

Plasma Components

This component information addresses:

- Fresh Frozen Plasma, Apheresis
- CPD Frozen Plasma
- CPD Cryosupernatant Plasma
- CPD Cryoprecipitate

Composition and properties

Fresh Frozen Plasma, Apheresis (FFPA) is collected by apheresis in approximately 70 – 90 mL of either trisodium citrate or ACD-A anticoagulant and is frozen within 8 hours of collection. The product label clearly indicates the anticoagulant used. **FFPA** contains both labile clotting factors V and VIII, plus all non-labile coagulation factors.

CPD Frozen Plasma (FP) is prepared from whole blood collected in approximately 70mL of CPD anticoagulant, centrifuged and then separated from the red blood cells and buffy coat. The plasma is frozen within 24 hours of collection. **FP** is not labelled as leukoreduced as some units may contain $\geq 5 \times 10^6$ leukocytes/unit. **FP** contains all coagulation factors at levels similar to the levels in **FFPA** with the exception of the labile factors, V and VIII, which may be slightly reduced in **FP**.

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

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

Notes:

CPD (citrate phosphate dextrose) anticoagulant contains citrate acid 3.27g/L, sodium citric 26.3g/L, sodium acid phosphate 2.51g/L, dextrose 25.5g/L.
ACD-A (adenine, citrate dextrose – formula A) anticoagulant contains sodium citrate 22.0g/L, citric acid 7.3g/L, dextrose 24.5g/L.
Tri-sodium citrate anticoagulant contains sodium citrate 40g/L and citric acid to adjust pH.

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

TABLE 1: Typical unit content is based on the number of units (n) tested from October 2007 to March 2008, inclusive.			
Plasma Component	Volume (mL) Mean \pm 2sd	Factor VIII (IU/mL) Mean \pm 2sd	Fibrinogen (mg/unit) Mean \pm 2sd
FFPA	ACD-A: 216 \pm 50 n = 628	1.24 \pm 0.72 n = 585	N/A
	Trisodium citrate: 498 \pm 49 n = 23,541		
CPD FP	289 \pm 33 n = 310	1.00 \pm 0.60 n = 253	N/A
CPD Cryosupernatant Plasma	284 \pm 49 n = 132	N/A	N/A
CPD Cryoprecipitate	11 \pm 4 n = 100	N/A	426 \pm 295 n = 100

Quality criteria that must be met:

FFPA: Factor VIII: ≥ 0.70 IU/mL in $\geq 75\%$ of units tested; **FFPA (ACD-A):** Volume: $\pm 10\%$ labelled volume in all units tested.

CPD FP: Volume: $\pm 10\%$ labelled volume and ≥ 100 mL in all units tested; Factor VIII: ≥ 0.52 IU/mL in $\geq 75\%$ of units tested.

CPD Cryosupernatant Plasma: Volume: $\pm 10\%$ labelled volume and ≥ 100 mL in all units tested.

CPD Cryoprecipitate: Volume: 5-15 mL in all units tested; Fibrinogen: ≥ 150 mg/unit in $\geq 75\%$ 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 the Canadian Blood Services and attending physician, partially tested or untested blood may be released for transfusion.

Packaging

FFPA, FP, CPD Cryosupernatant Plasma and CPD Cryoprecipitate may be stored in di-ethyl hexyl phthalate (DEHP) or non-DEHP plasticized bags depending on the manufacturer.¹

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 $30 - 37^{\circ}\text{C}$ or thaw in a microwave specifically manufactured for this use. Thawing may take 20 – 30 minutes for **FFPA, FP** and **CPD Cryosupernatant Plasma** and up to 10 minutes for **CPD Cryoprecipitate**.

- **FFPA, FP, and CPD Cryosupernatant Plasma:** store at $1 - 6^{\circ}\text{C}$ for a maximum storage period of 24 hours.
- **CPD Cryoprecipitate:** store at $20 - 24^{\circ}\text{C}$ 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). **CPD Cryoprecipitate** must be used within 4 hours after pooling or breaching the bag.

Action

Transfused **FFPA** 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 **FFPA**.

Transfused **CPD Cryosupernatant Plasma** provides a source of plasma with reduced levels of von Willebrand Factor including high molecular weight multimers.²

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

Indications

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

FFPA 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 haemolytic uremic syndrome (HUS).

CPD Cryosupernatant Plasma may be useful in the management of:

- plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP) or haemolytic uremic syndrome (HUS),
- patients on warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect.³

CPD 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.

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

Warnings and Precautions

FFPA, **FP** and **Cryosupernatant Plasma** must be ABO-compatible; for **CPD 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 **FFPA** 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 **CPD Cryosupernatant Plasma** for conditions which require von Willebrand Factor supplementation.

Do not use **CPD 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)⁴ or for pathogens that are either not recognized or for which there is no donor screening test.

TABLE 2: Estimated residual risk of transfusion-transmitted viral infections in Canada with incidence rates from observed donor seroconversions, 2001 to 2005.⁵

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 component 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.^{6,7} For further information, refer to the Canadian Standards Association, *Blood and Blood Components*, Section 17.2.2. and Transfusion Transmitted Injuries Surveillance System.^{6,8}

TABLE 3: The following adverse events have been described with transfusion of plasma components:^{7,9,10,11,12}

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 reference #7.
Infectious disease	See Table 2, Residual risk of tested viruses	Variable according to infectious disease.	Blood components 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 **FFPA**, **FP** and **CPD 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 **CPD 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 donations⁶. 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 are 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.

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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 their intended purpose. Attention to the specific indications for blood components is needed to prevent inappropriate transfusion.



Canadian Blood Services
it's in you to give

Canadian Blood Services
1800 Alta Vista Drive
Ottawa, Ontario, Canada
K1G 4J5

ISBN 978-1-926581-02-6
1000104990 01/09

This *Circular* is an extension of the component label and conforms to the applicable Regulations issued by the Health Products and Food Branch, Health Canada.¹³