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BACKGROUND

Whole blood donations are separated into specific cellular (red blood cells and platelets) and plasma products. This enhances the utilization of individual donations and decreases the need for blood donors. Transfusing the appropriate combination of blood products effectively provides for the clinical needs of patients and best utilizes the donated blood.

This chapter describes the manufacturing process for the most commonly prepared blood products: Red Blood Cells, Pooled Platelets, Frozen Plasma (FP), Apheresis Fresh Frozen Plasma (AFFF), Cryosupernatant Plasma (CSP) and Cryoprecipitate. Brief descriptions of the indications, contraindications, storage and transportation requirements, dose, administration and available alternatives are included in the sections below. Further information may be found in other chapters of this [Guide](#) as indicated within the different sections.

In addition, Canadian Blood Services publishes a [Circular of Information](#) to provide an extension of the component label and to provide information regarding component composition, packaging, storage and handling, indications, warnings and precautions, adverse events, dose and administration. The *Circular* conforms to the applicable regulations issued by Health Products and Food Branch, Health Canada.

COLLECTION OF BLOOD PRODUCTS

At Canadian Blood Services, whole blood is collected from donors into a collection pack in which multiple bags are connected, allowing blood and components to be transferred between bags aseptically during manufacturing. The collection packs include two different configurations. One, the buffy coat collection set (also referred to as B1 at Canadian Blood Services), is used in the production of red blood cell, plasma and platelet products; the other, a whole blood filtration set (also referred to as B2), is used in the production of red blood cell and plasma products. Figure 1 highlights the main steps of both manufacturing processes. Both collection sets contain a citrate-phosphate-dextrose (CPD) anticoagulant in the collection bag.

Apheresis technology instead of whole blood collection may also be used for collection of some blood components, including plasma and platelets. This collection procedure utilizes an automated in-line process in which whole blood from the donor enters a collection chamber where flow patterns separate the plasma from cellular blood constituents such as red blood cells and white blood cells. Plasma, or platelets suspended in plasma, are collected into a bag while the remaining constituents of the blood are returned to the donor.

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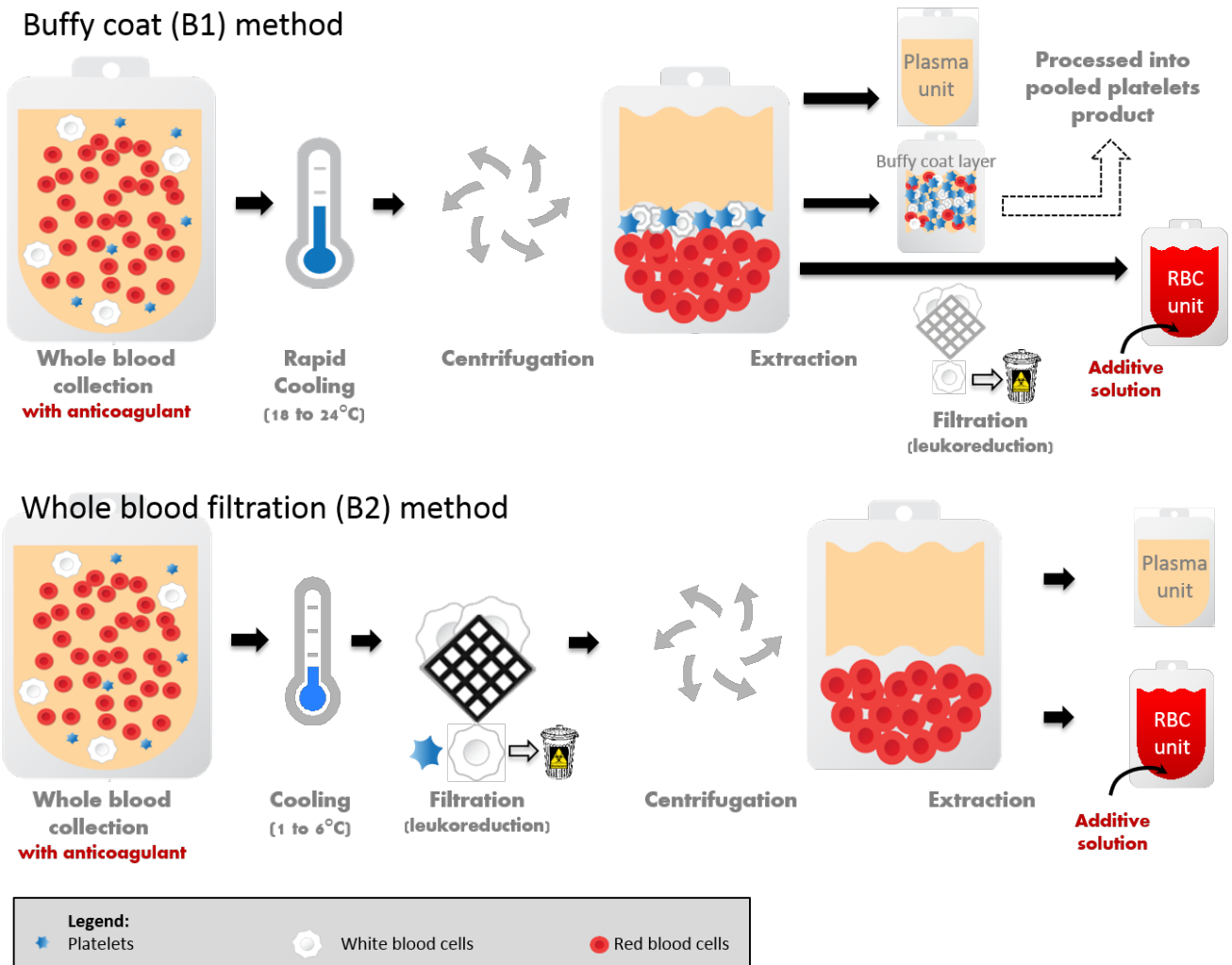


