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.
TABLE OF CONTENTS

NOTICE TO USERS ........................................................................................................... 1

I. GENERAL INFORMATION .............................................................................................. 2
   A. GENERAL INFORMATION .......................................................................................... 2
      A.1 Donor eligibility ...................................................................................................... 2
      A.2 Preventive measures .............................................................................................. 2
      A.3 Testing of donor blood .......................................................................................... 2
      A.4 Labelling of LBPs .................................................................................................. 3
      A.5 General instructions concerning transfusion of LBPs ........................................... 3
      A.6 Side effects and hazards of LBP transfusions ...................................................... 5
         A.6.1 Infectious diseases ........................................................................................... 5
         A.6.2 Creutzfeldt-Jakob disease (vCJD) ..................................................................... 6
         A.6.3 Immunological reactions ................................................................................. 6
         A.6.4 Physiological and metabolic complications .................................................... 9
         A.6.5 DEHP ................................................................................................................ 10
      A.7 Reporting serious adverse reactions ..................................................................... 11
      A.8 Traceback and lookback for HIV, HBV, HCV, HTLV, WNV and Trypanosoma cruzi .......................................................................................................................... 11
         A.8.1 Traceback ........................................................................................................... 11
         A.8.2 Lookback ............................................................................................................ 12
      A.9 Reporting other transfusion-related infections ..................................................... 12

II. LEUKOREDUCTED ALLOGENIC PRODUCTS .......................................................... 13
   B. RED BLOOD CELLS ................................................................................................. 13
      B.1 Description ............................................................................................................. 13
      B.2 Actions .................................................................................................................. 14
      B.3 Indications ............................................................................................................. 14
      B.4 Contraindications .................................................................................................. 14
      B.5 Side effects and hazards ....................................................................................... 14
      B.6 Dosage and administration .................................................................................. 15
      B.7 Storage .................................................................................................................. 15
   C. RED BLOOD CELLS, DEGLYCEROLIZED ............................................................ 15
      C.1 Description ............................................................................................................. 15
      C.2 Actions .................................................................................................................. 16
      C.3 Indications ............................................................................................................. 16
      C.4 Contraindications .................................................................................................. 16
      C.5 Side effects and hazards ....................................................................................... 16
      C.6 Dosage and administration .................................................................................. 16
      C.7 Storage .................................................................................................................. 17
D. RED BLOOD CELLS, WASHED

D.1 Description ................................................................. 17
D.2 Actions ........................................................................ 17
D.3 Indications .................................................................... 17
D.4 Contraindications ........................................................ 17
D.5 Side effects and hazards ............................................... 17
D.6 Dosage and administration ........................................... 18
D.7 Storage .......................................................................... 18

E. RED BLOOD CELLS PEDIATRIC PACKS (NON DIVIDED) .... 18

E.1 Description .................................................................... 18
E.2 Actions .......................................................................... 18
E.3 Indications ...................................................................... 18
E.4 Contraindications ........................................................ 18
E.5 Side effects and hazards ............................................... 18
E.6 Dosage and administration ........................................... 18
E.7 Storage .......................................................................... 19

F. PLATELETS ........................................................................ 19

F.1 Pooled platelets ............................................................ 19
  F.1.1 Description .................................................................. 19
  F.1.2 Actions ....................................................................... 19
  F.1.3 Indications .................................................................. 19
  F.1.4 Contraindications ...................................................... 20
  F.1.5 Side effects and hazards ........................................... 20
  F.1.6 Dosage and administration ....................................... 21
  F.1.7 Storage ...................................................................... 21

F.2 Platelets, apheresis .......................................................... 22
  F.2.1 Description .................................................................. 22
  F.2.2 Actions ....................................................................... 22
  F.2.3 Indications .................................................................. 22
  F.2.4 Contraindications ...................................................... 22
  F.2.5 Side effects and hazards ........................................... 22
  F.2.6 Dosage and administration ....................................... 23
  F.2.7 Storage ...................................................................... 23

G. GRANULOCYTES ............................................................... 23

G.1 Description ..................................................................... 23
G.2 Actions .......................................................................... 23
III. AUTOLOGOUS LABILE BLOOD PRODUCTS ........................................... 34

DIFFERENT with respect to their: ............................................................. 34
  1. Indications ................................................................................. 34
  2. Side effects and hazards .............................................................. 34

BIBLIOGRAPHY ............................................................................. 35

GLOSSARY .................................................................................... 36

LABILE BLOOD PRODUCTS AVAILABLE FROM HÉMA-QUÉBEC .................................................. 37
  Allogenic LBPs ............................................................................. 37
  Autologous LBPs ........................................................................ 40
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. Autologous transfusion is an option, when deemed appropriate, to reduce the risk of infectious diseases and immune reactions related to allogenic donations.

