

## CHAPTER 2

# BLOOD COMPONENTS

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## BACKGROUND

Whole blood donations are separated into specific cellular (red blood cells and platelets) and plasma components. Transfusing the appropriate blood component to effectively provide for the clinical needs of patients optimizes use of donated blood.

This chapter describes the manufacturing process for the most commonly prepared blood components:

- Red blood cells (RBC)
- Platelets: pooled and apheresis
- Frozen plasma (FP)
- Cryosupernatant plasma (CSP)
- Cryoprecipitate

Note: In January 2022, Canadian Blood Services introduced pathogen-reduced buffy coat platelets, also known as pooled platelets psoralen-treated (PPPT). **This chapter does not provide information on PPPT; for more information see Chapter 19, [Pathogen-reduced platelets](#).**

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.

Canadian Blood Services provides a [Circular of Information](#) with comprehensive 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 Canada](#).

## COLLECTION OF BLOOD PRODUCTS

At Canadian Blood Services, whole blood is collected from donors into a collection pack with multiple bags that are connected, allowing blood and components to be transferred between bags aseptically (closed system)

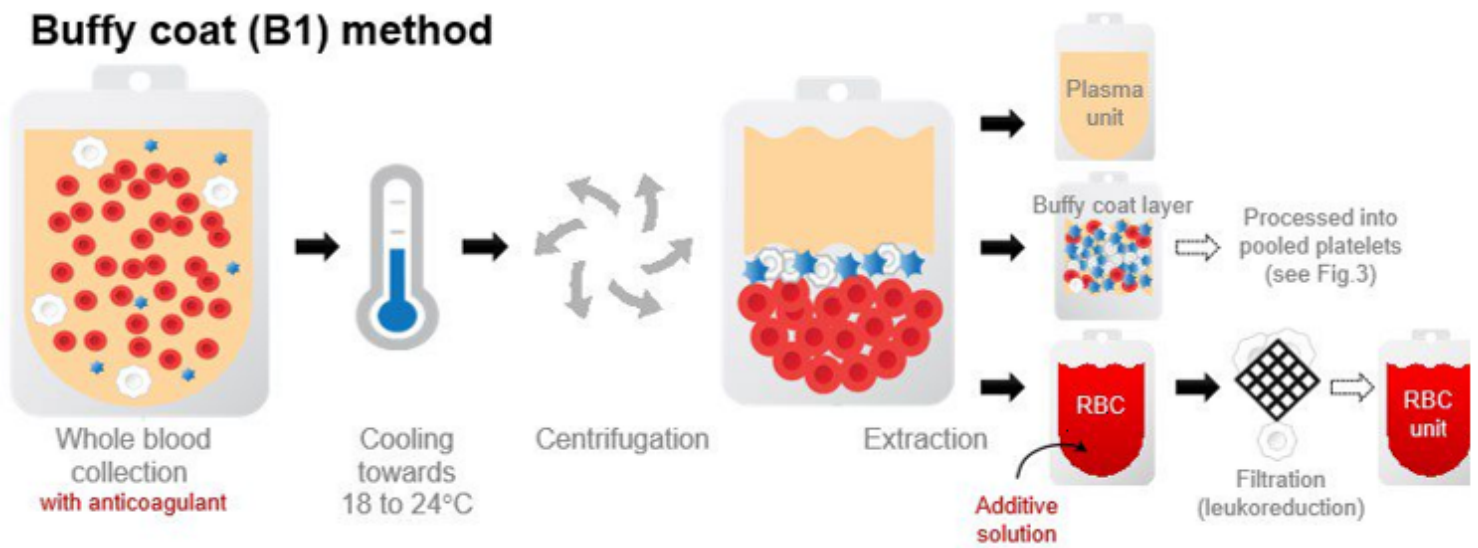
during manufacturing. The collection packs include two different configurations:

- The buffy coat collection set (also referred to as B1) is used in the production of RBC, plasma, and platelet components.
- The whole blood filtration set (also referred to as B2) is used in the production of RBC and plasma components (including cryoprecipitate).