Figure 1. The whole blood manufacturing processes used at Canadian Blood Services.

RED BLOOD CELLS

Product manufacturing and description (see Figure 1)

Whole blood collected in CPD anticoagulant is processed by either the B1 or B2 method (Figure 1). In the B1 method, whole blood is centrifuged to separate the red blood cells from the platelets and plasma. The red blood cells are then leukoreduced (LR) by filtration. In the B2 method, the whole blood is first filtered to remove platelets and leukocytes (LR), then centrifuged to separate the red blood cells from the plasma. For both B1 and B2 methods, the red blood cells are then mixed with an additive solution, saline-adenine-glucose-mannitol (SAGM) and labelled as a red blood cell unit.

Red blood cells LR is the only red blood cell product prepared by Canadian Blood Services. The average volume of a red blood cell unit issued by Canadian Blood Services is 293 (± 26) ml and it typically contains 56 (± 7) g of hemoglobin with a hematocrit of approximately 0.68 and has an average residual leukocyte count of 0.18 x 10⁶. Further modifications of red blood cell products such as washing, deglycerolizing and irradiation are covered in

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Chapter 15 of this [Guide](#).

Indications

The primary purpose for a red blood cell transfusion is to increase the oxygen-carrying capacity of the blood. Therefore, red blood cell transfusion is indicated in patients with anemia who have evidence of impaired oxygen delivery. For example, symptomatic acute blood loss, chronic anemia and cardiopulmonary compromise, or disease or medication effects associated with bone marrow suppression may be triggers for red blood cell transfusion. In patients with acute blood loss, volume replacement is often required and, depending on clinical circumstances, plasma and platelets may also be transfused. See Chapter 11 of this [Guide](#) for details on massive hemorrhage and emergency transfusion.

Effective oxygen delivery depends not only on the hemoglobin level, but also on the cardiovascular condition of the individual, and the associated ability to compensate for decreased hemoglobin concentration. Patients without cardio pulmonary compromise, therefore, will typically tolerate lower hemoglobin levels than patients with limited cardiopulmonary reserve. Similarly, the normal hemoglobin levels of infants and children vary from those seen in adults and transfusion triggers as well as usual blood component dose will also vary according to age. See Chapter 13 of this [Guide](#) for details on neonatal and pediatric transfusion. Finally, patients who develop anemia slowly develop compensatory mechanisms to allow them to tolerate lower hemoglobin values than patients who become acutely anemic.

The decision to transfuse anemic patients should be made in each individual case. There is no uniformly accepted hemoglobin value below which transfusion should always occur. However, many studies and guidelines support the use of a restrictive transfusion strategy, including in the intensive-care unit (ICU) setting and with postoperative anemia.¹

Red blood cells should not be given for volume replacement or for any reason other than correction of acute or chronic anemia when non-transfusion alternatives have been assessed and excluded. The decision to transfuse should not be based on a single hemoglobin or hematocrit value as a trigger without considering all critical physiologic and surgical factors affecting oxygenation and clinical status in that patient. See the Choosing Wisely Canada website for more information about transfusion guidelines.²

Dose and administration

One unit of red blood cells usually increases the hemoglobin concentration by approximately 10 g/l in an average size, non-bleeding adult. For pediatric or neonatal patients, as well as for adult patients who cannot tolerate a transfusion rate that would allow for infusion of the total volume within four hours, small volume or “split” units may be provided by some hospital transfusion services.

Reading of chapters 8 and 9 of this [Guide](#) is recommended for detailed information on pre-transfusion testing and administration, respectively. Chapter 13 of this [Guide](#) is also recommended for guidelines on neonatal and pediatric transfusion.