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.
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;
- had the opportunity to confidentially exclude their donation from transfusion.

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.

Table I.1 Tests done on donor blood

<table>
<thead>
<tr>
<th>Agents</th>
<th>Ac</th>
<th>Ag</th>
<th>NAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV 1/2 and group 0</td>
<td>✓</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>HIV-1</td>
<td>N/A</td>
<td>N/A</td>
<td>✓</td>
</tr>
<tr>
<td>HBV</td>
<td>*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HCV</td>
<td>✓</td>
<td>N/A</td>
<td>✓</td>
</tr>
<tr>
<td>HTLV I/II</td>
<td>✓</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Syphilis</td>
<td>✓</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>CMV</td>
<td>✓</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>WNV</td>
<td>N/A</td>
<td>N/A</td>
<td>✓</td>
</tr>
<tr>
<td>Chagas*** or Trypanosoma cruzi</td>
<td>✓</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A = Not applicable  * Anti-HBc  ** Done on a portion of the inventory  *** Test performed yearly between June 1st and November 30th. Outside this period, performed if travel outside of Canada in the last 56 days. **** Test performed 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)
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>
<thead>
<tr>
<th>Information</th>
<th>Bar codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The official name, including any qualifications and/or attributes</td>
<td>N/A</td>
</tr>
<tr>
<td>Product code in ISBT format</td>
<td>✓</td>
</tr>
<tr>
<td>2. The donation identification number, including establishment code</td>
<td>✓</td>
</tr>
<tr>
<td>3. Blood group; donor’s ABO group and, where applicable, Rh group in</td>
<td>✓</td>
</tr>
<tr>
<td>ISBT format. When “Rh negative” is indicated, the blood has been found</td>
<td></td>
</tr>
<tr>
<td>negative for both D and weak D antigens</td>
<td></td>
</tr>
<tr>
<td>4. The date and time of collection (except for pooled platelets : date and</td>
<td>✓</td>
</tr>
<tr>
<td>time of preparation)</td>
<td></td>
</tr>
<tr>
<td>5. The expiration date and time</td>
<td>✓</td>
</tr>
<tr>
<td>6. The method by which the LBP was prepared</td>
<td>N/A</td>
</tr>
<tr>
<td>7. The temperature range at which the LBP is to be stored</td>
<td>N/A</td>
</tr>
<tr>
<td>8. The preservatives and anticoagulants used</td>
<td>N/A</td>
</tr>
<tr>
<td>9. Real product volume</td>
<td>N/A</td>
</tr>
<tr>
<td>10. The type of donation (autologous, directed)</td>
<td>✓</td>
</tr>
<tr>
<td>11. General statements regarding this Circular and infectious disease risks</td>
<td>N/A</td>
</tr>
<tr>
<td>12. The manufacturer’s name and the establishment’s license number</td>
<td>N/A</td>
</tr>
<tr>
<td>13. The sedimenting agent used during granulocytes phteresis</td>
<td>N/A</td>
</tr>
<tr>
<td>14. Red blood cell phenotypes, platelet phenotypes CMV related information</td>
<td>✓</td>
</tr>
<tr>
<td>15. HLA phenotypes</td>
<td>N/A</td>
</tr>
</tbody>
</table>

✓ = Information encoded in an ISBT structure

A.5 General instructions concerning transfusion of LBPs

1) The intended recipient and the LBP must be properly identified before the transfusion is started.
2) The LBP container must be intact.
3) The LBP 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).
4) The LBPs must be mixed thoroughly before use.
5) 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.

