagulation factors are commercially available and are often preferred to frozen plasma due to their speed of action. Volume overload is also prevented. Consequently, frozen plasma is not indicated to correct coagulation deficiencies when a specific stable product is available. Also if time allows it, frozen plasma must not be used if the coagulopathy can be corrected more effectively with a specific treatment, such as vitamin K.

In non-urgent situations, frozen plasma must not be used when the blood volume can be adequately replaced by other volume expanders, such as 0.9% sodium chloride injection (USP), Ringer's lactate injection (USP), or albumin.

According to the [Guidelines for red blood cell and plasma transfusion for adults and children](#) of the Canadian Medical Association Journal, plasma must not be transfused in the following cases:

- a. intravascular volume expansion or repletion (except in massive transfusions) where crystalloids, synthetic colloids or purified human albumin solutions are preferred;
- b. the correction of hypoalbuminemia or protein malnutrition, where purified human albumin or synthetic amino acid solutions are preferred;

- c. the correction of hypogammaglobulinemia, where purified human immunoglobulin concentrates are preferred;
- d. the treatment of hemophilia and von Willebrand's disease where desmopressin (DDAVP) or existing virus-free factor concentrates are preferred;
- e. the treatment of any other isolated congenital procoagulant or anticoagulant factor deficiency, where virus-inactivated or recombinant factor concentrates are preferred if they exist.

In the past, plasma has been used for life-threatening complications of hereditary angioneurotic edema due to deficiency of C1-esterase inhibitor. A pasteurized concentrate now also exists for the treatment of this disorder.

H.5 Side effects and hazards

See [Section A.6, Side effects and hazards of LBP transfusions](#). **However, the comments regarding CMV and HTLV-I/II do not apply.**

H.6 Dosage and administration

Volume transfused depends on the patient's clinical picture and size, and may be determined according to laboratory coagulation test results.

Frozen plasma may be thawed rapidly in a water bath or any other device licensed for that matter, at a temperature between 30 to 37°C for about 30 minutes, using gentle agitation. Transfusion ports must be protected from water by placing the plasma bag in a watertight protective plastic over-wrap. The number of plasma to be thawed at the same time should be limited so the temperature of the water bath is not unduly modified and the time of thawing does not need to be extended.

Product must be transfused within 5 days of thawing. Do not use if there is evidence of container breakage or thawing during storage.

Guidelines for red blood cell and plasma transfusion for adults and children of the Canadian Medical Association Journal states: "These guidelines differ from others in not explicitly stating volumes of plasma to be administered". The EWG (Expert Working Group) agreed that published practical guides for appropriate initial-dose volumes in given clinical situations are prudent. It was recommended that plasma be given in doses calculated to achieve a minimum of 30% of normal concentrations for most plasma factors (usually achieved with administration of 10-15 mL of plasma per kilogram body weight), except for urgent reversal of warfarin anticoagulation, for which 5-8 mL/kg will usually suffice.

However, these values are derived not from systematic assessments of therapy, but from synthesis of physiologic measurements of factor concentrations, hemostatic function and clinical observations of the effect of plasma administration on abnormal coagulation. Ongoing clinical and laboratory assessments are necessary to determine subsequent action.

H.7 Storage

Frozen plasma may be stored for 12 months at -18°C or colder. When thawed for use, it can be stored in a closed system between 1 to 6°C and be transfused within 5 days after thawing. It must not be refrozen.

I FRESH FROZEN PLASMA, APHERESIS

I.1 Description

Fresh frozen plasma, apheresis (FFPA) is collected by apheresis (open system) and stored at -18°C or colder within **8 hours**. An anticoagulant, sodium citrate (average volume: 77 mL), is added during the apheresis process. The FFPA contains a minimum of 0.70 IU/mL of Factor VIII, as well as all other coagulation factors.

I.2 Actions

FFPA contains plasma proteins, including all coagulation factors.

FFPA also has oncotic and blood volume expansion properties.

I.3 Indications

FFPA is similar to frozen plasma, except that it has higher levels of Factors V, VIII and von Willebrand.

See [Section H.3, Indications](#).

I.4 Contraindications

Contraindications for FFPA are the same as for frozen plasma. See [Section H.4, Contraindications](#).