If transfusion of the red blood cell unit will not be initiated promptly after removal from the temperature-controlled blood product refrigerator or storage/transportation device, it should be returned immediately to prevent waste. Blood products may be returned to inventory only if the bag is intact, passes a visual inspection and has maintained an acceptable temperature or the red blood cells have not been out of a temperature controlled environment for more than 60 minutes (See CSTM Standard 5.8.7.1 for more information).³

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Storage and transportation

The proper storage and transportation of blood products are critical for safe transfusion. As a biological product, blood carries a risk of bacterial contamination if stored improperly. Improper storage may also affect the efficacy of blood products.

The shelf life of a red blood cell unit issued by Canadian Blood Services is 42 days from collection. Manipulation of the unit, including washing or irradiation, alters the shelf life. The expiry date is documented on the label of each unit. If the blood product is opened without the use of a sterile connection device, the shelf life is limited to 24 hours if stored at 1–6°C (or the original expiry date, whichever is sooner), or to four hours if stored above 6°C. Units selected for irradiation at Canadian Blood services must be less than or equal to 14 days after collection and following irradiation, the units may be stored for an additional 14 days. This change occurred on 2017-08-14 and aligns Canadian Blood Services with the British Committee for standards in Hematology.⁴ Red blood cell products must be stored at 1–6°C in a temperature-controlled storage device with an alarm system, air-circulating fan and continuous monitoring device. Records must be kept during storage and transportation that maintain the chain of traceability, in order to follow blood products from their source to final disposition and to ensure that appropriate conditions were present throughout this time frame.

Maintaining proper storage temperature during transportation is essential. Transportation time should not exceed 24 hours. Blood products with a required storage temperature of 1–6°C should be transported under validated conditions of 1–6°C; however, if the transit time is 24 hours or less, a transport system validated to maintain an environmental temperature of 1–10°C is allowable. Visual inspection of each blood product to be shipped must be performed and documented. Validated shipping containers and standardized packing procedures are critical to this process. Some hospitals and regions use temperature-monitoring devices, in one or more shipping containers in each shipment of blood and blood products, to ensure the correct temperature during transportation.

When red blood cell units accompany a patient, the issuing hospital transfusion service is responsible for notifying the receiving hospital transfusion service, which is then responsible for the final disposition documentation.

Further details about the red blood cell units manufactured by Canadian Blood Services can be found in the relevant [Circular of Information](#).

Available alternatives

Depending on the underlying cause of anemia, alternative treatments that may be considered include oral iron, intravenous iron, vitamin B12, folic acid, and erythropoietin stimulating agents. Monitoring the hemoglobin while treating the underlying condition(s) contributing to anemia may be an alternative to transfusion for some patients.²

PLATELETS

Product manufacturing and description (see Figures 1 and 2)

At Canadian Blood Services, there are two types of platelet preparations: Pooled Platelets and Apheresis Platelets.

Pooled Platelets are prepared from whole blood collected into a buffy coat collection set (B1 method) with CPD anticoagulant (Figure 1). The whole blood donations are rapidly cooled to room temperature after collection. After transportation to the production site, the blood components are separated by centrifugation. The top

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layer, containing the plasma, and the bottom layer, containing the red blood cells, are extracted. The buffy coat layer between the red blood cells and plasma contains platelets and white blood cells. The buffy coat layers from four donations of the same ABO blood group, along with plasma from one of the same four donations (generally a male donor), are pooled together and further processed, including LR by filtration, in order to produce Pooled Platelets (Figure 2). The pool is labeled as Rh negative only when all the donor units within the pooled product are Rh negative. The Pooled Platelets units are produced within 28 hours of collection and have a unique pool number identifier. Pooled Platelets have an average volume of 342 (\pm 15) ml and a typical platelet count of 298 (\pm 68) $\times 10^9$ per unit. The shelf life is seven days from the time of collection. The typical unit of Pooled Platelets has an average residual leukocyte count of 0.09 $\times 10^6$ and may also contain trace amounts of red blood cells.

Apheresis Platelets are collected and prepared by an automated in-line process using a chamber with flow patterns that separate the red blood cells and leukocytes from the platelets and plasma. A typical unit of Apheresis Platelets issued by Canadian Blood Services contains 370 (\pm 48) $\times 10^9$ platelets, with a mean residual leukocyte count of 0.067 $\times 10^6$ and an average volume of 242 (\pm 8) ml.