6) Hemolysis may become evident during the storage of LBPs containing red blood cells. LBPs should be carefully inspected before administration for signs of hemolysis.

7) Microbial growth may become evident during the storage of LBPs. LBPs should be carefully inspected before administration for microbial growth.

8) 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.

9) 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.

10) 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.

11) LBPs may be warmed, but to no more than 37 °C during transfusion, if clinically indicated.

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.
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, Trypanosoma cruzi (Chagas disease) and WNV. The table below describes the current residual risk.

Table I.3 Residual risk in Quebec

<table>
<thead>
<tr>
<th>Virus</th>
<th>Residual Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>1/4,583,505</td>
</tr>
<tr>
<td>HIV</td>
<td>1/12,838,319</td>
</tr>
<tr>
<td>HBV</td>
<td>1/1,115,505</td>
</tr>
<tr>
<td>HTLV</td>
<td>1/2,794,222</td>
</tr>
<tr>
<td>WNV</td>
<td>1/39,000</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>&lt; 1/100,000</td>
</tr>
</tbody>
</table>

** Estimated risk from 2001-2006 data and considering HBV NAT testing (2010)
*** Estimated risk for the summer season when the risk is at the maximum. Data collected during the 2005 and 2006 seasons. Off season, the risk is considered non-existent.
**** Based on an expected seroprevalence of 1/20,000 and an 80% efficacy or more of the test

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. The use of cellular components leukoreduced also lessens the risk of CMV transmission.

Other infectious agents transmitted by transfusion (although rarely in North America) include Plasmodium spp (malaria agents), Toxoplasma gondii, Babesia spp, Coxiella burnetii (Q-fever agent), Rickettsia rickettsii (Rocky Mountain spotted fever agent), Borrelia spp, Treponema pallidum (syphilis agent), parovirus B19, leishmania, brucella, hepatitis A virus, Colorado tick fever, Epstein-Barr virus, HHV-8, TT viruses and hepatitis G virus.
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 following the transfusion of red blood cells stored for three weeks or more, and platelets or plasma. The contamination of frozen LBPs is more rare, and occurs mainly during thawing in a water bath if the measures described in Section A.5.9 are not respected.

When a blood recipient experiences chills, high fever 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.

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 Creutzfeldt-Jakob disease, although no cases have been documented to date. Recent, convincing data suggest that the variant Creutzfeldt-Jakob disease is transmissible through transfusion.

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 most immediate reactions occur when clerical or identification errors lead to an ABO mismatch. All personnel who draw samples from patients or who start transfusions must know and follow procedures to ensure proper identification. 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 is suspected. **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;

– bacterial infection in the patient by a LBP (see Section A.6.1.2 Bacterial contamination);

– overheating or freezing of red blood cells.

**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 serious 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 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. 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 urticaria or wheezing may occur in 1% or more of recipients. Occasionally, chills and fever are also observed. The exact cause of these reactions is unknown. However, they 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.

Anaphylactoid reactions manifested by bronchospasm, dyspnea and pulmonary edema may occur in rare instances. Immediate treatment according to hospital protocol is indicated. Some of the patients involved have been shown to have IgG antibodies to IgA. Deglycerolized or washed red blood cells and IgA-deficient LBP are required for further transfusion of these patients.

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

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

Because these antibodies are more frequent in women with an history of pregnancy, the plasma and platelet products distributed to hospitals come from men or women without an history of pregnancy, except for HLA compatible or HPA typed apheresis platelets.

A.6.3.6 Febrile reactions

Febrile reactions, with or without chills, may occur in about 1% of transfusions. These reactions have mainly been ascribed to recipient antibodies that agglutinate donor leukocytes.

Febrile reactions are most common in patients previously sensitized by transfusion or pregnancy. The frequency of such reactions is diminished by using platelets and red blood cells leukoreduced before storage. Recent research, however, suggests that cytokines released by leukocytes during storage can cause febrile reactions in the recipient.

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 LBP, 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.

LBPs should 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 nutritive 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. This is a particular risk in the elderly, 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 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 to no more than 37 °C during its passage through the transfusion set 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) Other metabolic complications may occur further to rapid or massive transfusion of LBP s. These complications occur in patients with preexisting circulatory or metabolic problems, and include metabolic acidosis (rare) or alkalosis (secondary to the bicarbonate generated by the citrate metabolism), or hypokalemia or hyperkalemia (mainly in patients with renal failure).

