CIRCULAR OF INFORMATION

FOR THE USE OF HUMAN BLOOD AND BLOOD COMPONENTS

This Circular was prepared jointly by AABB, the American Red Cross, America's Blood Centers, and the Armed Services Blood Program. The Food and Drug Administration recognizes this *Circular of Information* as an acceptable extension of container labels.

AABB
Advancing Transfusion and Cellular Therapies Worldwide

America's Blood Centers
It's About Life.

American Red Cross

ASBP
Armed Services Blood Program

Federal Law prohibits dispensing the blood and blood components described in this circular without a prescription.

DO NOT COPY

Table of Contents

DO NOT COPY

Tables

DO NOT COPY

Notice to All Users

The *Circular of Information for the Use of Human Blood and Blood Components* (hereafter referred to as *Circular*) is an extension of container labels, as the space on those labels is limited.

Blood and blood components are biological products and living human tissue intended for use in patient treatment. Professional judgment based on clinical evaluation determines the selection of components, dosage, rate of administration, and decisions in situations not covered in this general statement.

This *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.

Because of the risks associated with transfusion, physicians should be familiar with alternatives to allogeneic transfusion. Blood banks and transfusion services are referred to the AABB *Standards for Blood Banks and Transfusion Services* for additional information and policies, especially in the areas of recipient sample identification, compatibility testing, issue and transfusion of blood and blood components, investigation of transfusion reactions, and proper record-keeping practices. Transfusionists are referred to the AABB *Technical Manual* for applicable chapters on adult and pediatric transfusion.

The specific product manufacturer's package insert should be reviewed for instructions pertaining to use of transfusion devices (eg, filters, blood administration sets, and blood warmers).

This *Circular* is supplied to conform with applicable federal statutes and regulations of the Food and Drug Administration (FDA), United States (US) Department of Health and Human Services. The blood components in this *Circular* marked with the symbol "Ω" are blood components for which the FDA currently has not received data to demonstrate that they meet prescribed requirements of safety, purity, and potency, and therefore are not licensed for distribution in interstate commerce.

General Information for Whole Blood and All Blood Components

Donors

Blood and blood components described in this *Circular* have been collected from volunteer blood donors for use in other

DO NOT COPY

patients (allogeneic transfusions) or from patients donating for themselves (autologous transfusions). The blood donors have satisfactorily completed a health assessment that includes a questionnaire on past and present illnesses, and have satisfied minimum physiologic criteria. The allogeneic donors have been questioned about risk factors for transmissible infectious agents and have been given instructions to call the blood center after donation if they develop illness or have concerns that their blood may not be safe to give to another person.

Testing of Donor Blood

Testing of a sample of donor blood is performed before units of blood or blood components are distributed for routine transfusion. The donor's ABO group and Rh type have been determined, including testing for the presence of weak D antigen.

A sample from each donation intended for allogeneic use has been tested by FDA-licensed tests and found to be nonreactive for antibodies to human immunodeficiency virus (anti-HIV-1/2), hepatitis C virus (anti-HCV), human T-cell lymphotropic virus (anti-HTLV-I/II), and hepatitis B core antigen (anti-HBc), and nonreactive for hepatitis B surface antigen (HBsAg). Licensed nucleic acid tests (NAT) for hepatitis B virus (HBV) deoxyribonucleic acid (DNA), HCV ribonucleic acid (RNA), HIV-1 RNA, and West Nile virus (WNV) RNA have been performed and found to be nonreactive. A serologic test for syphilis has been performed and found to be nonreactive. All blood has been collected from donors who have tested negative by a licensed test for antibodies to *Trypanosoma cruzi* either on the current donation or at least one previous donation. A blood collector may perform additional testing for pathogens; such additional testing may be performed under an approved investigational new drug (IND) application, and described in the *Circular* by the blood collector performing the test using language required by the IND sponsor.

For units labeled "FOR AUTOLOGOUS USE ONLY," infectious disease testing requirements vary, depending on whether the unit will be drawn in one facility and infused in another facility and whether the unit might be made available for allogeneic transfusion. Infectious disease testing may be omitted for autologous units drawn, stored, and infused at the same facility. Autologous units for which testing has not been performed are labeled "DONOR UNTESTED." Autologous units with reactive test results may be used for transfusion to the donor-patient with appropriate physician authorization. A biohazard label will be applied to autologous units that are tested for evidence of infection as listed above and determined to be reactive. If the units labeled "FOR AUTOLOGOUS USE ONLY" are infused at a different facility, at a minimum the first donation from the donor-patient in each 30-day period is tested

DO NOT COPY

for evidence of infection as listed above. Subsequent units that are not tested will be labeled as "DONOR TESTED WITHIN THE LAST 30 DAYS." Autologous units may be used for allogeneic transfusion only if the autologous donors meet all the allogeneic donor selection and testing requirements for each donation.

Tests for unexpected antibodies against red cell antigens have been performed on samples from all donors. The results of these tests are negative or have been determined to be clinically insignificant unless otherwise indicated on the label. Other tests may have been performed on donor blood as indicated by information that has been provided by the blood bank or transfusion service on an additional label or tie tag, or in a supplement to this *Circular*.

Blood and Component Labeling

All blood components identified in this *Circular* have the ISBT 128 product name listed first and other recognized component names in parentheses.

Blood and blood component labels will contain the following information:

1. The proper name, whole blood or blood component, including an indication of any qualification or modification.
2. The method by which the blood component was prepared, either by whole blood or apheresis collection.
3. The temperature range in which the blood component is to be stored.
4. The preservatives and anticoagulant used in the preparation of the blood or blood components, when appropriate.
5. The standard contents or volume is assumed unless otherwise indicated on the label or in *Circular* supplements.
6. The number of units in pooled blood components.
7. The name, address, registration number, and US license number (if applicable) of the collection and processing location.
8. The expiration date (and time, if applicable), which varies with the method of preparation (open or closed system) and the preservatives and anticoagulant used. When the expiration time is not indicated, the product expires at midnight.
9. The donation (unit or pool) identification number.
10. The donor category (paid or volunteer, and autologous, if applicable).
11. ABO group and Rh type, if applicable.
12. Special handling information, as required.
13. Statements regarding recipient identification, this *Circular*, infectious disease risk, and prescription requirement.
14. Any sedimenting agent used during cytapheresis, if applicable.

DO NOT COPY

Instructions for Use

The following general instructions pertain to Whole Blood and all the blood components described in this *Circular:*

1. All blood and blood components must be maintained in a controlled environment and stored under appropriate conditions as described in the AABB *Standards for Blood Banks and Transfusion Services*.
2. The intended recipient and the blood container must be properly identified before the transfusion is started.
3. Aseptic technique must be employed during preparation and administration. If the container is entered in a manner that violates the integrity of the system, the component expires 4 hours after entry if maintained at room temperature (20-24 C), or 24 hours after entry if refrigerated (1-6 C).
4. All blood components must be transfused through a filter designed to remove clots and aggregates (generally a standard 150- to 260-micron filter).
5. Blood and blood components should be mixed thoroughly before use.
6. Blood and blood components must be inspected immediately before use. If, upon visual inspection, the container is not intact or the appearance is abnormal (presence of excessive hemolysis, a significant color change in the blood bag as compared with the tubing segments, floccular material, cloudy appearance, or other problems), the blood or blood component must not be used for transfusion and appropriate follow-up with the transfusion service must be performed.
7. No medications or solutions may be added to or infused through the same tubing simultaneously with blood or blood components, with the exception of 0.9% Sodium Chloride, Injection (USP), unless: 1) they have been approved for this use by the FDA, or 2) there is documentation available to show that the addition is safe and does not adversely affect the blood or blood component.
8. Lactated Ringer's Injection (USP) or other solutions containing calcium should never be added to or infused through the same tubing with blood or blood components containing citrate.
9. Blood components should be warmed if clinically indicated for situations such as exchange or massive transfusions, or for patients with cold-reactive antibodies. Warming must be accomplished using an FDA-cleared warming device so as not to cause hemolysis.
10. Some life-threatening reactions occur after the infusion of only a small volume of blood or blood components. Therefore, unless otherwise indicated by the patient's clinical condition, the rate of infusion should initially be slow.

