



Plasma Components, Leukocytes Reduced (LR)

This component information addresses:

- CP2D Fresh Frozen Plasma LR
- CP2D Frozen Plasma LR
- CP2D Cryosupernatant Plasma LR
- Cryoprecipitate LR

Composition and properties

CP2D Fresh Frozen Plasma (FFP) LR is prepared from CP2D anticoagulated whole blood collected in approximately 63mL of CP2D, centrifuged and then separated from the red blood cells and leukoreduced by filtration. The plasma is frozen within 8 hours of collection. **FFP** contains both labile clotting factors V and VIII, plus all non-labile coagulation factors.

CP2D Frozen Plasma (FP) LR is prepared from CP2D anticoagulated whole blood collected in approximately 63mL of CP2D, centrifuged and then separated from the red blood cells and leukoreduced by filtration. The plasma is frozen within 24 hours of collection. **FP** contains all coagulation factors at levels similar to the levels in **FFP** with the exception of the labile factors, V and VIII, which may be slightly reduced in **FP**.

CP2D Cryosupernatant Plasma LR is prepared from slowly thawed **CP2D FFP** that has been centrifuged to separate the plasma from the insoluble cryoprecipitate. The insoluble cryoprecipitate is removed and the remaining plasma is refrozen.

Cryoprecipitate LR is prepared from slowly thawed **CP2D FFP** that has been centrifuged to separate the insoluble cryoprecipitate from the plasma. The insoluble cryoprecipitate is refrozen.

Notes:

CP2D (citrate phosphate dextrose) anticoagulant contains sodium citrate 26.3g/L, citric acid 3.27g/L, monobasic sodium phosphate 2.22g/L and dextrose 51.1g/L.

For approximate procoagulant and anticoagulant factor concentrations in some of these products, see www.transfusionmedicine.ca.

Plasma Component	Volume (mL) Mean ± 2sd	Factor VIII (IU/mL) Mean ± 2sd	Fibrinogen (mg/unit) Mean ± 2sd
CP2D FFP	202 ± 85 n = 396	1.35 ± 0.76 n = 396	N/A
CP2D FP	246 ± 58 n = 213	1.20 ± 0.79 n = 213	N/A
CP2D Cryosupernatant Plasma	266 ± 38 n = 450	N/A	N/A
Cryoprecipitate	10 ± 4 n = 201	N/A	431 ± 280 n = 201

Quality criteria that must be met:

CP2D FFP: Volume: > 100 mL in all units tested; Factor VIII: ≥ 0.70 IU/mL in ≥ 75% of units tested.

CP2D FP: Volume: ± 10% labelled volume and ≥ 100mL in all units tested; Factor VIII: ≥ 0.52 IU/mL in ≥ 75% of units tested.

CP2D Cryosupernatant Plasma: Volume: ± 10% labelled volume and ≥ 100mL in all units tested.

Cryoprecipitate: Volume: 5-15 mL in all units tested; Fibrinogen: ≥ 150 mg/unit in 75% of units tested.

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

Prior to making blood components available for transfusion, a sample of each donor's blood must test negative for:

- antibodies to human immunodeficiency virus (HIV-1 and HIV-2), hepatitis C virus (HCV), human T-cell lymphotropic virus, type I and II (HTLV-I/II), hepatitis B core antigen (HBcore)
- hepatitis B surface antigen (HBsAg)
- presence of viral RNA [HIV-1, HCV and West Nile Virus (WNV)]
- syphilis

In some cases, a donor sample is also tested for cytomegalovirus (CMV) antibody and/or the presence of IgA; if negative this is indicated on the label.

In some emergency situations, with the approval of both Canadian Blood Services and attending physician, partially tested or untested blood may be released for transfusion.

Packaging

FFP, FP, Cryosupernatant Plasma and **Cryoprecipitate** are stored in non-di-ethyl hexyl phthalate (DEHP) plasticized bags.

Storage and handling

Plasma components are stored at -18°C or colder for a maximum storage period of 12 months. Once thawed, transfuse immediately or store as described. Plasma components should not be refrozen.

Visual inspection should occur.

Thaw component in a watertight protective plastic overwrap using gentle agitation in a waterbath at 30 - 37°C or thaw in a microwave specifically manufactured for this use. Thawing may take 20 - 30 minutes for **FFP, FP** and **Cryosupernatant Plasma** and up to 10 minutes for **Cryoprecipitate**.