A.6.4.3 Clinically significant depletion of coagulation proteins and platelets

Clinically significant depletion of coagulation proteins and platelets is an infrequent 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 a standard 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 in the plastic used in collection bags, which leaches into the red blood cells during storage. The DEHP concentration in the nutritive solution increases significantly during storage of packed red blood cells stored at 1-6 °C, but does not change during storage of frozen products. DEHP is not used to manufacture the bags used for pooled platelets nor those for platelets obtained by apheresis.

There are no data confirming the toxicity of DEHP or its metabolites in humans. However, a toxic effect on the development of the male reproductive system in rodents has been shown. 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 or by removing a portion of the supernatant before transfusion.

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 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 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;
- it draws up a list of the deferred donor’s previous donations;
- it notifies hospitals that received LBP 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.

Thus, physicians should ask their patients infected with HIV, HBV, HCV, HTLV, WNV 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 LBP 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 LBP 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 and Trypanosoma cruzi.
All allogenic red blood cells and platelets are leukoreduced.

These products respect the following standard: less than \(5 \times 10^6\) leukocytes per unit.

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

### Table II.1

<table>
<thead>
<tr>
<th>Anticoagulant Solution</th>
<th>Sodium citrate</th>
<th>Citric acid</th>
<th>Monobasic sodium phosphate</th>
<th>Dextrose</th>
<th>Adenine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrate Phosphate Dextrose (CP2D)</td>
<td>26.3 g/L</td>
<td>3.27 g/L</td>
<td>2.22 g/L</td>
<td>51.1 g/L</td>
<td>N/A</td>
</tr>
<tr>
<td>CPD</td>
<td>26.3 g/L</td>
<td>3.27 g/L</td>
<td>2.22 g/L</td>
<td>25.6 g/L</td>
<td>N/A</td>
</tr>
<tr>
<td>ACD-A</td>
<td>22.0 g/L</td>
<td>7.3 g/L</td>
<td>N/A</td>
<td>24.5 g/L</td>
<td>N/A</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>40 g/L</td>
<td>To adjust pH</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Most LBPs supplied by Héma-Québec are collected into CP2D or CPD anticoagulant solution (63 mL). When units of red blood cells are prepared, a nutritive solution of AS-3 or SAGM is added (100 mL).

## 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 volume of 240 mL to 340 mL, an hemoglobin of 35 g / bag or more and a hematocrit of 0.80 L/L or less. After removal of most of the plasma, the nutritive solution AS-3 is mixed with the red blood cells. The nutritive solution AS 3 contains glucose (11 g/L), adenine (0.3 g/L), citric acid (0.42 g/L), sodium citrate (5.88 g/L), phosphate (2.76 g/L) and sodium chloride (4.1 g/L) in water for injection (USP).
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 volume between 288 et 362 mL, a hemoglobin of 35 g / bag or more and a hematocrit of 0,80 L/L or less. This product contains red blood cells with an AS-3 nutritive solution, as describe above.

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 volume of 240 mL to 340 mL, an hemoglobin of 35 g / bag or more and a hematocrit of 0.80 L/L or less. After removal of most of the plasma, the nutritive solution SAGM is mixed with the red blood cells. The nutritive solution SAGM contains glucose (9 g/L), adenine (0.169 g/L), mannitol (5.25 g/L) and sodium chloride (8.77 g/L) in water for injection (USP).

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.

The 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 nutritive solution. This must be done immediately before transfusion.

If it is indicated to decrease the nutritive 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 of 1-6 °C. Under these conditions, there is no significant loss of viability or function of red blood cells stored for 42 days.

The 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. This component contains more than 80% of the red blood cells in the original blood. The hematocrit level is 0.80 L/L or less. The hemoglobin is 35 g/bag or more. In LBP’s not filtered 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

The 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

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

C.5 Side effects and hazards

The side effects are similar to those for red blood cells, except for the reduced risk of febrile non-hemolytic reactions and allergic reactions. There is a greater risk of bacterial contamination because the container must be opened during production.