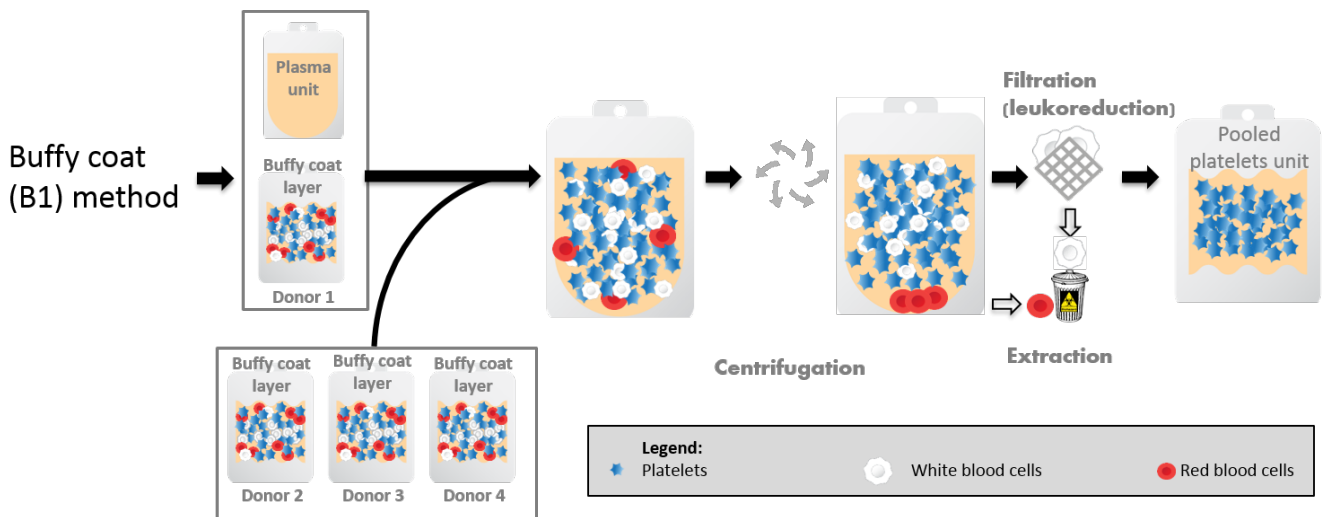


Figure 2. Pooled Platelets manufacturing at Canadian Blood Services.

Indications

The transfusion of platelets is indicated in the treatment of patients with bleeding due to severely decreased or dysfunctional platelets. Platelet transfusion may also be useful if given prophylactically to patients with rapidly falling or low platelet counts secondary to bone marrow disorders or chemotherapy. Platelet transfusions are not recommended for patients with rapid platelet destruction (e.g. ITP, heparin-induced thrombocytopenia (HIT), thrombotic thrombocytopenic purpura (TTP)) except in the setting of clinically significant and/or life threatening bleeding.⁵

Indications are similar for both Pooled Platelets and Apheresis Platelets. Apheresis Platelets may be selected on the basis of similar human leukocyte antigen (HLA) typing to the recipient's when a recipient fails to respond to platelet transfusion because of demonstrated anti-HLA antibodies (alloimmune refractoriness). See Chapter 18 of this [Guide](#) for details of treatment and testing for platelet-refractory patients.

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Dose and administration

The donor plasma in the platelet unit should be ABO compatible (but not necessarily group-specific) with the recipient's red blood cells. The same compatibility guidelines are used for platelets and plasma products (Table 1). See chapters 9 and 18 of this [Guide](#) for information on dose and administration of platelet products.

Table 1. ABO compatibility for plasma and platelet product recipients

Blood group of recipient	A/B Antigen(s) present on recipient red blood cells	A/B Antibodies present in recipient blood	Compatible plasma from groups	May receive platelets from groups
A	A	Anti-B	A, AB	A, AB, B, O
B	B	Anti-A	B, AB	B, AB, A, O
AB	A, B	None	AB	AB, A, B, O
O	None	Anti-A, Anti-B	All (A, B, AB, O)	O, AB, A, B

Transfusion of Apheresis Platelets should result in increments similar to those achieved by transfusion of Pooled Platelets. In practice, the post-transfusion platelet count often does not rise to the expected level. Sepsis, alloimmunization, fever, immune thrombocytopenic purpura (ITP) or disseminated intravascular coagulation (DIC) may contribute to a suboptimal response. See Chapter 18 of this [Guide](#) for more information.

Storage and transportation

Platelet components must be stored at 20–24°C under continuous agitation. Platelet agitators and incubators are required for storing platelet products. If the agitator is not contained in a platelet incubator, the ambient temperature must be recorded manually using a calibrated thermometer every four hours or through use of a constant room temperature monitoring device as long as platelet products are stored.

Their shelf life is seven days from the date of collection. Once opened, the expiry time is four hours from the time of opening unless aliquots are prepared using a sterile connection device. Aliquots obtained using such a device retain the seven day expiry date and must contain a minimum residual volume that is dependent on the collection pack. For Apheresis Gambro Trima collection packs the minimum volume is 100 ml. For Haemonetics MCS collection packs the minimum residual volume in the original storage container is 200 ml. The collection and expiry dates indicated on the platelet unit must be copied to the label of each aliquot pack made from the original unit.