DO NOT COPY

11. Periodic observation and recording of vital signs should occur before, during, and after the transfusion to identify suspected adverse reactions. If a transfusion reaction occurs, the transfusion must be discontinued immediately and appropriate therapy initiated. The infusion should not be restarted unless approved by transfusion service protocol.
12. Specific instructions concerning possible adverse reactions shall be provided to the patient or a responsible caregiver when direct medical observation or monitoring of the patient will not be available after transfusion.
13. Transfusion should be started before component expiration and completed within 4 hours.
14. All adverse events related to transfusion, including possible bacterial contamination of blood or a blood component or suspected disease transmission, must be reported to the transfusion service according to its local protocol.

Side Effects and Hazards for Whole Blood and All Blood Components

Transfusion-related adverse events may voluntarily be reported to the National Healthcare Safety Network (NHSN) hemovigilance program (http://www.cdc.gov/nhsn/acute-care-hospital/bio-hemo/). This program is intended to improve the safety and quality of blood transfusions through the collection and analysis of data on adverse events and medical errors. The NHSN Biovigilance Component Hemovigilance Module Surveillance Protocol (https://www.cdc.gov/nhsn/pdfs/biovigilance/bv-hv-protocol-current.pdf) provides case classification criteria for CDC-defined transfusion-associated adverse reactions.

Immunologic Complications, Immediate

1. *Hemolytic transfusion reaction*, the immune destruction of red cells, is typically the result of the exposure of transfused red cells to incompatible recipient plasma. The transfusion of blood components containing plasma which is incompatible with the recipient's red cells rarely results in clinically relevant hemolysis. Further details are discussed in the section on components containing red cells and in the platelet section.
2. *Immune-mediated platelet destruction*, one of the causes of refractoriness to platelet transfusion, is the result of alloantibodies in the recipient to HLA or platelet-specific antigens on transfused platelets. This is described in more detail in the section on platelets.

DO NOT COPY

3. *Febrile nonhemolytic reaction* is typically manifested by a temperature elevation of ≥1 C or 2 F occurring during or within 4 hours after a transfusion and in the absence of any other pyrexic stimulus or active warming. This may reflect the action of antibodies against white cells or the action of cytokines either present in the transfused component or generated by the recipient in response to transfused elements. Febrile reactions may occur in less than 1% of transfusions of leukocyte-reduced red cell components and about 5% of leukocyte-reduced apheresis platelet components. Febrile reactions occur more frequently in patients receiving non-leukocyte-reduced components and those previously alloimmunized by transfusion or pregnancy. No routinely available pre- or posttransfusion tests are helpful in predicting or preventing these reactions. Antipyretics usually provide effective symptomatic relief. Patients who experience repeated, severe febrile reactions may benefit from receiving leukocyte-reduced components. If these reactions are caused by cytokines in the component, prestorage leukocyte reduction may be beneficial.
4. *Allergic reactions* frequently occur (ie, with 1-3% of plasma-containing components) as mild or self-limiting urticaria or wheezing that usually responds to antihistamines. More severe manifestations, including respiratory and cardiovascular symptoms, are more consistent with anaphylactoid/anaphylactic reactions and may require more aggressive therapy (see below). No laboratory procedures are available to predict these reactions.
5. *Anaphylactoid/anaphylactic reactions*, characterized by hypotension, tachycardia, nausea, vomiting and/or diarrhea, abdominal pain, severe dyspnea, pulmonary and/or laryngeal edema, and bronchospasm and/or laryngospasm, are rare (<10/100,000 transfused units) but dangerous complications requiring immediate treatment with epinephrine and supportive care. While these reactions have been reported in IgA-deficient patients with anti-IgA antibodies and patients with haptoglobin deficiency, most reactions are idiosyncratic and not associated with a specific serum protein deficiency, polymorphism, or identifiable cause. In certain circumstances, patients may benefit from the use of washed cellular components to prevent or reduce the severity of allergic reactions not minimized by treatment with medication alone.
6. *Transfusion-related acute lung injury* (TRALI) is characterized by the acute onset of hypoxemia and noncardiogenic pulmonary edema within 6 hours of a blood or blood component transfusion in the absence of other causes of acute lung injury or circulatory overload. Various stimuli in blood components, most commonly white blood cell

DO NOT COPY

(WBC) antibodies from donors sensitized during pregnancy or prior transfusion or transplantation, or proinflammatory molecules that accumulate in stored blood components, may cause TRALI. These mechanisms may not be mutually exclusive and may act synergistically with underlying patient factors to lead to a final common pathway of acute lung injury. These stimuli may trigger an inflammatory response, granulocyte activation and degranulation, and injury to the alveolar capillary membrane and the development of permeability pulmonary edema. Although most TRALI cases are associated with donor antileukocyte antibodies, rare cases have implicated recipient antileukocyte antibodies that reacted with donor leukocytes. Widespread leukoreduction of blood components has likely mitigated this latter risk. Laboratory testing of blood donors for antileukocyte antibodies or blood components for biological mediators does not alter management of this reaction, which is diagnosed on clinical and radiographic findings. Treatment of TRALI involves aggressive respiratory support, and often mechanical ventilation. The preferential use of plasma collected from male donors has been associated with a significant reduction in the number of reported TRALI cases and associated fatalities. Transfusion services should immediately report suspected TRALI to the blood collection facility to facilitate the retrieval of other components associated with the involved donation(s) or prior donations.

Immunologic Complications, Delayed

1. *Delayed hemolytic reaction* is described in detail in the section on components containing red cells.
2. *Alloimmunization* to antigens of red cells, white cells, platelets, or plasma proteins may occur unpredictably after transfusion. Blood components may contain certain immunizing substances other than those indicated on the label. For example, platelet components may also contain red cells and white cells. Primary immunization does not become apparent until days or weeks after the immunizing event, and does not usually cause symptoms or physiologic changes. If components that express the relevant antigen are subsequently transfused, there may be accelerated removal of cellular elements from the circulation and/or systemic symptoms. Clinically significant antibodies to red cell antigens will ordinarily be detected by pretransfusion testing. Alloimmunization to antigens of white cells, platelets, or plasma proteins can be detected only by specialized testing.
3. *Posttransfusion purpura* (PTP) is a rare syndrome characterized by the development of dramatic, sudden, and self-

DO NOT COPY

limited thrombocytopenia, typically 7 to 10 days after a blood transfusion, in a patient with a history of sensitization by either pregnancy or transfusion. Although the immune specificity may be to a platelet-specific antigen the patient lacks, both autologous and allogeneic platelets are destroyed. High-dose Immune Globulin, Intravenous (IVIG) may correct the thrombocytopenia.