C.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.

C.7 Storage

Red blood cells, deglycerolized must be administered within 24 hours when stored at 1-6 °C and must be transfused before the expiration time indicated on the label.

D. RED BLOOD CELLS, WASHED

D.1 Description

Red blood cells are washed to eliminate all traces of plasma proteins, anticoagulant and nutritive solution.

This component contains more than 75% of the red blood cells from the original blood. Virtually all the residual anticoagulant, platelets and leukocytes are removed in the washing procedure.

The suspension medium is 0.9% sodium chloride injection (USP).

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.

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. There is a greater risk of bacterial contamination because the container must be open during production.
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

Red blood cells, washed must be administered within 24 hours when stored at 1-6 °C and must be transfused before the expiration time indicated on the 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. Pediatric packs enable multiple transfusions of red blood cells from the same unit.

E.2 Actions

The 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.

E.4 Contraindications

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

E.5 Side effects and hazards

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

E.6 Dosage and administration

The dosage and administration of pediatric packs are 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/SAGM) by washing or centrifugation and to resuspend the red blood cells in albumin or 0.9% sodium chloride injection (USP), as appropriate:

a) Extremely premature neonates or those with hepatic 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 into CPD anticoagulant and filtered to remove the leukocytes are used to prepare pooled platelets. This LBP contains at least $2.4 \times 10^{11}$ /L of platelets suspended in a maximum of 400mL of plasma. The plasma used in the pool is from one of the five buffy coat donors. Trace amounts of red blood cells are also present and the color of the unit of pooled platelets may vary from pink to salmon-colored. Pooled platelets contain less than $5 \times 10^6$ leukocytes per unit. Moreover, each unit of pooled platelets is cultured for bacterial contamination. The units are placed in inventory before the final results are obtained for the culture.

F.1.2 Actions

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

F.1.3 Indications

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

They 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 x 10^9/L) who are not bleeding. A transfusion of pooled platelets may also be useful in selected cases of postoperative bleeding (e.g. platelet count less than 50 x 10^9/L). 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. Certain studies show that filtration could decrease 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. 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 is 1 or less in 37,000 transfusions of pooled platelets or 60,000 transfusions of apheresis platelets. Information on the use of irradiated blood products can be found in Section A.6.3.7, Graft-versus-host disease.

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, collected by apheresis.

Pooled platelets may be indicated for patients with thrombopenia secondary to disseminated intravascular coagulation (DIC), idiopathic thrombocytopenic purpura (ITP), hypersplenism, fever and sepsis.
Immunization to red blood cell antigens may occur because of the presence of trace amounts of red blood cells in the platelets unit. 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**

Compatibility testing is not necessary. The plasma chosen for the pool should ideally be ABO-compatible with the recipient’s red blood cells. In specific cases or in an emergency, this compatibility need not be considered.

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 /µL) when measured 20-60 minutes post transfusion. The expected response will not occur in the following cases: sepsis, fever, ITP, anti-platelet or HLA 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 /µL/ m²), 1-2 hours post-transfusion, may signify that the patient is refractory to the transfused platelets.

This dose may need to be repeated 1-3 days later because of the short life span of the transfused platelets (3-4 days).

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.

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 5 days, as indicated on the label.

Pooled platelets must be stored at 20-24 °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 (average volume/bag: from a single donation → 282 mL; from a double donation → 218 mL) contains at least 300 x 10⁹ platelets. If necessary, this dose can be obtained from a donor who is HLA-matched with the patient.

The volume of plasma used for platelet suspension may vary between 150 and 400 mL. The component contains less than 5 x 10⁶ leukocytes. Moreover, each unit of platelets is cultured for bacterial contamination. The units are placed in inventory before the final results are obtained for the culture.

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, although they are reduced due to the fact that the recipient is exposed to blood from only one donor.

The administration of type-O platelets, apheresis to a type-A recipient rarely causes significant hemolysis.
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 $10^9$/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. 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 5 days when stored at 20-24 °C. Platelets, apheresis must be agitated gently and continuously 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 x $10^{10}$ granulocytes and a variable number of red blood cells, lymphocytes and platelets in 200 to 300 mL of plasma.