Further details on the platelet products manufactured by Canadian Blood Services can be found in the [Circular of Information](#) and Chapter 18 of this [Guide](#).

Available alternatives

Apheresis Platelets may be used instead of Pooled Platelets whenever supply and demand allow.

There are no known alternatives to platelet concentrates.

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PLASMA PRODUCTS

Product manufacturing and description

The main types of plasma products produced and distributed by Canadian Blood Services are Frozen Plasma CPD, Apheresis Fresh Frozen Plasma and Cryosupernatant Plasma CPD. Canadian Blood Services also distributes solvent detergent treated (SD) plasma produced by Octapharma to specific patients who have conditions requiring use of this product (Table 2). Canadian Blood Services also produces and distributes Cryoprecipitate, for which a separate section is identified at the end of this chapter.

Frozen Plasma CPD (FP) is prepared from whole blood collected in CPD anticoagulant that is red blood cell-reduced by centrifugation. Depending on the processing method, FP is platelet-reduced and leukocyte-reduced by either centrifugation (B1 method) or filtration (B2 method) (Figure 1). The extracted plasma is frozen within 24 hours of collection and labelled as a Frozen Plasma CPD unit. Although the processing steps inherently reduce the number of leukocytes to a residual leukocyte level that averages $< 5 \times 10^6$ per unit, the label for plasma components does not indicate that leukoreduction has been performed because leukocyte level can be highly variable.

Apheresis Fresh Frozen Plasma (AFFP) is collected using an automated in-line process in which whole blood from the donor enters a collection chamber where flow patterns separate the plasma from cellular blood constituents such as red blood cells and leukocytes. Plasma collected by apheresis is frozen within eight hours of collection and labelled as an Apheresis Fresh Frozen Plasma unit.

The average volume of FP and AFFP products issued by Canadian Blood Services and their coagulation factors content are described in Table 2. Coagulation Factors V and VIII, known as the labile coagulation factors, are not stable in plasma stored for prolonged periods at 1–6°C; therefore, plasma is stored in the frozen state at -18°C or lower. AFFP contains approximately 87% of the Factor VIII present at the time of collection, and according to Canadian standards must contain at least 0.70 IU/ml of Factor VIII. FP contains Factor VIII levels that are approximately 70–75% of the levels present at the time of collection, and according to Canadian standards must contain at least 0.52 IU/ml of Factor VIII. The levels of Factor V, as well as the levels of other coagulation factors, are not significantly decreased from baseline in plasma frozen within 24 hours of collection.

Cryosupernatant Plasma CPD (CSP) is prepared from slowly thawed FP that is centrifuged to separate the plasma from the insoluble cryoprecipitate. The insoluble cryoprecipitate is removed and the remaining plasma is refrozen and labelled as Cryosupernatant Plasma CPD.

Canadian Blood Services also distributes Octaplasma™ to a limited number of patients who meet specific criteria. This is a solvent detergent (SD) treated, pooled fresh frozen plasma product produced by Octapharma. Octaplasma™ is filtered to remove cells and debris, which may help reduce adverse events linked to residual blood cells, and the pooling process dilutes and neutralizes allergens and antibodies, theoretically reducing the risk of TRALI. The SD treatment destroys enveloped viruses, and the manufacturing process reduces the risk of infection by non-enveloped viruses and prions, but the possibility of transmission of the latter agents cannot be eliminated.

Table 2. Description of plasma products distributed by Canadian Blood Services

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Type	Description
Frozen Plasma CPD (FP)	Approximately 283 ml of plasma separated from an individual unit of whole blood collected in CPD anticoagulant and placed in a freezer at $<-18^{\circ}\text{C}$ within 24 hours after donation; contains all coagulation factors but has slightly reduced amounts of clotting Factors V and VIII. On average, FP contains 0.87 IU of Factor VIII per ml.
Apheresis Fresh Frozen Plasma (AFFP)	Plasma collected by apheresis and frozen within eight hours of donation; contains both labile clotting Factors V and VIII, plus non-labile coagulation factors. Sodium citrate anticoagulated AFFP units have an average volume of 494 ml while ACD-A anticoagulated AFFP units have an average volume of 249 ml. AFFP units contain an average of 1.29 IU of Factor VIII per ml.
Cryosupernatant Plasma CPD (CSP)	Approximately 273 ml of plasma separated from an individual unit of whole blood prepared following Cryoprecipitate production; contains all coagulation factors but has reduced levels of the high molecular weight Von Willebrand factor (vWF) multimers.
Solvent Detergent (SD) plasma	Plasma pooled from many donors, treated with processing steps (solvent detergent, immune neutralisation, sterile filtration) to remove or inactivate pathogens, cells, allergens and antibodies. Each unit is 200 ml of cell-free plasma that contains 9.0–14.0 g of human plasma proteins (45–70 mg/ml). A minimum of 0.5 IU per ml is obtained for all clotting factors.
FP, AFFP and CSP are manufactured and distributed by Canadian Blood Services. SD plasma (Octaplasma™) is produced by Octapharma and distributed by Canadian Blood Services for specific indications. See product monograph for more details.	