- **FFP, FP, and Cryosupernatant Plasma:** store at 1 - 6°C for a maximum storage period of 24 hours.
- **Cryoprecipitate:** store at 20 - 24°C for a maximum storage period of 4 hours. For pooling, mix 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).

Action

Transfused **FFP** and **FP** act as plasma protein supplements and plasma volume expanders. Both plasma components contain all clotting factors. **FP** levels of Factor V and Factor VIII may be reduced compared to levels in **FFP**.

Transfused **Cryosupernatant Plasma** provides a source of plasma with reduced levels of von Willebrand Factor including high molecular weight multimers.¹

Transfused **Cryoprecipitate** provides a source of fibrinogen, coagulation factors VIII, XIII, and von Willebrand Factor (AHF-vWF). Fibronectin is also present.

Indications

Alternatives to plasma components should be considered prior to the transfusion.

FFP and **FP** may be useful in the management of:

- bleeding patients or patients undergoing invasive procedures who require replacement of multiple plasma coagulation factors,
- patients with massive transfusion with clinically significant coagulation abnormalities,
- patients on warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect,
- patients with selected coagulation factor or with rare specific plasma protein deficiencies for which a more appropriate alternative therapy is not available,
- preparation of reconstituted whole blood for exchange transfusion in neonates,
- plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS).

Cryosupernatant Plasma may be useful in the management of:

- plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS),
- patients on warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect.²

Cryoprecipitate may be useful in the management of patients requiring fibrinogen or Factor XIII supplementation.

Contraindications

Recipients with known anti-IgA should receive IgA deficient plasma. Patients with known anaphylaxis to plasma components should only receive plasma components under appropriate medical supervision.

Plasma components should not be used to treat hypovolemia without coagulation factor deficiencies.

Cryoprecipitate is not recommended as replacement therapy for patients with Hemophilia A or von Willebrand disease (vWD).

Warnings and Precautions

FFP, **FP** and **Cryosupernatant Plasma** must be ABO-compatible; for **Cryoprecipitate**, ABO compatibility is preferred. Rh need not be considered.

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

Do not use the component if there is evidence of container breakage or of thawing during storage.

Do not use **FFP** or **FP** when coagulopathy can be more appropriately corrected with specific therapy, such as vitamin K or specific factor replacement.

Hemophilia A and B and vWD are more appropriately treated with recombinant or virally inactivated fractionation products or 1-deamino-8-D-arginine vasopressin (DDAVP) as initial treatment. For replacement

of fibrinogen and Factor XIII, commercial virally inactivated concentrates are also available. Some products are only available through the Special Access Programme of Health Canada.

Do not use **Cryosupernatant Plasma** for conditions which require von Willebrand Factor supplementation.

Do not use **Cryoprecipitate** to make fibrin glue. Virally inactivated products should be used for this purpose.

Careful donor selection and available laboratory tests do not eliminate the hazard of transmitting infectious disease agents for which testing is performed (see Table 2)³ or for pathogens that are either not recognized or for which there is no donor screening test.

Virus	Residual risk	
	Per million donations (95% CI)	Per number of donations
HIV	0.13 (0.05-0.28)	1 in 7.8 million
HCV	0.43 (0.27-0.66)	1 in 2.3 million
HBV	6.55 (3.90-10.29)	1 in 153,000
HTLV*	0.23 (0.04-0.83)	1 in 4.3 million†

*95 percent CI is not available for HTLV window period, the listed numbers in brackets are the range.

†This estimate represents potentially infectious units released into inventory. The risk to recipients would be much lower due to universal leukoreduction.

For some patients at particularly high risk of severe CMV disease (e.g., fetus requiring an intrauterine transfusion [IUT], or CMV-seronegative recipients of allogeneic, hematopoietic stem cell transplants from CMV-seronegative donors), clinicians may choose, in addition to the use of LR components, to transfuse components from CMV-seronegative donors.

Some collection needles are in contact with latex. Canadian Blood Services cannot guarantee that this product is latex free.