I.5 Side effects and hazards

See [Section A.6, Side effects and hazards of LBP transfusions](#). **Note, however, that the comments about CMV and HTLV-I/II do not apply.**

I.6 Dosage and administration

See [Section H.6, Dosage and administration](#) except for the storage delay. The product must be transfused within 24 hours of thawing.

I.7 Storage

FFPA may be stored for 12 months at -18°C or colder. When thawed for use, it may be stored between 1 to 6°C for 24 hours.

It must not be refrozen.

J CRYOPRECIPITATE

J.1 Description

Cryoprecipitate is prepared by thawing frozen plasma (collected into CP2D) at a temperature between 1 to 6°C and recovering the insoluble precipitate, which is then refrozen. Each bag of cryoprecipitate contains approximately 500 mg of fibrinogen and some factor VIII but not used for recipient with factor VIII deficiency.

J.2 Actions

Cryoprecipitate is mostly used as a source of fibrinogen and Factor XIII even though it contains factor VIII.

J.3 Indications

If commercial concentrates are not available, this component:

- a) is indicated for Factor XIII deficiencies;
- b) may be used to treat hypofibrinogenemia or dysfibrinogenemia.

J.4 Contraindications

Specific factor concentrates are preferred, when available, due to the decreased risk of transmissible diseases (because of viral inactivation during manufacturing). Cryoprecipitate is therefore no longer used for factor VIII deficiency.

Cryoprecipitate should not be used to make fibrin glue. Viral-inactivated commercial products should be used for this purpose.

J.5 Side effects and hazards

See [Section A.6, Side effects and hazards of LBP transfusions](#). **Note, however, that the comments about CMV and HTLV-I/II do not apply.**

Hyperfibrinogenemia is possible in patients infused with large amounts of this component. If ABO-incompatible cryoprecipitate is used, positive direct antiglobulin test results may occur and the patient may, in very rare cases, develop mild hemolysis.

J.6 Dosage and administration

The product is rapidly thawed in a water bath at 30 to 37 °C for up to 10 minutes. Cryoprecipitate units must be inserted in a watertight protective plastic over-wrap and gently shaken. The number of cryoprecipitate units to be thawed must be restricted in order to keep a steady bath temperature and limit thawing time. The use of a microwave device certified for this purpose is allowed. Do not use if there is evidence of container breakage or thawing during storage. Do not refreeze after thawing. Cryoprecipitate must be transfused within 4 hours of thawing. As a source of fibrinogen, if stored at 1-6 °C, it may be transfused up to 24 hours after thawing. It must be used within 4 hours after pooling or opening the container.

For pooling, the first cryoprecipitate in each concentrate should be mixed well with 10-15 mL of diluent to ensure complete removal of all material from the container. The preferred diluent is 0.9% sodium chloride injection (USP).

The following formula is helpful to calculate the fibrinogen required:

1. Patient's weight (kg) x 70 mL/kg = blood volume (mL)
2. Blood volume (mL) x (1.0 – hematocrit) = plasma volume (mL)
3. Quantity of fibrinogen required in mg = (Desired fibrinogen level in mg/dL – initial fibrinogen level in mg/dL) x plasma volume (mL) ÷ 100 mL/dL
4. Amount of cryoprecipitate required = mg of fibrinogen required ÷ 500 mg of fibrinogen/unit of cryoprecipitate

Hypofibrinogenemic recipients should be monitored with fibrinogen assays.

J.7 Storage

Cryoprecipitate may be stored for 12 months at –18 °C or colder.

K CRYOPRECIPITATE SUPERNATANT

K.1 Description

This product is prepared from whole blood collected into a CP2D anticoagulant solution.

Cryoprecipitate supernatant is prepared by thawing frozen plasma at a temperature between 1 to 6 °C and recovering the residual plasma following the preparation of cryoprecipitate. The plasma is then refrozen.

Proteins such as albumin, Factors II, V, VII, IX, X and XI are present in cryoprecipitate supernatant.

K.2 Actions

Cryoprecipitate supernatant is a source of plasma proteins, with the exception of fibrinogen and Factors VIII and XIII.

K.3 Indications

This product is primarily used in some patients with thrombotic thrombocytopenic purpura (TTP), or in cases of adult hemolytic uremic syndrome (HUS) as part of plasma exchange therapy.