Indications

Given the fact that AFFP is no longer used to treat patients with isolated Factor VIII or Von Willebrand factor deficiencies and that studies have shown that the levels of Factor VIII in FP are only slightly lower than those in AFFP, in most clinical situations where these products are indicated (Table 3), FP and AFFP may be used interchangeably.

There is broad general consensus that the appropriate use of AFFP/FP is limited almost exclusively to the treatment or prevention of clinically significant bleeding due to a deficiency of one or more plasma coagulation factors. Such situations potentially include the treatment of:

<ul style="list-style-type: none"> bleeding patients or patients undergoing invasive procedures who require replacement of multiple coagulation factors (such as patients with severe liver disease or DIC); patients with massive transfusion (replacement of patient's blood volume in less than 24 hours) with clinically significant coagulation abnormalities; patients on warfarin anticoagulation who are bleeding or need to undergo an invasive procedure before vitamin K can reverse the warfarin effect and for whom prothrombin complex concentrates are not indicated, or not available; 	<ul style="list-style-type: none"> patients with rare specific plasma protein deficiencies for which no more appropriate or specific alternative therapy is available; patients requiring treatment of TTP and adult hemolytic uremic syndrome (HUS) by plasma exchange; other conditions treated by therapeutic plasma exchange where the exchange fluid must include coagulation factors. See Chapter 14 of this Guide.
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AFFP or FP may also be used in the preparation of reconstituted whole blood for exchange transfusion in neonates. See Chapter 13 of this [Guide](#) for more information about neonatal and pediatric plasma transfusion.

CSP is used in the treatment of TTP and adult hemolytic uremic syndrome (HUS) by plasma exchange, or may be used in treatment of multifactor deficiency, particularly when fibrinogen replacement is not required. For example, CSP may also be used for treatment of patients on warfarin anticoagulation who are bleeding or need

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to undergo an invasive procedure before vitamin K can reverse the warfarin effect and for whom prothrombin complex concentrates are not indicated, or not available. AAFP or FP is usually used in these situations when CSP is not available.

SD plasma (Octaplasma™) is licensed and approved for use in Canada for a number of indications where plasma might otherwise be used. However, the supply is limited, and only patients with high volume plasma transfusions who meet criteria identified by the National Advisory Group⁶ for blood and blood products may be treated with SD plasma, including patients with:

- Thrombotic thrombocytopenic purpura (TTP) or
- Hemolytic uremic syndrome (HUS) with associated factor H deficiency or
- Clotting factor deficiencies for which specific licensed concentrates may not be readily available (e.g. Factor V, Factor XI, Factor XIII)

Who also:

- Have experienced an allergic reaction to a frozen plasma product (e.g. AAFP, FP) or
- Have a pre existing lung disorder or
- Need FP but a blood group compatible product is not available in a timely manner.

Table 3. Indications for plasma component transfusion by condition/clinical circumstance

Condition/Clinical Circumstance	Frozen Plasma CPD (FP)	Apheresis Fresh Frozen Plasma (FFPA)	Cryosupernatant Plasma CPD (CSP)	Solvent Detergent (SD) Plasma
Reversal of warfarin therapy when prothrombin complex concentrates and/or vitamin K is contra-indicated or unavailable	X	X	X	
Correction of microvascular bleeding when laboratory testing demonstrates coagulopathy	X	X		
Liver disease	X	X		
Massive transfusion	X	X		
Exchange transfusion in neonates	X	X		
TTP or adult HUS plasma exchange therapy	X	X	X	
Patients with selected coagulation factor deficiency or rare plasma protein deficiencies when specific alternative therapy is not available	X	X		
Patients who meet the qualifying criteria for SD plasma (see above)				X

Guidelines for reversal of oral anticoagulant therapy using plasma or prothrombin complex concentrates (PCC) are available from the National Advisory Committee on Blood and Blood products.⁷ See also Chapter 17 of this

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Guide and/or the relevant Canadian Blood Services *Circular of Information* for further information.

Contraindications

Plasma transfusion is **not** indicated for volume replacement alone, or for a single coagulation factor deficiency if specific recombinant products or plasma-derived virally inactivated products are available. Plasma transfusion is generally not indicated or effective in reversal of an International Normalized Ratio (INR) below 1.8.⁸

Hypovolemia without coagulation factor deficiencies should be treated with other plasma volume expanders such as 0.9% sodium chloride, Ringer's lactate solution, albumin or hydroxyethyl starches. See Chapter 3 of this *Guide* for more details on albumin and therapeutic alternatives to albumin.