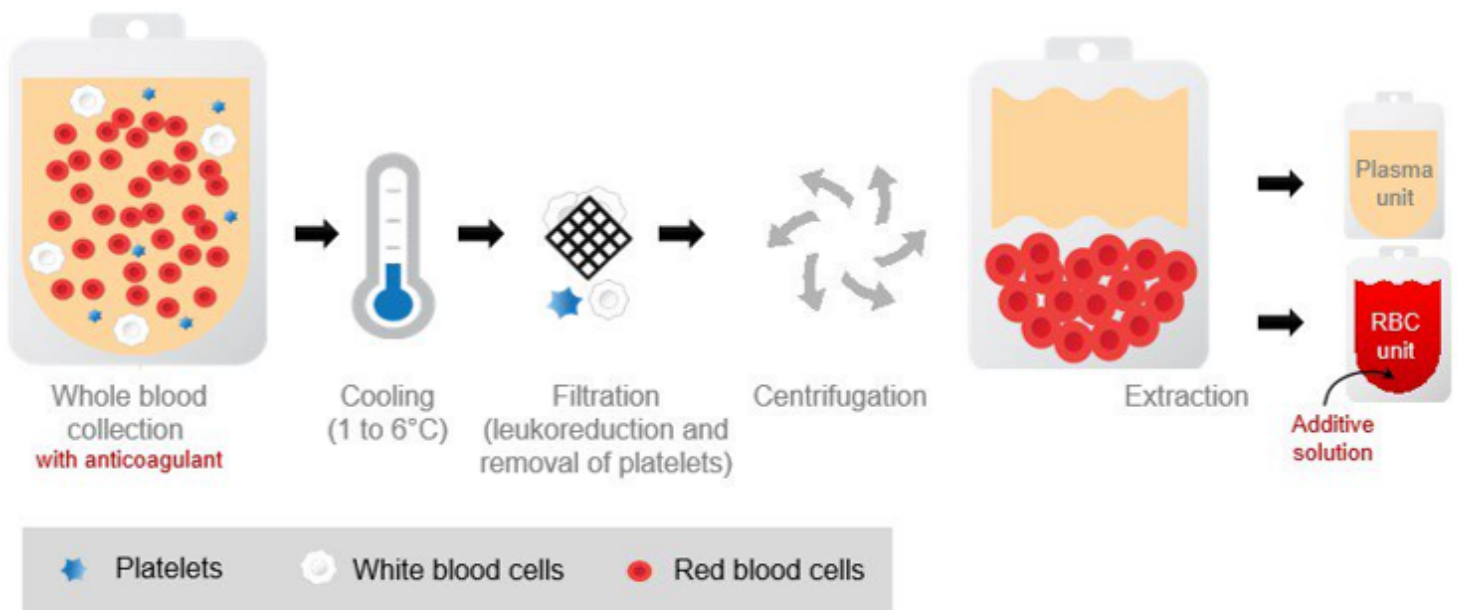
Figure 1 highlights the main steps of both manufacturing processes. Collection bags contain a citrate-phosphate-dextrose (CPD) anticoagulant.

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 centrifugation separates the plasma from cellular blood constituents such as red blood cells and white blood cells. Information about the anticoagulants used can be found in the [Circular of Information](#) for each component type and in Table 1. Depending on the process, either plasma or platelets suspended in plasma are collected into a bag while the remaining constituents of the blood are returned to the donor.

## Buffy coat (B1) method



## Whole blood filtration (B2) method



**Figure 1.** The manufacturing processes used at Canadian Blood Services to produce blood components from whole blood. Note: Manufacturing of pathogen-reduced platelets is not shown here (see [Chapter 19](#)).

## RED BLOOD CELLS

### COMPONENT MANUFACTURING AND DESCRIPTION

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 the additive solution saline-adenine-glucose-mannitol (SAGM) and labelled as a red blood cell unit.