Adverse events

Potential adverse events related to a blood transfusion range in severity from minor with no sequelae to life-threatening. All adverse events occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted. All adverse events suspected to be related to a transfusion (whether during or after a transfusion) should be reported to your local transfusion service and when required (i.e. when the adverse event could be attributed to the quality of a blood component), to Canadian Blood Services and the hospital/regional hemovigilance network. Canadian Standards Association requires reporting of adverse events associated with blood component quality (e.g.: bacterial contamination) to Canadian Blood Services.^{5,6} For further information, refer to the Canadian Standards Association, *Blood and Blood Components*, Section 17.2.2. and Transfusion Transmitted Injuries Surveillance System.^{5,7}

TABLE 3: The following adverse events have been described with transfusion of plasma components:^{6,8,9,10,11}

Event	Approximate Frequency	Symptoms and Signs	Notes
Mild allergy	1 in 100	Urticaria, pruritis and/or erythema.	Transfusion can be restarted after assessment and necessary intervention.
Transfusion associated circulatory overload (TACO)	1 in 700	Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.	Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI.
Transfusion related acute lung injury (TRALI)	1 in 1,200-5,000	New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.	Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.
Isolated hypotensive reaction	Unknown	Hypotension, occasionally accompanied by urticaria, dyspnea and nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Immediate hemolytic transfusion reactions (HTR)	Rare	Shock, chills, fever, dyspnea, chest pain, back pain, headache and/or abnormal bleeding.	May be associated with ABO plasma incompatibility.
Anaphylaxis	Rare	Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea and vomiting.	Resuscitation according to institutional guidelines. IgA deficient patients who have formed anti-IgA antibodies may experience anaphylactic reactions. However, in most cases of anaphylactic reactions, no specific antibodies are found in the patient.
Transfusion-related alloimmune thrombocytopenia	Rare	Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.	Passive transfer of platelet antibodies leading to thrombocytopenia.
Bacterial contamination	Very rare	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and/or disseminated intravascular coagulation.	For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to references #6.
Infectious disease	See Table 2, Residual risk of tested viruses	Variable according to infectious disease.	Blood products have been described to transmit viruses other than HIV, HBV, HCV, HTLV I/II and WNV as well as parasites and prions.
Complications of massive transfusion	Dependent on clinical situation	Complications may include hypothermia, citrate toxicity, acidosis.	Appropriate monitoring may abrogate some complications.

Reporting of suspected cases of transfusion-related infections such as HIV, HCV, HTLV, HBV, WNV and other transfusion-related infections is described in the Clinical Guide to Transfusion, section 1: Vein to Vein: A Summary of Blood Collection and Transfusion in Canada.

Dose and administration

The volume of **FFP**, **FP** and **Cryosupernatant Plasma** transfused depends on the clinical situation and patient size. Common pediatric dosing is 10-15mL per kg body weight.

The volume needed to raise fibrinogen concentration 0.5 - 1.0g/L can be estimated as one unit of **Cryoprecipitate** per 5 – 10kg body weight.

Serial laboratory assays of coagulation function may be of assistance in planning dose. A standard blood administration set containing a 170 – 260 micron filter or a filter of equivalent efficacy, approved by Health Canada, must be used for infusion.

No medications or solutions, with the exception of 0.9% Sodium Chloride, may be added to or infused through the same tubing with the plasma components. In particular, the addition of commonly used solutions such as D5W (5% dextrose in water) or additives such as calcium (e.g. in Lactated Ringers), should never be added to, or administered concurrently through the same vascular access as blood or blood components. Co-administration of platelets, red cells or 5% albumin can be performed at the discretion of the treating physician.

Transfusion rate is dependent on clinical factors. For more information, refer to the Clinical Guide to Transfusion. All transfusions should be complete within 4 hours of removal from storage. Patients should be under observation during transfusion with close observation during the first 15 minutes and in accordance with institutional guidelines.

Modification and additional information

TABLE 4: Modified Components

Modification	Description	Indication	Storage	Benefits	Adverse events
Divided	One unit of plasma divided into two smaller units.	Neonates and infants.	Once thawed, 1 - 6°C: transfuse within 24 hours.	Reduced donor exposure if both units transfused to the same patient.	As per Table 3.

Autologous Donations

Autologous donor samples are typically tested as described above. Syphilis and anti-HBcore are not mandatory tests for autologous donations⁵. Autologous units found to be repeat reactive, but negative/indeterminate on confirmatory/supplemental testing for any of the transmissible disease markers will be labelled as “Biohazard” and providing all other requirements have been met, may be released with the approval of both the Canadian Blood Services and attending physician. In addition, syphilis confirmatory positive units may also be released with “Biohazard” labelling.

Directed Donations

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

References

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The Circular as a whole or in part cannot be considered or interpreted as an expressed or implied warranty of the safety or fitness of the described blood or blood components when used for its intended purpose. Attention to the specific indications for blood components is needed to prevent inappropriate transfusion.



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it's in you to give

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ISBN 978-1-926581-12-5
1000104993 01/09

This *Circular* is an extension of the product label and conforms to the applicable Regulations issued by the Health Products and Food Branch, Health Canada.¹²