K.4 Contraindications

This product is not indicated for labile coagulation factor deficiencies or the replacement of a patient's plasma volume.

K.5 Side effects and hazards

See [Section A.6, Side effects and hazards of LBP transfusions](#). **Note, however, that the comments about CMV and HTLV I/II do not apply.**

K.6 Dosage and administration

See [Section A.6, Side effects and hazards of LBP transfusions](#).

The volume transfused depends on the patient's clinical picture and size.

Do not use the product if there is evidence of container breakage or thawing during storage. Cryoprecipitate supernatant may be thawed in a water bath at a temperature of 30-37 °C (in a watertight protective plastic over-wrap using gentle agitation) or in a microwave intended for this purpose. Thawing may take 20-30 minutes.

K.7 Storage

Cryoprecipitate supernatant may be stored for 12 months at -18 °C or colder. It may be stored between 1 to 6 °C for 5 days.

Do not refreeze.

III AUTOLOGOUS LABILE BLOOD PRODUCTS

Except for the selection criteria, autologous labile blood products (LBP) in CP2D are IDENTICAL to allogenic LBPs with respect to their description, actions, contraindications, dosage and administration and storage but:

DIFFERENT with respect to their:

1. Indications

Autologous red blood cells may be indicated in cases where the recipient has a rare blood type with multiple antibodies and/or alloantibodies to a high-incidence antigens.

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GLOSSARY

Ab	Antibody
Additive solution	Nutritive solution (AS-3 and SAGM)
Ag	Antigen
Adverse reaction to a transfusion or transfusion reaction	Is defined as a harmful, non-intentional reaction following the transfusion of blood or a blood component, whether or not it is considered to be due to the transfusion or an error or accident. Adverse reactions to products derived from human plasma are treated in the same manner as adverse reactions to drugs and are subject to the applicable sections of the Food and Drug Regulations.
B19	Parvovirus B19
Serious adverse reaction to a transfusion	<p>Is defined as a transfusion reaction, regardless of the quantity administered, wherein the patient must be hospitalized or medical or surgical intervention is required, which results in a malignancy, congenital abnormality or a persistent or serious disability, or which is life-threatening or fatal.</p> <p>The following are examples of serious adverse reactions (this should not be considered a comprehensive list):</p> <ul style="list-style-type: none"> A) Hemolytic transfusion reaction (acute or delayed), B) Anaphylactic shock, C) Graft-Versus-Host Disease (GVHD), D) Bacterial contamination, including toxins and parasites, E) Non-hemodynamic pulmonary edema (within 24 hours of transfusion), transfusion-related acute lung injury (TRALI), non-hemodynamic overload respiratory distress. F) Any other reaction that could cause a permanent disability or death.
Adverse, unforeseen reaction to a transfusion	Is defined as a transfusion reaction, the nature, seriousness or frequency of which is not listed among the known adverse reactions to transfusion of blood or blood components.
Chagas disease	Parasite infection caused by <i>Trypanosoma cruzi</i>
CMV	Cytomegalovirus
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV 1/2	Human Immunodeficiency Virus type 1 and 2
HTLV I/II	Human T-cell lymphotropic Virus type 1 and 2
LBP	Labile blood products
Massive transfusion	Is defined as the replacement, within a 24-hour period, of a volume of blood superior to the recipient's total blood volume.
NAT	Nucleic Acid Test
Syphilis	Sexually transmissible disease caused by <i>Treponema pallidum</i> .
T.E.N.D / H.T.N.D.	Titre Élevé Non Détecté / High Titer Not Detected
vCJD	variant Creutzfeldt-Jakob disease
WNV	West Nile Virus