All red blood cells prepared by Canadian Blood Services have undergone leukoreduction (LR). The typical red blood cell unit issued by Canadian Blood Services is 285 mL, contains 55 g of hemoglobin with a hematocrit of approximately 0.67% and has an average residual leukocyte count of  $6 \times 10^6$ . Specific parameters are described and updated in the [Circular of Information](#). Further modifications of red blood cell components such as washing, deglycerolizing and irradiation are covered in [Chapter 15](#) of this *Guide*.

Each donation is tested for various antigens and for certain infectious disease markers as outlined in [Chapter 6](#). In addition, all donor red blood cells undergo ABO and Rh D typing and are labelled accordingly (Figure 2). Kell typing is performed on every donor twice and, when negative, this result is printed on the label. A proportion of donors are also phenotyped for additional red cell antigens corresponding to common clinically significant antibodies (C,c,E,e,Jka, Jkb, Fya, Fyb, S,s). Negative results for any of these antigens appear on the label. The complete set of results, including positive and negative antigen tests, appears in the bar code label.



**Figure 2:** Canadian Blood Services label for a red blood cell unit. Available on [blood.ca](http://blood.ca).

## 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 cardiopulmonary 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 blood component dose, 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 based on an individual case assessment. There is no uniformly accepted hemoglobin value below which transfusion should occur for every patient, in every scenario. 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.

Red blood cells are not given for volume replacement or for any reason other than correction of acute or chronic anemia and should be given only after non-transfusion alternatives have been either assessed and excluded or do not adequately manage anemia. The decision to transfuse should not be based on a single hemoglobin or hematocrit value as a trigger without considering relevant physiologic and surgical factors affecting oxygenation and clinical status in that patient. Cardiovascular status along with other co-morbid conditions, the acuity and severity of the anemia, and the presence or risk for ongoing blood loss are also considered in determining the need for correction of anemia with transfusion. See the Choosing Wisely Canada [website](#) for more information about transfusion guidelines.

## DOSE AND ADMINISTRATION

One unit of red blood cells usually increases the hemoglobin concentration by approximately 10 g/L in a 70 kg non-bleeding adult. For pediatric or neonatal patients who require a smaller dose, small volume or “split” units may be provided by some hospital transfusion services.

[Chapter 8](#) and [Chapter 9](#) of this *Guide* provide 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 component refrigerator or storage/transportation device, it should be returned to inventory immediately to prevent waste. An unused RBC unit may be returned only if the bag is intact, passes a visual inspection and has either been maintained at an acceptable temperature (see Storage and transportation), or has not been out of a temperature-controlled environment for more than 60 minutes (See CSTM Standard 5.8.7.1 for more information).

## STORAGE AND TRANSPORTATION

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

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, shortens the shelf life. The expiry date is documented on the label of each unit. If the red blood cell unit 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 4 hours if stored above 6°C. Units selected for irradiation at Canadian Blood Services must be less than or equal to 14 days old after collection and following irradiation, irradiated cells must be transfused as soon as possible, but not later than 14 days after irradiation. <sup>4-6</sup> Red blood cell components 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 of blood components from their source to final disposition, and to ensure that appropriate conditions were present throughout this time frame. [Chapter 15](#) provides additional information on washing and irradiation.

Maintaining proper storage temperature during transportation is essential. Transportation time for red blood cells should not exceed 27 hours, using shipping containers and standardized packing procedures that have been validated to maintain an environmental temperature of 1–6°C. For transit times of 24 hours or less, a transport system validated to maintain an environmental temperature of 1–10°C is allowable. Visual inspection of each blood component to be shipped must be performed and documented at the time of shipping and receiving. Some hospitals and regions use temperature-monitoring devices in one or more shipping containers with each shipment of blood and blood components to ensure the correct temperature during transportation.

When red blood cell units accompany a patient who is transferred from one facility to another, traceability of the RBC must be maintained. Accordingly, the issuing hospital transfusion service is responsible for notifying the receiving hospital transfusion service, which is then responsible for the final disposition documentation including whether the RBC was transfused to a patient or was discarded.

Further details about the red blood cell units manufactured by Canadian Blood Services can be found in the [\*Circular of Information for the Use of Human Blood Components, Red Blood Cells, Leukocytes Reduced.\*](#)

## 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/or erythropoietin stimulating agents. Monitoring the patient while <sup>2</sup>treating the underlying condition(s) contributing to anemia may be an alternative to transfusion for some patients.