Pentastarch* 10% is used to facilitate the collection of granulocytes. Less than 30 mL of pentastarch can be found in the final product. A 6% concentration of sodium citrate solution in pentastarch is used to collect granulocytes. (Average volume : 32 mL).

* Products not approved for this use.

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, it is recommended to irradiate granulocytes, where clinically justified.

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 pentastarch in the product is usually less than 30 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 date 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

If absolutely necessary, the product may be stored at 20-24 °C for no longer than 24 hours \textit{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 stable coagulation factors, such as Factor IX and fibrinogen in concentrations similar to those in fresh frozen plasma, although they contain less of Factors V and VIII.

Frozen plasma :

a) is prepared from whole blood collected in a closed system into CP2D or CPD and has a volume of 140 mL or more.

b) is harvested by apheresis in a closed system, in ACD-A and has a volume of 200 mL or more.

H.2 Actions

Frozen plasma is a source of plasma proteins, including stable coagulation factors, i.e. 2-4 mg of fibrinogen per mL, and one unit per mL of other coagulation factors. These products are used as a source of plasma proteins to treat patients with plasma protein deficiencies (with the exception of Factors V and VIII).

H.3 Indications

Frozen plasma is indicated to replace several coagulation factors (with the exception of Factors V, VIII and von Willebrand Factor) in cases of acquired coagulopathy caused by a vitamin K deficiency or liver disease. For severe cases of Factor V deficiency, if frozen plasma does not give the expected therapeutic results, it may be necessary to use fresh frozen plasma, apheresis.

According to the “Guidelines for red blood cell and plasma transfusion for adults and children” of the \textit{Canadian Medical Association Journal}, plasma
should be transfused to patients with acquired deficiencies of several coagulation factors in the following circumstances:

Legend – Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from at least one properly randomized controlled trial.</td>
</tr>
<tr>
<td>II</td>
<td>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.</td>
</tr>
<tr>
<td>III</td>
<td>Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.</td>
</tr>
</tbody>
</table>

a) Plasma is recommended when 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) Plasma is recommended when there is actual bleeding in patients with liver disease and increased PT, INR or aPTT. Plasma may 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. Prophylactic plasma transfusion is not indicated for certain invasive procedures (e.g. percutaneous liver biopsy, paracentesis, thoracentesis) in patients with liver disease if their INR is 2.0 or less.

(Level of evidence: II)

c) Plasma is recommended in patients with acute disseminated intravascular coagulation with active bleeding associated with increased PT, INR or aPTT, provided that the triggering condition can also be treated effectively.

(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 an attempt to stop diffuse nonsurgical bleeding.

(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 as replacement fluid. 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. Frozen plasma or fresh frozen plasma may be used depending on the specific factor involved.

(Level of evidence: III)

H.4 Contraindications

Frozen plasma is not indicated to correct coagulation deficiencies when a specific stable product is available. 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.

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), albumin or 10% pentastarch.

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 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**

Compatibility tests before transfusion are not necessary. However, the frozen plasma must be ABO-compatible with the recipient’s red blood cells.

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

The frozen plasma 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.

The product must be transfused within 24 hours of thawing. Do not use if there is evidence of container breakage or thawing during storage.

The “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 at 1-6 °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, and has a volume of approximately 500 mL.

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. It can be used to reduce the number of donors to which a patient is exposed. 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.

I.7 Storage

FFPA may be stored for 12 months at −18 °C or colder. When thawed for use, it may be stored at 1-6 °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 of 1-6 °C and recovering the insoluble precipitate, which is then refrozen. On average, each bag of cryoprecipitate contains at least 150 mg of fibrinogen in 5-15 mL of plasma.

J.2 Actions

Cryoprecipitate is a source of Factor XIII and fibrinogen.

J.3 Indications

This component is indicated for Factor XIII deficiencies. This component may be used to treat hypofibrinogenemia or dysfibrinogenemia if fibrinogen concentrates are not available.

J.4 Contraindications

Do not use cryoprecipitate unless results of laboratory tests indicate a specific hemostatic defect for which this product is indicated.