4. *Transfusion-associated graft-vs-host disease* (TA-GVHD) is rare but has a fatality rate of nearly 100% due to overwhelming infection in the setting of pancytopenia. This condition occurs when viable T lymphocytes in the transfused component engraft in the recipient and react against recipient tissue antigens. TA-GVHD can occur if the host does not recognize and reject the foreign transfused cells, and it can follow transfusion of any component that contains even very small numbers of viable T lymphocytes. Immunologically normal recipients who are heterozygous for a tissue antigen haplotype for which the donor is homozygous are at risk. Recipients with severe cellular immunodeficiency (except for HIV infection) are also at greatest risk (eg, fetuses receiving intrauterine transfusions, at-risk neonates, recipients of hematopoietic progenitor cell transplants, and selected patients with severe immunodeficiency conditions). Patients with oncologic and rheumatologic diseases receiving purine analogues (eg, fludarabine, cladribine) or certain other biological immunmodulators (eg, alemtuzumab, antithymocyte globulin) may be at risk for TA-GVHD, depending on clinical factors and the source of the biological agent. TA-GVHD remains a risk with leukocyte-reduced components because they contain sufficient residual T lymphocytes. Irradiation of the component renders T lymphocytes incapable of proliferation. Pathogen inactivation may also be used to prevent TA-GVHD if the pathogen inactivation technology has been shown to inactivate residual lymphocytes.

Nonimmunologic Complications

1. *Because Whole Blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents [eg, viruses, bacteria, parasites, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the CJD agent].* Careful donor selection, available laboratory tests, and pathogen inactivation (when it is utilized) do not totally eliminate these hazards. Also, septic and toxic reactions can result from transfusion of bacterially contaminated blood and blood components. Such complications are infrequent but may be life-threatening. Infectious disease transmission may occur despite careful selection of donors and testing of blood. Donor selection

DO NOT COPY

criteria are designed to screen out potential donors with increased risk of infection with HIV, HTLV, hepatitis, and syphilis, as well as other agents (see section on Testing of Donor Blood). These procedures do not totally eliminate the risk of transmitting these agents. Transfusion services should immediately report infections that may be related to the blood donor or to the manufacture of the blood components to the collection facility.

2. *Cytomegalovirus* (CMV) may be present in white-cell-containing components from donors previously infected with this virus, which can persist for a lifetime despite the presence of serum antibodies. Up to 70% of donors may be CMV seropositive. Transmission of CMV by transfusion may be of concern in low-birthweight (≤1200 g) premature infants born to CMV-seronegative mothers and in intrauterine transfusions and/or certain other categories of immunocompromised individuals such as hematopoietic progenitor cell or solid organ transplant patients, if they are CMV seronegative. For at-risk recipients, the risk of CMV transmission by cellular components can be reduced by transfusing CMV-seronegative or leukocyte-reduced components, or pathogen-reduced components when applicable.

   For *other infectious agents* (eg, *Babesia* spp, *Leishmania* spp and *Plasmodia* spp) there are no licensed tests available to predict or prevent disease transmission; however, some of these may be mitigated by pathogen reduction technology if it is utilized. All potential blood donors are subjected to screening procedures intended to reduce to a minimum the risk that they will transmit infectious agents.

3. *Bacterial sepsis* occurs rarely but can cause acute, severe, sometimes life-threatening effects. Onset of high fever (≥2 C or ≥3.5 F increase in temperature), severe chills, hypotension, or circulatory collapse during or shortly after transfusion should suggest the possibility of bacterial contamination and/or endotoxin reaction in the transfused products. Although platelet components stored at room temperature have been implicated most frequently, previously frozen components thawed by immersion in a waterbath and red cell components stored for several weeks at 1 to 6 C have also been implicated. Although most platelet components are controlled for bacterial contamination, this does not completely eliminate the risk.

   Both gram-positive and gram-negative organisms have been identified as causing septic reactions. Organisms capable of multiplying at low temperatures (eg, *Yersinia enterocolitica*) and those using citrate as a nutrient are most often associated with components containing red cells. A variety of pathogens, as well as skin contaminants, have been found in platelet components. Endotoxemia in recipients has resulted from multiplication of gram-negative bacteria in blood components.

Prompt recognition of a possible septic reaction is essential, with immediate discontinuation of the transfusion and aggressive therapy with broad-spectrum antimicrobials and vasopressor agents, if necessary. In addition to prompt sampling of the patient's blood for cultures, investigation should include examination of material from the blood container by Gram stain, and cultures of specimens from the container and the administration set. It is important to report all febrile transfusion reactions to the transfusion service for appropriate investigation. If post-transfusion sepsis is suspected, the transfusion service should immediately report the reaction to the blood collection facility to facilitate retrieval of other potentially contaminated components associated with the collection.

4. *Transfusion-associated circulatory overload* (TACO) is a frequent complication of transfusion leading to cardiogenic (hydrostatic) pulmonary edema and can occur after transfusion of excessive volumes or at excessively rapid rates. This is a particular risk in individuals with underlying cardiopulmonary or renal disease, the very young and the elderly, and in patients with chronic severe anemia in whom low red cell mass is associated with high plasma volume. Small transfusion volumes can precipitate symptoms in at-risk patients who already have a positive fluid balance.

   Pulmonary edema should be promptly and aggressively treated, and infusion of colloid preparations, including plasma components and the supernatant fluid in cellular components, reduced to a minimum.
5. *Hypothermia* carries a risk of cardiac arrhythmia or cardiac arrest and exacerbation of coagulopathy. Rapid infusion of large volumes of cold blood or blood components can depress body temperature, and the danger is compounded in patients experiencing shock or surgical or anesthetic manipulations that disrupt temperature regulation. A blood warming device should be considered if rapid infusion of blood or blood components is needed. Warming must be accomplished using an FDA-cleared blood warming device so as not to cause hemolysis.
6. *Metabolic complications* may accompany large-volume transfusions, especially in neonates and patients with liver or kidney disease.
   a. Citrate "toxicity" reflects a depression of ionized calcium caused by the presence in the circulation of large quantities of citrate anticoagulant. Because citrate is

DO NOT COPY

promptly metabolized by the liver, this complication is rare. Patients with severe liver disease or those with circulatory collapse that prevents adequate hepatic blood flow may have physiologically significant hypocalcemia after rapid, large-volume transfusion. Citrated blood or blood components administered rapidly through central intravenous access may reach the heart so rapidly that ventricular arrhythmias occur. Standard measurement of serum calcium does not distinguish ionized from complexed calcium. Ionized calcium testing or electrocardiogram monitoring is more helpful in detecting physiologically significant alteration in calcium levels.

b. Other metabolic derangements can accompany rapid or large-volume transfusions, especially in patients with preexisting circulatory or metabolic problems. These include acidosis or alkalosis (deriving from changing concentrations of citric acid and its subsequent conversion to pyruvate and bicarbonate) and hyper- or hypokalemia.