# PLATELETS

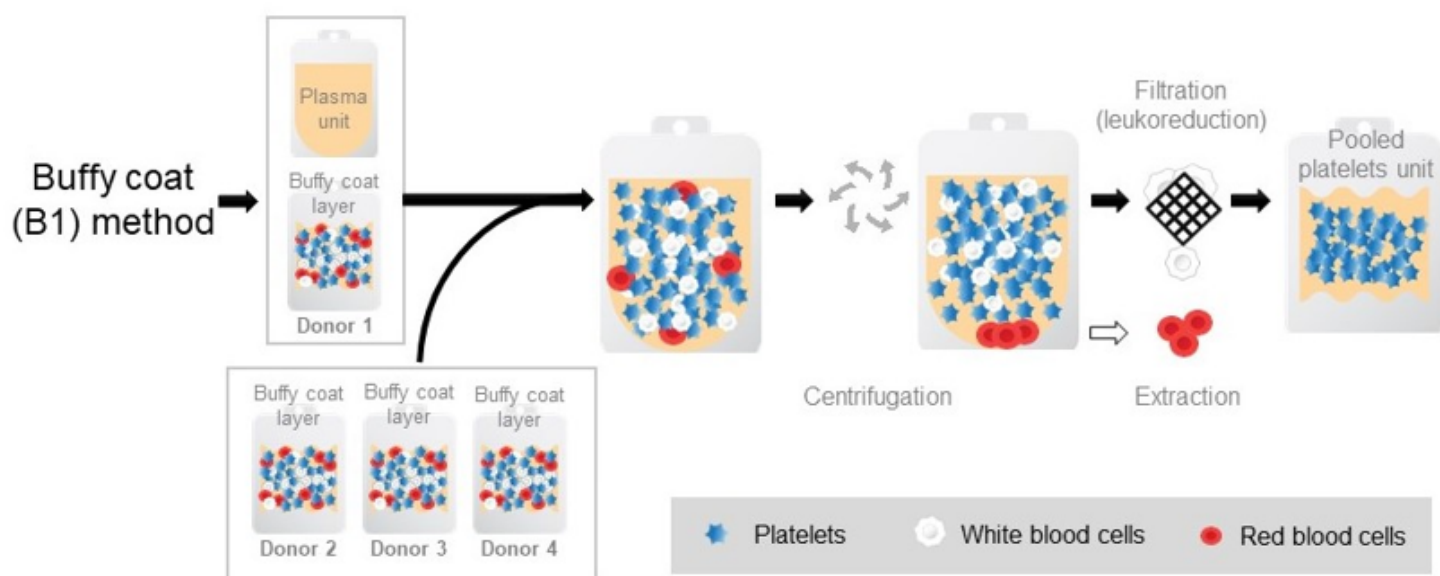
## COMPONENT MANUFACTURING AND DESCRIPTION

At Canadian Blood Services, there are two types of platelet preparations: pooled platelets and apheresis platelets. This chapter provides information on pooled platelets and apheresis platelets but does not include [pathogen-](#)



### reduced buffy coat 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 cooled to room temperature after collection. After transportation to the production site, the blood components are separated by centrifugation. The top 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 (a male donor), are pooled together and processed further, including LR by filtration, to produce one pooled platelet unit or dose (Figure 2). The pool is labeled as Rh negative only when all the donor units within the pooled component are Rh negative. The pool is labeled as “Low Anti-A/B” only when all the donors contributing to the pool were found to have anti-A and anti-B levels below a predetermined cut-off (see [our FAQ: Donor high titre isohemagglutinin \(anti-A,anti-B\) testing at Canadian Blood Services](#)). Pooled platelet units are produced within 28 hours of collection and have a unique pool number identifier. A typical pooled platelet component has a volume of 320 mL, a platelet count of  $340 \times 10^9$  and residual leukocyte count of  $5 \times 10^6$  per unit and may have trace amounts of red cells. The shelf life is seven days from the time of collection. Apheresis platelets are collected and prepared by an automated in-line process using apheresis machines that separate and extract platelets (suspended in the donor's plasma) from other cellular whole blood components by centrifugation. A typical unit of apheresis platelets issued by Canadian Blood Services contains  $333 \times 10^9$  platelets, with residual leukocyte count of  $10 \times 10^6$  and a volume of 220 mL.