Specific factor concentrates are preferred, when available, because of the decreased risk of transmissible diseases (because of viral inactivation during manufacturing).

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

For treatment of bleeding associated with a deficiency and if desmopressin (DDAVP) is not effective, Héma-Québec recommends the use of commercial products like Factor VIII.
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

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.

The frozen product is thawed in a water bath at 30-37 °C for up to 10 minutes (in a watertight protective plastic over-wrap using gentle agitation) or in a microwave intended for this purpose. 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 ÷ 250 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 and has a volume of 160-260 mL.

Cryoprecipitate supernatant is prepared by thawing frozen plasma at a temperature of 1-6 °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 Factor 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

Compatibility tests before transfusion are not necessary. However, cryoprecipitate supernatant must be ABO-compatible with the recipient’s
red blood cells (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 at 1-6 °C for 24 hours.

**Do not refreeze.**
III. AUTOLOGOUS LABILE BLOOD PRODUCTS

Autologous products provided by Héma-Québec, packed red blood cells and red blood cells deglycerolized are prepared from whole blood and are not leukoreduced by filtration.

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** are indicated in elective surgery to replace red blood cells lost during surgery.

2. Side effects and hazards

The use of autologous blood protects the recipient from all microbial contamination, except for bacterial infection of the LBP during collection. The use of autologous blood also protects the recipient from immunological side effects (as described in Section A.6, Side effects and hazards of LBP transfusions). The other side effects are the same as those for allogenic products, except for those related to clerical or identification errors.
BIBLIOGRAPHY


CONSENSUS DEVELOPMENT PANEL (United States National Institutes of Health) “*Fresh-frozen plasma: indications and risks*”. JAMA 1985; 253:551-3

CONSENSUS CONFERENCE. “*Platelet Transfusion Therapy*”. JAMA 1987; 257:1777-80.


## Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ab</td>
<td>Antibody</td>
</tr>
<tr>
<td>Ag</td>
<td>Antigen</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>HTLV I/II</td>
<td>Human T-cell lymphotropic virus type 1 and 2</td>
</tr>
<tr>
<td>Chagas disease</td>
<td>Parasite infection caused by <em>Trypanosoma cruzi</em></td>
</tr>
<tr>
<td>Adverse reaction to a transfusion or transfusion reaction</td>
<td>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 like adverse reactions to drugs and are subject to the applicable sections of the Food and Drug Regulations.</td>
</tr>
<tr>
<td>Serious adverse reaction to a transfusion</td>
<td>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. The following are examples of serious adverse reactions (this should not be considered a comprehensive list): 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.</td>
</tr>
<tr>
<td>Adverse, unforeseen reaction to a transfusion</td>
<td>Is defined as a transfusion reaction, the nature, seriousness or frequency of which is not listed among the known adverse reactions to the transfusion of blood or blood components.</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Sexually transmissible disease caused by <em>Treponema pallidum</em>.</td>
</tr>
<tr>
<td>NAT</td>
<td>Nucleic Acid Test</td>
</tr>
<tr>
<td>Massive transfusion</td>
<td>Is defined as the replacement within a 24-hour period, of a volume of blood superior to the recipient’s total blood volume.</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>HCV</td>
<td>Hepatitis C Virus</td>
</tr>
<tr>
<td>HIV 1/2</td>
<td>Human Immunodeficiency Virus type 1 and 2</td>
</tr>
<tr>
<td>WNV</td>
<td>West Nile Virus</td>
</tr>
<tr>
<td>ALLOGENIC LBPs</td>
<td>Major Indications</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Red blood cells, leukoreduced</td>
<td>Symptomatic anemia</td>
</tr>
<tr>
<td>Red blood cells, deglycerolized</td>
<td>Patient with rare blood type, numerous alloantibodies or high incidence antigen</td>
</tr>
<tr>
<td>Red blood cells, leukoreduced and washed</td>
<td>Reaction to plasma proteins</td>
</tr>
</tbody>
</table>