Fatal Transfusion Reactions

When a fatality occurs as a result of a complication of blood or blood component transfusion, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research (CBER), should be notified as soon as possible (telephone: 240-402-9160; e-mail: fatalities2@fda.hhs.gov). Within 7 days after the fatality, a written report must be submitted to the FDA: Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, Attn: Fatality Program Manager, Document Control Center, 10903 New Hampshire Avenue, W071, G112, Silver Spring, MD 20993-0002. A copy of the report should be sent to the collecting facility, if appropriate. Updated information about CBER reporting requirements may be found at http://www.fda.gov/biologicsbloodvaccines/safetyavailability/reportaproblem/transfusiondonationfatalities/default.htm.

Red Blood Cell Components

Overview

Description

Red cells contain hemoglobin and serve as the primary agent for transport of oxygen to tissues. The primary red-cell-containing transfusion component is Red Blood Cells (RBCs). This component is prepared by centrifugation or sedimentation of Whole

DO NOT COPY

Blood to remove much of the plasma. RBC components can also be prepared by apheresis methods.

Depending upon the collection system used, a single whole blood donation typically contains either 450 mL (±10%) or 500 mL (±10%) of blood collected from allogeneic blood donors with a minimum hematocrit of 36% to 38% (females) or 39% (males), withdrawn in a sterile container that includes an anticoagulant solution licensed for this component. In the case of autologous adult blood donors, a hematocrit minimum as low as 33% is acceptable. Occasionally, units of other volumes are collected and those volumes are stated on the label.

Red-cell-containing components can be stored for an interval ("shelf life") determined by the properties of the anticoagulant-preservative solution (see Table 1). Whole Blood units are prepared in an aseptic manner in a ratio of 14 mL of anticoagulant-preservative solution per 100 mL of whole blood targeted for collection. Apheresis components are collected into anticoagulants as recommended by the manufacturer. Specific additive solutions (AS; eg, AS-7) may allow 24-hour storage at room temperature prior to processing.

After plasma is removed, the resulting component is Red Blood Cells, which has a hematocrit of 65% to 80% and a usual volume between 225 mL and 350 mL. AS may be mixed with the red cells remaining after removal of nearly all of the plasma (see Table 2). The typical hematocrit of AS RBCs is 55% to 65%, and the volume is approximately 300 to 400 mL. AS RBCs have a shelf life of 42 days. Descriptions of specific components containing red cells are given at the end of this section.

Actions

All RBC components and Whole Blood increase the recipient's oxygen-carrying capacity by increasing the mass of circulating red cells. Processing and/or storage deplete the component of virtually all potential therapeutic benefit attributable to the functions of white cells and platelets; cellular elements remain in these blood components and may cause adverse immunologic or physiologic consequences. Residual plasma in the component provides the recipient with volume expansion and nonlabile plasma proteins to the extent that residual plasma is present in the preparation. Depending on the method of production, RBCs may contain approximately 20 to 100 mL of residual plasma. RBCs prepared with additive solutions are the most commonly used red cell product and have limited residual plasma.

Indications

Red-cell-containing components are indicated for treatment of symptomatic or critical deficit of oxygen-carrying capacity. They are also indicated for red cell exchange transfusion.

DO NOT COPY

DO NOT COPY

Table 1. Contents of Anticoagulant-Preservative Solutions*

Anticoagulant-Preservative (g/L)	Trisodium Citrate	Citric Acid	Monobasic Sodium Phosphate	Dextrose	Adenine	Shelf Life
Anticoagulant citrate-dextrose A (ACD-A)[†]	22.0	8.0	0	24.5	0	21 days
Citrate-phosphate dextrose (CPD)	26.3	3.27	2.22	25.5	0	21 days
Citrate-phosphate-dextrose-dextrose (CP2D)	26.3	3.27	2.22	51.1	0	21 days
Citrate-phosphate-dextrose-adenine (CPDA-1)	26.3	3.27	2.22	31.9	0.275	35 days

*63 mL/450 mL collection, 70 mL/500 mL collection.

[†]ACD is used for apheresis components.

DO NOT COPY

Table 2. Contents of Red Blood Cells Additive Solutions*

Additive Solution (mg/100 mL)	Dextrose Mono-hydrate	Adenine	Monobasic Sodium Phosphate	Dibasic Sodium Phosphate	Mannitol	Sodium Bicarbonate	Sodium Chloride	Sodium Citrate	Citric Acid	Shelf Life
AS-1 (Adsol)	2200	27	0	0	750	0	900	0	0	42 days
AS-3 (Nutricel)	1100	30	276	0	0	0	410	588	42	42 days
AS-5 (Optisol)	900	30	0	0	525	0	877	0	0	42 days
AS-7 (SOLX)	1585	27	0	170	1000	218	0	0	0	42 days

*100 mL AS/450 mL collection, 110 mL AS/500 mL collection.

Contraindications

Red-cell-containing components should not be used to treat anemias that can be corrected with specific hematinic medications such as iron, vitamin B_{12}, folic acid, or erythropoietin.

RBCs or Whole Blood should not be used solely for volume expansion or to increase oncotic pressure of circulating blood.

Dosage and Administration

Each unit of RBCs or Whole Blood contains enough hemoglobin to increase the hemoglobin concentration in an average-sized adult by approximately 1 g/dL (increase hematocrit by 3%). Smaller aliquots can be made available for use with neonatal or pediatric patients, or adults with special transfusion needs.

The ABO group of all red-cell-containing components must be compatible with ABO antibodies in the recipient's plasma. Whole Blood must be ABO group-specific with the recipient; RBCs, which contain a reduced volume of antibody-containing plasma, need only be ABO compatible.

Serologic compatibility between recipient and donor must be established before any red-cell-containing component is transfused. This may be accomplished by performing ABO/Rh typing, antibody screening, and crossmatching by serologic technique or use of a computer crossmatch. In cases when delay in transfusion will be life-threatening, uncrossmatched group O RBCs or ABO group-specific RBCs may be transfused before completion of pretransfusion compatibility testing.

The initial portion of each unit transfused should be infused cautiously and with sufficient observation to detect onset of acute reactions. Thereafter, the rate of infusion can be more rapid, as tolerated by the patient's circulatory system. It is undesirable for components that contain red cells to remain at room temperature longer than 4 hours. If the anticipated infusion rate must be so slow that the entire unit cannot be infused within 4 hours, it is appropriate to order smaller aliquots for transfusion.

See Table 3 for pediatric dosage information.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the earlier section titled Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are **additional** hazards that apply specifically to components that contain red cells.