**Figure 3.** 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 can cause harm and thus are not recommended for patients with rapid platelet destruction (e.g., immune thrombocytopenic purpura (ITP), heparin-induced thrombocytopenia (HIT), thrombotic thrombocytopenic purpura (TTP)) except to treat clinically significant and/or life-threatening bleeding.

Indications are similar for both pooled platelets and apheresis platelets. Apheresis platelets may be selected based on 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.

## DOSE AND ADMINISTRATION

While ABO-identical platelets may be preferred for transfusion of some patients, ABO compatible platelets are often used. See [Chapter 9](#) and [Chapter 18](#) of this *Guide* for information on ABO compatibility, dose and administration of platelet components.

Transfusion of apheresis platelets should result in increments similar to those achieved by transfusion of pooled platelets. Each dose of platelets should increase the patient's platelet count at 1 hour by at least  $15\text{--}25 \times 10^9 / \text{L}$  in a standard sized-adult. In practice, the post-transfusion platelet count often does not rise to the expected level. Sepsis, alloimmunization, fever, 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. If the agitator is not a closed 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.

Both pooled platelets and apheresis platelets have a shelf life of seven days from the date of collection. Once opened, the unit 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 original seven-day expiry date and must contain a minimum residual volume that is dependent on the collection pack. Canadian Blood Services collects apheresis platelets using Terumo Trima collection packs, which have a minimum volume of 100 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 components manufactured by Canadian Blood Services can be found in the [Circular of Information for the Use of Human Blood Components, Platelets](#), and [Chapter 18](#) and [Chapter 19](#) of this *Guide*.

## AVAILABLE ALTERNATIVES



Apheresis platelets or pooled platelets psoralen-treated may be substituted for pooled platelets if supply and demand allow.

There are no known alternatives to platelet concentrates.

## PLASMA COMPONENTS

### COMPONENT MANUFACTURING AND DESCRIPTION

Canadian Blood Services manufactures and distributes the following main types of plasma components:

- Frozen plasma CPD (FP)
- Cryosupernatant plasma CPD (CSP)
- Cryoprecipitate (see cryoprecipitate section later in this chapter)

Canadian Blood Services also provides:

- Octaplasma (Solvent detergent treated (S/D) plasma) produced by Octapharma.

Blood donors are screened for the presence of antibodies to red cell antigens. If a clinically significant antibody is identified, the plasma is discarded.

Frozen plasma CPD (FP) is prepared from whole blood collected in CPD anticoagulant that is red blood cell-reduced by centrifugation. FP produced by the B1 method is both leukoreduced and platelet-reduced by centrifugation but not leukoreduced by filtration. FP produced by the B2 method is both platelet-reduced and leukoreduced by filtration (Figure 1). The extracted plasma is frozen within 24 hours of collection and labelled as a frozen plasma CPD unit. The processing steps inherently reduce the number of leukocytes to a residual leukocyte level that averages  $< 5 \times 10^6$  per unit, although individual unit leukocyte level can be highly variable. Hence, FP components are not labeled as LR.

For pediatric patients requiring small volume transfusions, Canadian Blood Services offers divided plasma units (FP-Divided) which contain 125–150 ml of plasma. FP-Divided is blood group AB, unless otherwise requested.

The typical volume of FP issued by Canadian Blood Services and their coagulation factors content are described in Table 1. Coagulation factors V and VIII are labile coagulation factors and 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. 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, in at least 75% of the units tested. The levels of factor V and 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 refrozen and the remaining plasma is also refrozen and labelled as cryosupernatant plasma CPD.