**Rate of infusion**
- As patient can tolerate, but less than 4 hours
- As patient can tolerate, but less than 4 hours
- As patient can tolerate, but less than 4 hours
<table>
<thead>
<tr>
<th>Allogenic LBPs</th>
<th>Major Indications</th>
<th>Actions</th>
<th>Contraindications</th>
<th>Special precautions</th>
<th>Hazards</th>
<th>Rate of infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets pooled, leukoreduced</td>
<td>Bleeding from thrombocytopenia or platelet function abnormality, bleeding prevention</td>
<td>Improvement of hemostasis</td>
<td>Bleeding from plasma coagulation factor deficits and some conditions with rapid platelet destruction (e.g. ITP)</td>
<td>ABO-compatible preferred Should not use certain microaggregate filters (check manufacturer’s instructions)</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Platelets, leukoreduced, apheresis</td>
<td>Bleeding from thrombocytopenia or platelet function abnormality, bleeding prevention</td>
<td>Improvement of hemostasis</td>
<td>Bleeding from plasma coagulation factor deficits and some conditions with rapid platelet destruction (e.g. ITP)</td>
<td>ABO-compatible preferred Should not use certain microaggregate filters (check manufacturer’s instructions)</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Granulocytes</td>
<td>Serious neutropenia Adjunct to antimicrobial or antifungal treatments in severe bacterial or fungal infections that do not respond in an adequate way to undergoing treatments</td>
<td>Phagocytize and kill bacteria</td>
<td>Pursuit of the administration of Granulocytes as a treatment to a resistant infection to antimicrobials or antifungals</td>
<td>Must be ABO-compatible Must be irradiated for patients with immune deficiencies</td>
<td>Bacterial contamination, TRALI, toxic, allergic, hemolytic and febrile reactions; circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Allogenic LBPs</td>
<td>Major Indications</td>
<td>Actions</td>
<td>Contraindications</td>
<td>Special precautions</td>
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</tr>
<tr>
<td>Frozen plasma</td>
<td>Deficit of stable coagulation factors</td>
<td>Source of stable coagulation factors</td>
<td>Volume replacement&lt;br&gt;Replacement of labile coagulation factors</td>
<td>Must be ABO-compatible but, compatibility tests before transfusion are not necessary</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Fresh frozen plasma, apheresis</td>
<td>Deficit of labile and stable coagulation factors</td>
<td>Source of labile and stable coagulation factors</td>
<td>Volume replacement</td>
<td>Must be ABO-compatible but, compatibility tests before transfusion are not necessary</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>Hypofibrinogenemia or dysfibrinogenemia</td>
<td>Source of fibrinogen and Factor XII</td>
<td>Specific factors available</td>
<td>Should be ABO-compatible&lt;br&gt;Frequent repeat dose may be necessary to obtain therapeutic levels</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Cryoprecipitate supernatant</td>
<td>Thrombotic thrombocytopenic purpura Adult hemolytic uremic syndrome</td>
<td>Source of stable coagulation factors</td>
<td>Deficit of labile coagulation factors or plasma volume replacement</td>
<td>Must be ABO-compatible but, compatibility tests before transfusion are not necessary</td>
<td>Bacterial contamination, TRALI, febrile and allergic reactions, circulatory overload, infectious diseases</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
</tbody>
</table>
## AUTOLOGOUS LBPs

<table>
<thead>
<tr>
<th>Autologous LBPs</th>
<th>Major Indications</th>
<th>Actions</th>
<th>Contraindications</th>
<th>Special precautions</th>
<th>Hazards</th>
<th>Rate of infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS-3 red blood cells</td>
<td>During elective surgery where blood loss will lead to symptomatic anemia</td>
<td>Restoration of oxygen-carrying capacity</td>
<td>Elective surgery which, statistically, rarely requires transfusion</td>
<td>Ensure the patient receives his (her) unit of blood</td>
<td>Bacterial contamination, circulatory overload</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
<tr>
<td>Red blood cells, deglycerolized</td>
<td>Patients with rare blood type, numerous alloantibodies or directed against high-incidence antigen</td>
<td>Restoration of oxygen-carrying capacity</td>
<td>Pharmacologically treatable anemia</td>
<td>Ensure the patient receives his (her) unit of blood</td>
<td>Bacterial contamination, circulatory overload</td>
<td>As patient can tolerate, but less than 4 hours</td>
</tr>
</tbody>
</table>