Do not use plasma when coagulopathy can be more appropriately corrected with specific therapy such as vitamin K, prothrombin complex concentrates (PCCs), Cryoprecipitate, or specific coagulation factor replacement. See Chapter 5 of this *Guide* for information about coagulation factors available in Canada and their use.

Do not use cryosupernatant plasma for conditions that require fibrinogen, Factor VIII or Von Willebrand factor replacement.

Dose and administration

Reading of chapters 9 and 13 of this *Guide* is recommended for detailed information on blood administration and on neonatal and pediatric transfusion, respectively.

The volume transfused depends on the clinical situation and recipient size, and when possible should be guided by serial laboratory assays of coagulation function. In general, the dose to achieve a minimum of 30% of plasma clotting factor concentration is attained with the administration of 10–15 ml/kg of body weight, except for the treatment of warfarin reversal in which 5–8 ml/kg body weight will usually suffice (and only in the rare circumstance where PCCs are contraindicated or unavailable).

Plasma products must be ABO compatible with the recipient's blood type but not necessarily be group specific (see Table 1). To be compatible, the plasma product should not contain ABO antibodies that may be incompatible with the ABO antigens on the patient's red blood cells. If there is no ABO group available for the recipient, a typing will be required to determine compatibility or group AB plasma can be used.

Thawing of FP, AAFP and CSP may take 12–30 minutes depending on the product volume, thawing method and equipment used by the hospital transfusion service. SD plasma should be thawed in the outer wrapper in a circulating water bath (30–37°C) for 30 to 60 minutes or in a dry tempering system according to manufacturer instructions; detailed device-specific recommendations are available from Octapharma.

Upon completion of thawing, transfuse immediately or store plasma products in an alarmed, continuously monitored refrigerator at 1–6°C. Once thawed, plasma products cannot be refrozen; some institutions have a thawed plasma bank. FP, CSP, and AAFP anticoagulated with ACD-A can be stored up to five days; however, AAFP anticoagulated with sodium citrate) is collected in an open system and can be stored for only 24 hours (at 1–6°C) after thawing.

If transfusion of the plasma unit will not be initiated promptly after removal from the temperature-controlled blood product refrigerator or storage/transportation device, it should be returned immediately to prevent waste. Blood products may be returned to inventory only if the bag is intact, passes a visual inspection and has maintained an acceptable temperature (See CSTM Standard 5.8.7.1 for more information).³

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Storage and transportation

Frozen plasma products must be stored frozen at -18°C or colder in a controlled, monitored freezer for a maximum of 12 months (FP, AFFP, CSP) or four years (Octaplasma™). Product must not be out of the controlled blood storage freezer for longer than 30 minutes.

Available alternatives

FP and AFFP may be used interchangeably depending on indication, supply and demand.

SD plasma is available for specific indications as described above.

Vitamin K should be used for warfarin reversal when the patient is not bleeding and does not require an invasive procedure. Patients requiring rapid reversal of warfarin due to bleeding, bleeding risk or an urgent invasive procedure may benefit from use of a PCC.

Specific plasma protein concentrates are available and are described in chapters 5 and 17 of this [Guide](#).

CRYOPRECIPITATE

Product manufacturing and description

Canadian Blood Services prepares Cryoprecipitate from slowly thawed FP that is centrifuged to separate the insoluble cryoprecipitate from the plasma. The plasma is removed and the insoluble cryoprecipitate is refrozen and labelled as Cryoprecipitate. Each 10 (± 2) ml bag of cryoprecipitate contains a mean of 285 (± 88) mg of fibrinogen.

Indications

Over the last several years a number of factors have changed the clinical indications for the use of Cryoprecipitate. These factors include a better understanding of the coagulation system; more attention to the non-factor VIII factors within Cryoprecipitate; concern about viral inactivation; and the development of alternative products.

The current primary uses of Cryoprecipitate are for fibrinogen replacement in acquired hypofibrinogenemia or as empiric therapy in a bleeding patient. Generally, a plasma fibrinogen level of less than 1.0 g/l, as might occur in DIC or fibrinogenolysis, provides an objective basis for Cryoprecipitate therapy. Certain populations have a higher threshold (e.g. fibrinogen >1.5 g/l is recommended in patients with acute promyelocytic leukemia and in massively bleeding patients).^{3, 9, 10}

Apart from the historical use of Cryoprecipitate as a Factor VIII concentrate for hemophilia and Von Willebrand disease, there are no prospective studies demonstrating evidence-based outcomes for the use of Cryoprecipitate. See the “Available alternatives” section below for information on use of recombinant products for these conditions.