Canadian Blood Services also supplies Octaplasma. This is a solvent detergent (S/D) treated, pooled fresh frozen plasma component 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 transfusion-related acute lung injury (TRALI). The manufacturing process with S/D treatment destroys enveloped viruses and resin adsorption removes prions, reducing the risk of infection and variant-Creutzfeldt Jakob disease (vCJD).

Convalescent plasma is plasma that is collected from people who have recovered from an infection and their plasma contains neutralizing antibodies against the causative pathogen. Convalescent plasma has been used as an experimental therapy to treat SARS , H1N1 , Ebola<sup>11 12</sup> and, most recently, COVID-19.<sup>13 15</sup> Prior to the COVID-19 pandemic, there were no large-scale randomized trials that demonstrated efficacy of convalescent plasma. Systematic reviews of trials that used convalescent plasma or hyperimmune products to treat viral pneumonias concluded that convalescent plasma may be associated with efficacy and lack of harm (very low quality evidence), and that well-designed clinical trials are needed.<sup>16 17</sup> During the year 2020, hundreds of studies were initiated world-wide to determine safety and efficacy of convalescent plasma in treating COVID-19. Canadian Blood Services and Héma-Québec have supported Health Canada approved clinical trials by collecting and manufacturing COVID-19 convalescent plasma. Convalescent plasma donors must meet eligibility criteria for routine apheresis plasma collection; in addition, the donors must be previously confirmed positive for COVID-19 by a laboratory test, fully recovered from the virus and symptom free for at least 28 days.

**Table 1.** Description of plasma components distributed by Canadian Blood Services

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°C within 24 hours after collection; 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.
Cryosupernatant Plasma CPD (CSP)	Approximately 273 mL of plasma separated from an individual unit of whole blood prepared following cryoprecipitate manufacturing; contains all coagulation factors but has reduced levels of the high molecular weight Von Willebrand factor (vWF) multimers and fibrinogen.
Octaplasma, Solvent Detergent (S/D) 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.
Convalescent Plasma (CCP)	Plasma collected from people who have recovered from an infection and that contains neutralizing antibodies against the causative pathogen. Plasma must demonstrate a pre-specified neutralizing antibody titre.
CCP is currently manufactured for ongoing clinical trials and is not part of the Canadian Blood Service license for distribution outside of these clinical trials. FP and CSP are manufactured and distributed by Canadian Blood Services. Octaplasma (S/D plasma) is produced by Octapharma and provided to hospitals by Canadian Blood Services. See component monograph for more details.	

INDICATIONS

The use of FP and S/D plasma is limited almost exclusively to the treatment or prevention of clinically significant bleeding due to a deficiency of one or more coagulation factors for which more appropriate or specific alternative therapy is not available. Such situations potentially include the treatment of:

- Bleeding patients or patients undergoing invasive procedures who require replacement of multiple coagulation factors (such as patients with severe liver disease or disseminated intravascular coagulation)
- Patients with massive hemorrhage with clinically significant coagulation abnormalities
- Patients on warfarin anticoagulation who are bleeding or undergoing an invasive procedure before vitamin K can reverse the warfarin effect and for whom prothrombin complex concentrates (PCC) are contraindicated or unavailable
- Patients requiring treatment of TTP by plasma exchange
- Other conditions treated by therapeutic plasma exchange where the exchange fluid must include coagulation factors. See [Chapter 14](#) of this *Guide*.

FP or S/D plasma may also be used in the preparation of reconstituted whole blood. See [Chapter 13](#) of this *Guide* for more information about neonatal and pediatric plasma transfusion.

Cryosupernatant plasma CPD (CSP) is used in the treatment of TTP by plasma exchange, or may be used in treatment of multiple factor deficiencies, 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 to undergo an invasive procedure before vitamin K can reverse the warfarin effect and for whom PCC is contraindicated or unavailable.<sup>18</sup> FP may also be used in these situations and has equivalent efficacy.<sup>19, 20</sup>

Octaplasma is available and approved for use in Canada for the same indications as FP. See the National Advisory Committee on Blood and Blood Products (NAC) [Recommendations for the use of solvent-detergent plasma in Canada](#) for more information on indications, including indications for special populations.