1. **Hemolytic transfusion reaction** is the immunologic destruction of transfused red cells, nearly always the result of incompatibility of antigen on the transfused cells with antibody in the recipient's circulation (see item 5 below for discussion of nonimmunologic hemolysis). The most common cause of severe, acute hemolytic reactions is

DO NOT COPY

DO NOT COPY

Table 3. Suggested Pediatric (Patients <50 kg) Dosing

(adapted from Wong ECC, Roseff SD, eds. Pediatric hemotherapy data card. 4th ed. Bethesda, MD: AABB, 2015)

Component	Attributes	Dosage	Expected Increment
Red Blood Cells (RBCs)	CPD, CPDA-1 (65-80% Hct)	10-15 mL/kg	3 g/dL rise in Hb
	AS-1, AS-3, AS-5, AS-7 (55-65% Hct)	10-15 mL/kg	2 g/dL rise in Hb
Washed RBCs	70-80% Hct, suspended in normal saline	10-15 mL/kg	3 g/dL rise in Hb
Plasma components*	Near-normal levels of coagulation factors, citrate anticoagulant	10-15 mL/kg	15-20% rise in factor level (assume ideal recovery)
Platelets	Whole-blood-derived platelets: $\geq 5.5 \times 10^{10}$ platelets suspended in 50 mL of plasma	5-10 mL/kg OR 1 unit/ 10 kg (patients >10 kg)	50,000-100,000/µL rise in platelet count (assume ideal recovery)
	Apheresis platelets: $\geq 3.0 \times 10^{11}$ platelets in 250-300 mL plasma, equivalent to approx. 4-6 units of whole-blood-derived platelets	Same as above	Same as above (assume ideal recovery)

Cryoprecipitated AHF	≥150 mg fibrinogen/unit ≥80 units Factor VIII/unit, von Willebrand factor (vWF), Factor XIII	1-2 units/10 kg (volume of a unit will vary, maximum to 15 mL)	60-100 mg/dL rise in fibrinogen
Granulocytes[†]	Apheresis or pooled from whole blood buffy coats	10-15 mL/kg (1×10^9 to 2×10^9 polymorphonuclear cells/kg) for neonates. For older children, minimum of 1×10^{10} granulocytes.	None. Administered daily until an adequate neutrophil count is maintained and/or the patient shows clinical improvement.

*See Table 7 for specific components.

[†]Wong ECC, Punzalan RC. Neonatal and pediatric transfusion practice. In: Fung MK, Eder AF, Spitalnik SL, Westhoff CM, eds. Technical manual. 19th ed. Bethesda, MD: AABB, 2017:613-40.

CPD = citrate-phosphate-dextrose; CPDA = citrate-phosphate-dextrose-adenine; Hct = hematocrit; Hb = hemoglobin; AS = additive solution; AHF = antihemophilic factor.

DO NOT COPY

transfusion of ABO-incompatible blood, resulting from identification errors occurring at some point(s) in the transfusion process. Serologic incompatibility undetected during pretransfusion testing is a much less common cause of acute hemolysis. If a hemolytic transfusion reaction is suspected, the transfusion must be stopped and the transfusion service laboratory notified immediately. Information identifying the patient, the transfusion component, and associated forms and labels must be reviewed promptly to detect possible errors. A postreaction blood sample, preferably drawn from a site other than the transfusion access, must be sent to the laboratory along with the implicated unit of blood and administration set.

Acute hemolytic reactions characteristically begin with an increase in temperature and pulse rate; symptoms may include chills, dyspnea, chest or back pain, abnormal bleeding, or shock. Instability of blood pressure is frequent, the direction and magnitude of change depending upon the phase of the reaction and the magnitude of compensatory mechanisms. In anesthetized patients, hemoglobinuria, hypotension, and evidence of disseminated intravascular coagulopathy (DIC) may be the first signs of incompatibility. Laboratory findings can include hemoglobinemia and/or hemoglobinuria, followed by elevation of serum indirect bilirubin. The direct antiglobulin test (DAT) result is usually positive, with rare exceptions (ie, complete hemolysis of incompatible red cells). Treatment includes measures to maintain or correct arterial blood pressure; correct coagulopathy, if present; and promote and maintain urine flow. Lack of symptoms does not exclude an acute hemolytic reaction.

Delayed hemolytic reactions occur in previously red-cell-alloimmunized patients in whom antigens on transfused red cells provoke anamnestic production of antibody. The anamnestic response reaches a significant circulating level while the transfused cells are still present in the circulation; the usual time frame is 2 to 14 days after transfusion. Signs may include unexplained fever, development of a positive DAT result, and unexplained decrease in hemoglobin/hematocrit. Hemoglobinemia and hemoglobinuria are uncommon, but elevation of lactate dehydrogenase (LDH) or bilirubin may be noted. Most delayed hemolytic reactions have a benign course and require no treatment.

Hemolytic transfusion reactions in patients with sickle cell anemia may be particularly severe, with destruction of autologous as well as transfused red cells, resulting in a lower hemoglobin level after transfusion. This is suggestive of hyperhemolysis syndrome. In such patients, sero-

DO NOT COPY

logic investigations may not reveal the specificity of the causative antibody. Immediate treatment may include steroid use, IVIG, and avoiding transfusions, if possible. Consultation with a transfusion medicine specialist is required in these cases. Prospective matching for Rh and Kell antigens may decrease risk.

2. Antigens on transfused red cells may cause red cell **alloimmunization** of the recipient. Clinically significant antibodies to red cell antigens will usually be detected in pretransfusion antibody screening tests. For most patients, red cell antigen matching beyond ABO and Rh is unnecessary.
3. **TACO** can accompany transfusion of any component at a rate more rapid than the recipient's cardiac output can accommodate. Whole Blood creates more of a risk than RBCs because the transfused plasma adds volume without increasing oxygen-carrying capacity. Patients with chronic anemia have increased plasma volumes and are at increased risk for circulatory overload.
4. **Iron overload** is a complication of chronic RBC transfusion therapy. Each transfusion contributes approximately 250 mg of iron, and significant accumulation can occur after 10 to 20 RBC transfusions. Patients requiring multiple transfusions due to decreased red cell production or increased RBC destruction are at far greater risk than patients transfused for hemorrhagic indications, because blood loss is an effective means of iron excretion. Patients with predictably chronic transfusion requirements should be considered for treatment with iron-chelating agents, a program of exchange transfusion therapy, or therapeutic phlebotomy, if applicable.
5. **Nonimmunologic hemolysis** occurs rarely, but can result from: 1) introduction of hypotonic fluids into the circulation; 2) effects of drugs coadministered with transfusion; 3) effects of bacterial toxins; 4) thermal injury by freezing or overheating; 5) metabolic damage to cells, as from hemoglobinopathies or enzyme deficiencies; or 6) mechanical injury or osmotic stresses. Examples of situations capable of causing nonimmune red cell hemolysis include: exposure to excessive heat by non-FDA-approved warming methods, mixture with hypotonic solutions, or transfusion under high pressure through small-gauge or defective needles.

Components Available

1. **RED BLOOD CELLS (RED BLOOD CELLS)** are prepared from blood collected into any of the anticoagulant-preservative solutions approved by the FDA, and separated from the plasma by centrifugation or sedimentation. Sepa-

DO NOT COPY

ration may be done at any time during the allowable shelf life. Red Blood Cells may contain from 160 to 275 mL of red cells (50-80 g of hemoglobin) suspended in varying quantities of residual plasma.