Despite the paucity of evidence, Cryoprecipitate is widely accepted as one of the products used to treat bleeding due to hypofibrinogenemia. These conditions include rare cases of hypofibrinogenemia or dysfibrinogenemia and, more commonly, acquired conditions with multiple factor deficiencies (e.g. DIC, post-thrombolytics, massive transfusion or liver disease). These are complicated conditions and Cryoprecipitate is only one part of the clinical management of such patients. Fibrinogen deficiency should be documented, and the

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product should only be used if there is active bleeding or a planned surgical procedure. While studies documenting efficacy in these settings are very limited, these are relatively common conditions and there is considerable clinical experience using Cryoprecipitate. In some cases, fibrinogen concentrates may be considered an equally effective alternative (see chapters 5 and 8 of this [Guide](#)).

Contraindications

Usually, Cryoprecipitate **is not indicated** unless results of laboratory studies indicate a fibrinogen concentration of 1.0 g/l or less or in the setting of massive hemorrhage with coagulopathy. Specific factor and/or recombinant concentrates are preferred, when available, because of the reduced risk of transfusion-transmissible diseases.

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

Cryoprecipitate is not recommended in the treatment of hemophilia A, or in most cases (see below) in the treatment of Von Willebrand disease.

Dose and administration

Group-specific Cryoprecipitate is not necessary outside of the pediatric setting, and should be considered according to local policy for pediatric recipients. Reading of chapters 9 and 13 of this [Guide](#) is recommended for detailed information on administration and on neonatal and pediatric transfusion, respectively.

One unit of Cryoprecipitate contains approximately 285 mg of fibrinogen. The amount of Cryoprecipitate required for transfusion will depend on the severity and nature of the bleeding condition.

The amount of Cryoprecipitate needed to raise the fibrinogen concentration of plasma can be calculated as follows:

- Step 1. Weight of the patient (kg) x 70 ml/kg = blood volume in ml.
- Step 2. Blood volume in ml x (1.0 - patient hematocrit) = plasma volume in ml.
- Step 3. Desired fibrinogen - actual fibrinogen x plasma volume (ml) = mg fibrinogen required.
- Step 4. mg fibrinogen required/285 mg per cryoprecipitate unit = units of cryoprecipitate required.

Many facilities use the generic dose of up to 1-2 units per 10 kg body weight, as required to maintain fibrinogen above 1 g/l, as directed by the hospital transfusion service medical director for treatment of hypofibrinogenemia. An order for 10 units of Cryoprecipitate for an average sized patient is typical at many hospitals, with subsequent requests in increments of 10 units depending on clinical need. The same standards as for the other blood components concerning prescription, informed consent and addition of medications apply to Cryoprecipitate.

Cryoprecipitate is often pooled by the hospital transfusion medicine service personnel or may be given sequentially. Small quantities of normal saline are introduced to rinse each bag in the pooling process. Pooled Cryoprecipitate may have a single pool number and the label will indicate the number of units in the pool. This number and the number of units in the pool must be documented. If no pool number exists, each donor unit number must be documented on the medical record. If the Cryoprecipitate is pooled, all units will have been opened and must be used within four hours.

Cryoprecipitate may be administered through a blood administration set with a standard blood filter or as a

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bolus injection by trained personnel. Infusion should be as rapid as can be tolerated by the patient or as specified by the ordering physician. See the [Circular of Information](#) on plasma components for further information.

Storage and transportation

Cryoprecipitate must be stored frozen at -18°C or colder in a controlled, monitored freezer for a maximum of 12 months. Product must not be out of the controlled blood storage freezer for longer than 30 minutes and cannot be refrozen. If the transfusion will not be initiated promptly after removal from the temperature-controlled blood product storage device, the product should be returned immediately to prevent deterioration and waste (CSTM Standard 5.8.7.1).³

Additional information on storage may be found in the [Circular of Information](#) on plasma components.

Available alternatives

The primary use of Cryoprecipitate is for fibrinogen replacement, or empirically in a bleeding patient or patient with new microvascular bleeding.

See Chapter 5 of this [Guide](#) for information on coagulation factor concentrates available in Canada and their use. There are fibrinogen concentrates available. In Canada, the current indication is for treatment of congenital hypofibrinogenemia.

See also Chapter 17 of this [Guide](#) for information on how to treat hemostatic disorders including hemophilia and Von Willebrand disease. Cryoprecipitate does contain fibronectin that has been suggested and used to improve reticuloendothelial function in critically ill patients with sepsis. There is, however, insufficient information to recommend its use in this setting.

CONTINUING PROFESSIONAL DEVELOPMENT CREDITS

Fellows and health-care professionals who participate in the Canadian Royal College's Maintenance of Certification (MOC) Program can claim the reading of the Clinical Guide to Transfusion as a continuing professional development (CPD) activity under Section 2: Self-learning credit. The reading of one chapter is equivalent to **two credits**.

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We're here to answer your questions about the Clinical Guide to Transfusion. We'd also appreciate your ideas on how to improve the Guide. Please contact us through the [Clinical Guide feedback form](#).

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