LABILE BLOOD PRODUCTS (LBP) AVAILABLE FROM HÉMA-QUÉBEC

Allogenic LBPs	Major Indications	Actions	Contraindications	Special precautions	Hazards	Rate of infusion
Red blood cells, leukoreduced	Symptomatic anemia	Restoration of oxygen-carrying capacity	Pharmacologically treatable anemia	Must be ABO-compatible	Febrile reactions, allergic reactions, circulatory overload, hemolytic reactions, TRALI, Bacterial contamination, Others reactions and Infectious diseases	As patient can tolerate, but less than 4 hours
Red blood cells, deglycerolized	Patients with rare blood type, numerous alloantibodies or directed against high-incidence antigen	Restoration of oxygen-carrying capacity.	Pharmacologically treatable anemia	Must be ABO-compatible	Febrile reactions, allergic reactions, circulatory overload, hemolytic reactions, TRALI, Bacterial contamination, Others reactions and Infectious diseases	As patient can tolerate, but less than 4 hours
Red blood cells, leukoreduced and washed	Patient with IgA deficiency Reaction to plasma proteins Repeat FNHTR (as a last resort)	Restoration of oxygen-carrying capacity	Pharmacologically treatable anemia	Must be ABO-compatible	Febrile reactions, allergic reactions, circulatory overload, hemolytic reactions, Bacterial contamination, Others reactions and Infectious diseases	As patient can tolerate, but less than 4 hours

Allogenic LBPs	Major Indications	Actions	Contraindications	Special precautions	Hazards	Rate of infusion
Platelets pooled, leukoreduced And Platelets, leukoreduced , apheresis	Bleeding from thrombocytopenia or platelet function abnormality, bleeding prevention	Improvement of hemostasis	Bleeding from plasma coagulation factor deficits and some conditions with rapid platelet destruction (e.g. ITP)	ABO-compatible preferred For platelets, leukoreduced, apheresis only, possible substitution by a group O product, if H.T.N.D. Should not use certain microaggregate filters (check manufacturer's instructions)	Febrile reactions, allergic reactions, circulatory overload, TRALI, Bacterial contamination and Infectious diseases	As patient can tolerate, but less than 4 hours
Granulocytes	Serious neutropenia Adjuvant to antimicrobial or antifungal treatments in severe bacterial or fungal infections that do not respond in an adequate way to undergoing treatments.	Phagocytize and kill bacteria	Pursuit of the administration of Granulocytes as a treatment to a resistant infection to antimicrobials or antifungals	Must be ABO-compatible Must be irradiated for patients with immune deficiencies	Febrile reactions, allergic reactions, hemolytic reactions, circulatory overload, TRALI, Bacterial contamination, Other reactions and Infectious diseases	As patient can tolerate, but less than 4 hours

Allogenic LBP's	Major Indications	Actions	Contraindications	Special precautions	Hazards	Rate of infusion
Frozen plasma And Fresh frozen plasma, apheresis	Deficit of labile (for FP only) and stable coagulation factors	Source of labile (for FP only) stable coagulation factors	Volume replacement Replacement of labile coagulation factors (for FP only)	Must be ABO-compatible but, compatibility tests before transfusion are not necessary	Febrile reactions, allergic reactions, circulatory overload, TRALI, Bacterial contamination, and Infectious diseases	As patient can tolerate, but less than 4 hours
Cryoprecipitate	Hypofibrinogenemia or dysfibrinogenemia	Source of Fibrinogen, Factor XIII	Specific factors available	Should be ABO-compatible Frequent repeat dose may be necessary to obtain therapeutic levels	Febrile reactions, allergic reactions, circulatory overload, TRALI, Bacterial contamination, and Infectious diseases	As patient can tolerate, but less than 4 hours
Cryoprecipitate supernatant	Thrombotic thrombocytopenic purpura Adult hemolytic uremic syndrome	Source of stable coagulation factors	Deficit of labile coagulation factors or plasma volume replacement	Must be ABO-compatible but, compatibility tests before transfusion are not necessary	Febrile reactions, allergic reactions, circulatory overload, TRALI, Bacterial contamination, and Infectious diseases	As patient can tolerate, but less than 4 hours

MEAN VOLUMES OF ALLOGENIC LABILE BLOOD PRODUCTS AVAILABLE FROM HÉMA-QUÉBEC

Product	Mean Volume (mL) \pm 1 SD
Red blood cells	See section II ALLOGENIC LABILE BLOOD PRODUCTS
Cryoprecipitate	9 \pm 5,5
Granulocytes	272 \pm 22,9
Fresh Frozen Plasma, Apheresis	495 \pm 4,4
Frozen plasma, Apheresis	252 \pm 5,5
Frozen Plasma	264 \pm 17,8
Pooled platelets	325 \pm 24,7
Platelets, apheresis	220 \pm 14
Cryoprecipitate supernatant	262 \pm 18,7



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