2. **RED BLOOD CELLS ADENINE SALINE ADDED (RED BLOOD CELLS ADENINE SALINE ADDED)** are prepared by centrifuging Whole Blood to remove as much plasma as possible, and replacing the plasma with usually 100 to 110 mL of an additive solution that contains some combination (see Table 2) of dextrose, adenine, sodium chloride, sodium bicarbonate, monobasic or dibasic sodium phosphate, or mannitol; the hematocrit is usually between 55% and 65%. Red Blood Cells in an additive solution have lower viscosity than Red Blood Cells, and flow through administration systems in a manner more comparable to that of Whole Blood. Red Blood Cells stored with an additive solution have an extended shelf life.
3. **RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS LEUKOCYTES REDUCED)** and **RED BLOOD CELLS ADENINE SALINE ADDED LEUKOCYTES REDUCED (RED BLOOD CELLS ADENINE SALINE ADDED LEUKOCYTES REDUCED)** are prepared from a unit of Whole Blood (collected in anticoagulant-preservative solution as noted above) containing ≥1 to 10×10^9 white cells. In general, leukocyte reduction is achieved by filtration: 1) soon after collection (prestorage) or 2) after varying periods of storage in the laboratory. Leukocyte reduction will decrease the cellular content and volume of blood according to characteristics of the filter system used. RBCs Leukocytes Reduced must have a residual content of leukocytes $<5.0 \times 10^6$. Leukocyte reduction filters variably remove other cellular elements in addition to white cells. The leukocyte-reduced component contains ≥85% of the original red cell content.
4. **APHERESIS RED BLOOD CELLS (RED BLOOD CELLS PHERESIS)** are red cells collected by apheresis. This component must be collected in an approved anticoagulant. The red cell volume collected and the anticoagulant used are noted on the label. Aside from the automated collection method used, the component is comparable to whole blood-derived RBCs in all aspects. The dose can be calculated, as for RBCs, from the red cell content of the product. Apheresis RBCs contain approximately 60 g of hemoglobin per unit.
5. **APHERESIS RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS PHERESIS LEUKOCYTES REDUCED)** and **APHERESIS RED BLOOD CELLS ADENINE SALINE ADDED LEUKOCYTES**

DO NOT COPY

REDUCED (RED BLOOD CELLS PHERESIS ADENINE SALINE ADDED LEUKOCYTES REDUCED) are collected by apheresis methods. Leukocyte reduction is achieved by filtration during the manufacturing process resulting in a final product containing $<5.0 \times 10^6$ leukocytes and ≥85% of the target red cell content.

6. **RED BLOOD CELLS, LOW VOLUME (RED BLOOD CELLS, LOW VOLUME)** are prepared when 300 to 404 mL of Whole Blood is collected into an anticoagulant volume calculated for 450 mL ± 45 mL or when 333 to 449 mL of Whole Blood is collected into an anticoagulant volume calculated for 500 mL ± 50 mL. These products reflect a collection with an altered ratio of anticoagulant to red cells and may not be an indication of a lower dose of hemoglobin. Plasma and platelet components should not be prepared from low-volume collections.
7. **WHOLE BLOOD (WHOLE BLOOD)** is rarely used for transfusion. In situations where Whole Blood is indicated but RBCs are used, a suitable plasma volume expander should be administered. See also General Information for Whole Blood and All Blood Components, Instructions for Use. All Whole Blood transfusions must be ABO identical.
8. **FROZEN RED BLOOD CELLS (RED BLOOD CELLS FROZEN)** and **FROZEN REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED FROZEN)** are prepared by adding glycerol to red cells as a cryoprotective agent before freezing. The glycerol must be removed from the thawed component before it is infused. Frozen RBCs stored for longer than 10 years, if there is a particular need for specific units, are unlicensed products. Frozen storage is especially suitable for red cells with unusual antigenic phenotypes.
9. **DEGLYCEROLIZED RED BLOOD CELLS (RED BLOOD CELLS DEGLYCEROLIZED)** is the form in which cryopreserved red cells (Frozen Red Blood Cells) are made available for infusion. Glycerol is added to red cells as a cryoprotective agent before freezing, and must be removed from the thawed component before it is infused.

   Deglycerolized RBCs contain 80% or more of the red cells present in the original unit of blood, and have approximately the same expected posttransfusion survival as RBCs. Glycerol is removed by washing the cells with successively lower concentrations of Sodium Chloride, Injection (USP); the final suspension is in 0.9% Sodium Chloride, Injection (USP), with or without small amounts of dextrose. Small amounts of residual free hemoglobin may cause the supernatant fluid to be pink-tinged.

DO NOT COPY

Deglycerolized RBCs provide the same physiologic benefits as RBCs, but their use is usually restricted to situations in which standard transfusion components are inappropriate or unavailable. Deglycerolized RBCs may be useful for transfusions to patients with previous severe allergic transfusion reactions, because the process efficiently removes plasma constituents.

In addition to the side effects and hazards of RBC transfusion, Deglycerolized RBCs carry a risk of intravascular hemolysis if deglycerolization has been inadequate.

Deglycerolized RBCs must be transfused within 24 hours after thawing if prepared in an open system. If prepared in a closed system, they can be infused within a 2-week interval after thawing.

10. **REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED)** may be prepared from red cells stored in CPD, CPDA-1, and AS-1 storage solutions up to 3 days after expiration. Addition of an FDA-approved solution containing inosine, phosphate, and adenine restores 2,3-diphosphoglycerate and adenosine triphosphate to levels approximating those of freshly drawn cells. These products must be washed before infusion to remove the inosine, which may be toxic. Rejuvenated RBCs may be prepared and **transfused within 24 hours or frozen for long-term storage.**
11. **DEGLYCEROLIZED REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED DEGLYCEROLIZED)** is the form in which rejuvenated, cryopreserved red cells (Frozen Rejuvenated Red Blood Cells) are made available for infusion. For additional information, see sections on Rejuvenated RBCs and Deglycerolized RBCs above.
12. **Autologous Whole Blood and RBCs** are collected from patients who anticipate requiring blood transfusions. Donor-safety screening criteria and testing procedures applicable to collection from allogeneic donors do not always apply to these components. All units intended for transfusion to the donor/patient must be labeled "AUTOLOGOUS DONOR." The unit must be labeled "FOR AUTOLOGOUS USE ONLY" if the donor fails to meet donor suitability requirements or has reactive or positive test results for evidence of infection. A biohazard label is required if these units have a reactive test result. In addition, if these units are untested, they must be labeled as "DONOR UNTESTED." Autologous Whole Blood or RBCs can be modified into any of the components described above. If a facility allows for autologous units to be crossed over for inclusion in the general blood inventory, the donors and units must be subjected to the same

DO NOT COPY

donor eligibility requirements and test requirements as allogeneic donors and units.

13. See section on Further Processing.

Plasma Components

Overview

Plasma is the aqueous part of blood and can be derived from the separation of a whole blood collection or by apheresis collection. Important elements in plasma include albumin, coagulation factors, fibrinolytic proteins, immunoglobulin, and other proteins. Once plasma is collected, it can be maintained in the liquid state or stored frozen and subsequently thawed and kept in a liquid state. If Fresh Frozen Plasma (FFP) is thawed at 1 to 6 C, and the insoluble cryoprecipitate (see Cryoprecipitated Components) is removed by centrifugation, the supernatant plasma can be refrozen and labeled as Plasma Cryoprecipitate Reduced. Labile coagulation factor levels vary based upon ABO group, storage conditions, and/or further processing (see Tables 4 and 5).

Fresh Frozen Plasma

Description

FRESH FROZEN PLASMA (FRESH FROZEN PLASMA) is prepared from a whole blood or apheresis collection and frozen at −18 C or colder within the time frame as specified in the directions for use for the blood collection, processing, and storage system. The anticoagulant solution used and the component volume are indicated on the label. On average, units contain 200 to 250 mL, but apheresis-derived units may contain as much as 400 to 600 mL. Fresh Frozen Plasma (FFP) contains plasma proteins, including all coagulation factors. FFP contains normal levels of the labile coagulation factors, Factors V and VIII.