**Table 2.** Indications for plasma component transfusion by condition/clinical circumstance

Condition/Clinical Circumstance	Frozen Plasma CPD (FP)	Cryosupernatant Plasma CPD (CSP)	Solvent Detergent (S/D) 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 treated with plasma exchange	X	X	X

Condition/Clinical Circumstance	Frozen Plasma CPD (FP)	Cryosupernatant Plasma CPD (CSP)	Solvent Detergent (S/D) Plasma
Patients with selected coagulation factor deficiency or rare plasma protein deficiencies when specific alternative therapy is not available	X		X
*The Octaplasma product monograph indicates that the product can be mixed with red blood cells and platelets. Data on use in neonates is limited and the product should only be administered to these individuals if the likely benefits clearly outweigh potential risks.			

See also [Chapter 17](#) of this *Guide* and/or the relevant Canadian Blood Services [Circular of Information](#) for the Use of Human Blood Components, Plasma Components, 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 a non-bleeding patient for primary prophylaxis when the International Normalized Ratio (INR) is below 1.8.<sup>22</sup>

Hypovolemia without coagulation factor deficiencies should be treated with crystalloids 0.9% sodium chloride, or Ringer's lactate solution.

Do not use plasma when coagulopathy can be more appropriately corrected with specific therapy such as vitamin K, PCC, 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 CSP for conditions that require fibrinogen, factor VIII or Von Willebrand factor replacement.

## DOSE AND ADMINISTRATION

[Chapter 9](#) and [Chapter 13](#) of this *Guide* are 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. The dose of FP to achieve a minimum of 30% of plasma clotting factor concentration is attained with administration of 10–15 ml/kg of body weight, approximately 3–4 units in an adult. The product monograph of Octaplasma suggests that 12–15 mL/kg is a generally accepted starting dose, depending on the clinical situation and underlying disorder and that an adequate hemostatic effect on minor or moderate hemorrhages or surgery is normally achieved after the infusion of 5–20 mL/kg of Octaplasma.<sup>23</sup>

Plasma components must be ABO compatible with the recipient but are not necessarily required to be group specific. In most clinical circumstances, the plasma component 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. For the initial management of massive hemorrhages, group AB plasma is predominantly used in Canada. Although many North American trauma centres have been using group A plasma over group AB plasma in their massive hemorrhage protocols. In Canada, some

group A plasma is now tested and labelled as "[Low anti-A/B titre](#)" and is being adopted by some trauma centres as an alternative for AB plasma.

Thawing of FP and CSP may take 12–30 minutes depending on the component volume, thawing method and equipment used by the hospital transfusion service. S/D plasma (Octaplasma) 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 components in a continuously temperature-monitored refrigerator at 1–6°C for up to five days. Once thawed, plasma components cannot be refrozen.

If transfusion of the plasma unit will not be initiated promptly after removal from the temperature-controlled blood component refrigerator or storage/transportation device, it should be returned immediately to inventory to prevent waste. Blood components may be returned 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).

## STORAGE AND TRANSPORTATION

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

## AVAILABLE ALTERNATIVES

FP and S/D plasma may be used interchangeably depending on indication, supply and demand.

Vitamin K should be used for warfarin reversal when the patient is not bleeding or does not require an invasive procedure urgently. Patients requiring rapid reversal of warfarin due to bleeding, bleeding risk or an urgent invasive procedure may benefit from use of a PCC along with Vitamin K. Practical guidance on warfarin reversal can be found on [Treat the Bleed](#), an evidence-based, online resource.

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

## CRYOPRECIPITATE

### COMPONENT 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 component is refrozen and labelled as cryoprecipitate. Typically, one unit of cryoprecipitate (10 ± 2 mL) is obtained from one unit of FP. A [typical unit of cryoprecipitate](#) contains approximately 365 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 constituents within cryoprecipitate, concern about viral inactivation, and the development of alternative components.