FFP should be infused immediately after thawing or stored at 1 to 6 C. After 24 hours, the component must be discarded or, if collected in a functionally closed system, may be relabeled as Thawed Plasma Ω (see Thawed Plasma).

See section on Further Processing.

Action

FFP serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins.

DO NOT COPY

DO NOT COPY

Table 4. Coagulation Factor Activity in FFP and PF24 (whole blood) at the Time of Thaw and after 120 Hours of 1 to 6 C Storage

(adapted from Table 1. Scott EA, et al. Transfusion 2009;49:1584-91)

	Thaw, mean ± SD (range) by product		120 hr, mean (range) by product		% Change after 120 hr at 1 to 6 C	
Analyte	**FFP (n=20)**	**PF24 (n=14)***	**FFP (n=20)**	**PF24 (n=14)***	**FFP**	**PF24**
FII (IU/dL)	97 ± 10 (83-125)	97 ± 8 (80-113)	95 ± 10 (82-126)	96 ± 11 (74-120)	3‡	1
FV (U/dL)	85 ± 13 (63-104)	86 ± 16 (54-124)	67 ± 19 (17-92)	59 ± 22 (15-109)	21‡	31‡
FVII (IU/dL)	105 ± 25 (50-163)	89 ± 22 (54-145)	70 ± 18 (34-102)	77 ± 27 (50-159)	33‡	14‡
FVIII (IU/dL)§	81 ± 19 (47-117)	66 ± 17 (30-100)†	43 ± 10 (27-60)	48 ± 12 (26-73)	47‡	28‡
F IX (IU/dL)	82 ± 13 (62-108)	88 ± 13 (70-105)	80 ± 12 (64-107)	84 ± 12 (65-99)	2	4‡
FX (IU/dL)	94 ± 10 (71-112)	94 ± 11 (72-112)	87 ± 11 (65-111)	91 ± 12 (67-114)	7‡	3‡
vWF:Ag (IU/dL)§	98 ± 27 (57-156)	132 ± 41 (78-211)	97 ± 30 (48-150)	127 ± 40 (79-224)	1	4

vWF:RCo (IU/dL)[§]	101 ± 26 (61-152)	123 ± 47 (58-238)	93 ± 30 (48-149)	102 ± 38 (50-191)	8[‡]	17[‡]
Fibrinogen (mg/dL)	280 ± 52 (223-455)	309 ± 70 (211-500)	278 ± 50 (223-455)	303 ± 50 (205-490)	1	2[‡]
Antithrombin (IU/dL)	97 ± 9 (85-118)	97 ± 11 (77-110)	100 ± 10 (85-131)	101 ± 14 (73-116)	3	4[‡]
Protein C (IU/dL)	107 ± 20 (74-148)	88 ± 16 (65-120)[†]	107 ± 19 (77-148)	89 ± 17 (65-115)[†]	0	2
Protein S (IU/dL)	97 ± 18 (61-123)	92 ± 18 (54-121)	90 ± 22 (52-134)	78 ± 19 (46-114)[†]	7[‡]	15[‡]

*N = 25 for FII, FV, FVIII, fibrinogen, vWF:RCo, and Protein S.

[†]p <0.05 compared with mean activity in FFP of the same age.

[‡]p <0.05 when comparing mean activity at thaw to mean activity after 120 hours of 1 to 6 C storage.

[§]Only results from group O products were used for statistical comparisons of Factor VIII, vWF:Ag, and vWF:RCo activities.

FFP = Fresh Frozen Plasma; PF24 = Plasma Frozen Within 24 Hours After Phlebotomy; SD = standard deviation; FII = Factor II; vWF:Ag = von Willebrand factor antigen; vWF:RCo = von Willebrand factor ristocetin cofactor.

DO NOT COPY

Table 5. Statistically Significantly Different Coagulation Factor Activity in FFP and PF24RT24 (apheresis) after 24 Hours at 1 to 6 C Storage after Thawing

[adapted from Tables 2 and 3 of the 102nd Meeting of the Blood Products Advisory Committee (May 16, 2012)]

	Sponsor A			Sponsor B		
	Mean ± SD (range) by product		Mean difference:	Mean ± SD (range) by product		Mean difference:
Analyte	FFP (n=52)	PF24RT24 (n=52)	PF24RT24 – FFP (95% CLs)	FFP (n=54)	PF24RT24 (n=54)	PF24RT24 – FFP (95% CLs)
FV (IU/dL)	101 ± 18 (52-138)	100 ± 17 (52-136)	–1.1 (–2.1, –0.1)*	90 ± 19 (35-136)	89 ± 18 (35-131)	–1.0 (–2.6, 0.6)
FVIII (IU/dL)	81 ± 25 (37-163)	73 ± 24 (36-157)	–7.3 (–9.4, –5.2)†	99 ± 32 (49-193)	86 ± 27 (40-156)	–13.2 (–16.0, –10.5)†
Protein S (IU/dL)	94 ± 20 (53-161)	83 ± 19 (48-145)	–10.6 (–12.7, –8.5)†	82 ± 18 (29-124)	73 ± 14 (47-109)	–9.0 (–11.7, –6.2)†

*p = <0.05.

†p = <0.0001.

FFP = Fresh Frozen Plasma; PF24RT24 = Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy; SD = standard deviation; CLs = confidence limits; FV = Factor V.

DO NOT COPY

Indications

FFP is indicated in the following conditions:

1. Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors (eg, liver disease, DIC).
2. Patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
3. Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect.
4. Transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP).
5. Management of patients with selected coagulation factor deficiencies, congenital or acquired, for which no specific coagulation concentrates are available.
6. Management of patients with rare specific plasma protein deficiencies, such as C1 inhibitor, when recombinant products are unavailable.

Contraindications

Do not use this product when coagulopathy can be corrected more effectively with specific therapy, such as vitamin K, Cryoprecipitated AHF (Antihemophilic Factor), prothrombin complex concentrates approved to reverse warfarin in emergency situations, or specific coagulation factor concentrates.

Do not use this product when blood volume can be safely and adequately replaced with other volume expanders.

Dosage and Administration

Compatibility tests prior to transfusion are not necessary. Plasma must be ABO compatible with the recipient's red cells. The volume transfused depends on the clinical situation and patient size, and may be guided by laboratory assays of coagulation function.

Do not use FFP if there is evidence of container breakage or of thawing during storage. FFP must be thawed in a waterbath at 30 to 37 C or in an FDA-cleared device. If a waterbath is used, thaw the component in a protective plastic overwrap using gentle agitation.

See Table 3 for pediatric dosage information.

Side Effects and Hazards

Hazards that pertain to all transfusion components, including FFP, are described in the earlier section on Side Effects and Hazards for Whole Blood and All Blood Components.

DO NOT COPY

Plasma Frozen Within 24 Hours After Phlebotomy

Description

PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY (PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY) is prepared from a whole blood or apheresis collection. The anticoagulant solution used and the component volume are indicated on the label. On average, units contain 200 to 250 mL, but apheresis-derived units may contain as much as 400 to 600 mL. This plasma component is a source of nonlabile plasma proteins. Plasma proteins such as albumin; ADAMTS13; fibrinogen; and Factors II, VII, IX, X, and XI remain in levels similar to FFP. Levels of Factor VIII and Protein C are reduced, and levels of Factor V and other labile plasma proteins are variable compared with FFP.