The current primary uses of cryoprecipitate are for fibrinogen replacement in acquired hypofibrinogenemia or in a bleeding patient.<sup>24,25</sup> Although either cryoprecipitate or fibrinogen concentrate can be utilized for fibrinogen replacement therapy, the concentrate has the advantage of being pathogen-reduced and available in a freeze-dried, powdered form, which makes it easier to reconstitute and administer than cryoprecipitate, which must remain frozen until use. For these reasons, fibrinogen concentrate is increasingly used in Canada for treatment of acquired hypofibrinogenemia.<sup>24,25</sup> Production of cryoprecipitate from a donor unit precludes platelet production; thus, in the event of a platelet shortage, optimizing platelet production may lead to decreased cryoprecipitate production and recommendations for use of fibrinogen as an alternative. See [Chapter 5](#) of this *Guide*.

Generally, a plasma fibrinogen level of less than 1.0 g/L, as might occur in DIC or fibrinogenolysis, provides an objective basis for fibrinogen replacement. Certain populations have a higher threshold (e.g., fibrinogen <2.0 g/L in massively bleeding obstetrical patients, and fibrinogen <1.5 g/L for non-obstetric patients with massive hemorrhage or primary prophylaxis in acute promyelocytic leukemia).<sup>3 25 27</sup>

The historical use of cryoprecipitate as a factor VIII and VWF concentrate for hemophilia and Von Willebrand disease has now been replaced through treatment regimens that utilize recombinant clotting factor concentrates. A recent study confirms the efficacy of fibrinogen concentrate in treating acquired hypofibrinogenemia consequently many hospitals have shifted to use of concentrates rather than cryoprecipitate.<sup>24</sup>

## CONTRAINDICATIONS

Usually, cryoprecipitate **is not indicated** unless laboratory testing demonstrates 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 used 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. Fibrinogen concentrates may be preferred in treatment of hypofibrinogenemia.

## 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. [Chapter 9](#) and [Chapter 13](#) of this *Guide* are recommended for detailed information on blood 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 (see Figure 4). It is common practice to use a generic dose of 1–2 cryoprecipitate units per 10 kg body weight as a single dose, with additional doses as required to maintain the fibrinogen level for the clinical scenario. An order of 10 units of cryoprecipitate for an average-sized adult patient to target between 3 to 4 g of fibrinogen is a typical dose.

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.

**Figure 4.** Steps to calculate the amount of cryoprecipitate needed to raise the fibrinogen concentration of plasma.

Cryoprecipitate is often pooled by hospital transfusion medicine service personnel or may be given as individual units 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 filtered bolus injection by trained personnel. Infusion should be as rapid as can be tolerated by the patient or as specified by the ordering physician.

## STORAGE AND TRANSPORTATION

Cryoprecipitate must be stored frozen at -18°C or colder in a temperature controlled, monitored freezer for a maximum of 12 months. Components must not be out of the temperature-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 component storage device<sup>3</sup>, the component should be returned immediately to prevent deterioration and waste (CSTM Standard 5.8.7.1). Once thawed, cryoprecipitate should be stored at 20–24°C, and transfused within 4 hours.

More information about cryoprecipitate can be found in the [Circular of Information for the Use of Human Blood Components, 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 and these may be used instead of cryoprecipitate for fibrinogen

replacement. See also [Chapter 17](#) of this *Guide* for information on treating hemostatic disorders including hemophilia and Von Willebrand disease. Cryoprecipitate does contain fibronectin, which is hypothesised to improve reticuloendothelial function in critically ill patients with sepsis as well as FXIII, which is critical for wound healing in critically ill or post-operative patients. There is, however, insufficient evidence to recommend its use in these contexts.

## ADDITIONAL RESOURCES

**Manufacturing blood components from whole blood.** Download [this poster](#) that includes an overview of how blood components are produced from whole blood using the buffy coat (B1) and whole blood (B2) methods.

## 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**.

Medical laboratory technologists who participate in the Canadian Society for Medical Laboratory Science's [Professional Enhancement Program](#) (PEP) can claim the reading of the [Clinical Guide to Transfusion](#) as a non-verified activity.

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If you have questions about the *Clinical Guide to Transfusion* or suggestions for improvement, please contact us through the [Feedback form](#).

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