Plasma Frozen Within 24 Hours After Phlebotomy (PF24) should be infused immediately after thawing or stored at 1 to 6 C. After 24 hours' storage, the component must be discarded or, if collected in a functionally closed system, may be relabeled as Thawed Plasma Ω (see Thawed Plasma).

Action

This plasma component serves as a source of nonlabile plasma proteins for patients who are deficient in or have defective plasma proteins. Some coagulation factor levels may be lower than those of FFP, especially labile coagulation Factors V, VIII, and Protein C.

Indications

See Fresh Frozen Plasma.

Contraindications

See Fresh Frozen Plasma. In addition, this product is not indicated for treatment of deficiencies of labile coagulation factors, including Factors V and VIII and Protein C.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Components Available

1. **PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY (PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY)** is prepared from a whole blood

DO NOT COPY

collection and must be separated and placed at –18 C or colder within 24 hours from whole blood collection.

2. **APHERESIS PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY (PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY PHERESIS)** is prepared from apheresis and stored at 1 to 6 C within 8 hours of collection and frozen at –18 C or colder within 24 hours of collection.
3. See section on Further Processing.

Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy

Description

PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY HELD AT ROOM TEMPERATURE UP TO 24 HOURS AFTER PHLEBOTOMY (PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY HELD AT ROOM TEMPERATURE UP TO 24 HOURS AFTER PHLEBOTOMY) is prepared from whole blood or an apheresis collection. The product can be held at room temperature for up to 24 hours after collection and then frozen at –18 C or colder. The anticoagulant solution used and the component volume are indicated on the label. On average, units contain 200 to 250 mL, but apheresis-derived units may contain as much as 400 to 600 mL. This plasma component is a source of nonlabile plasma proteins. Plasma proteins such as albumin; ADAMTS13; fibrinogen; and Factors II, VII, IX, X, and XI remain at levels similar to FFP. Levels of Factor V, Factor VIII, and Protein S are reduced, and levels of other labile plasma proteins are variable compared with FFP.

Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy (PF24RT24) should be infused immediately after thawing or stored at 1 to 6 C. After 24 hours, the component must be discarded or, if collected in a functionally closed system, may be relabeled as Thawed Plasma Ω (see Thawed Plasma).

See section on Further Processing.

Action

This plasma component serves as a source of nonlabile plasma proteins for patients who are deficient in or have defective plasma proteins. Some coagulation factor levels may be lower than those of FFP, especially labile coagulation Factors V and VIII and Protein S.

Indications

See Fresh Frozen Plasma.

DO NOT COPY

Contraindications

See Fresh Frozen Plasma. In addition, this product is not indicated for treatment of deficiencies of labile coagulation factors, including Factors V and VIII and Protein S.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Plasma Cryoprecipitate Reduced

Description

PLASMA CRYOPRECIPITATE REDUCED (PLASMA, CRYOPRECIPITATE REDUCED) is prepared from whole-blood-derived FFP after thawing and centrifugation and removal of the cryoprecipitate. The remaining product is plasma that is deficient in fibrinogen, Factor VIII, Factor XIII, von Willebrand factor (vWF), cryoglobulin, and fibronectin. This supernatant plasma must be refrozen within 24 hours of thawing at –18 C or colder. Proteins such as albumin, ADAMTS13, and Factors II, V, VII, IX, X, and XI remain in levels similar to FFP. High-molecular-weight forms of vWF (multimers) are significantly decreased during production; however, smaller multimers are retained.

Plasma Cryoprecipitate Reduced should be infused immediately after thawing or stored at 1 to 6 C. This product can be stored at 1 to 6 C for up to 5 days but must be relabeled as Thawed Plasma Cryoprecipitate Reduced Ω.

Action

This component serves as a source for plasma proteins except for fibrinogen, Factor VIII, Factor XIII, and vWF.

Indications

Plasma Cryoprecipitate Reduced is used for transfusion or plasma exchange in patients with TTP. It may be used to provide clotting factors except fibrinogen, Factor VIII, Factor XIII, and vWF.

Contraindications

Plasma Cryoprecipitate Reduced is contraindicated for the repletion of coagulation factors known to be depleted in this product: fibrinogen, vWF, Factor VIII, and Factor XIII. This component should not be used as a substitute for FFP, PF24, or Thawed Plasma.

DO NOT COPY

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Liquid Plasma Components

Description

Other plasma components may be made from whole blood collected in all approved anticoagulants. Levels and activation state of coagulation proteins in these products are variable. The volume is indicated on the label.

THAWED PLASMA Ω (THAWED PLASMA) is derived from FFP, PF24, or PF24RT24 prepared using aseptic techniques (functionally closed system). It is thawed at 30 to 37 C, and maintained at 1 to 6 C for up to 4 days after the initial 24-hour postthaw period has elapsed. The volume is indicated on the label. Thawed Plasma contains stable coagulation factors such as Factor II and fibrinogen in concentrations clinically similar to those of FFP, but variably reduced amounts of other factors (see Table 4).

Action

This component serves as a source of nonlabile plasma proteins. Levels and activation state of coagulation proteins in thawed plasma are variable and change over time.

Indications

Thawed Plasma is indicated in the following conditions:

1. Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors (eg, liver disease, DIC).
2. Initial treatment of patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
3. Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect.
4. Transfusion or plasma exchange in patients with TTP.

Contraindications

See Fresh Frozen Plasma. Do not use Thawed Plasma as the treatment for isolated coagulation factor or specific plasma protein deficiencies where other products are available with higher concentrations of the specific factor(s) or proteins.

DO NOT COPY

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

THAWED PLASMA *CRYOPRECIPITATE REDUCED* Ω (THAWED PLASMA, CRYOPRECIPITATE REDUCED) is derived from Plasma Cryoprecipitate Reduced. It is thawed at 30 to 37 C, and maintained at 1 to 6 C for up to 4 days after the initial 24-hour postthaw period has elapsed. The volume is indicated on the label. Thawed Plasma Cryoprecipitate Reduced is deficient in fibrinogen, Factor VIII, Factor XIII, vWF, cryoglobulin, and fibronectin and contains variable levels of albumin, ADAMTS13, and Factors II, V, VII, IX, X, and XI.

Action

See Plasma Cryoprecipitate Reduced.

Indications

See Plasma Cryoprecipitate Reduced.

Contraindications

See Plasma Cryoprecipitate Reduced.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

LIQUID PLASMA (LIQUID PLASMA) is separated and infused no later than 5 days after the expiration date of the Whole Blood and is stored at 1 to 6 C.

The profile and activity of plasma proteins involved in coagulation in Liquid Plasma are not completely characterized. Levels and activation state of coagulation proteins in Liquid Plasma are dependent upon and change with time in contact with cells, as well as the conditions and duration of storage. This product contains viable lymphocytes that may cause graft-versus-host reactions in susceptible patients.

See section on Further Processing.

Action

This component serves as a source of plasma proteins. Levels and activation state of coagulation proteins are variable and change over time.

DO NOT COPY

Indications

Liquid Plasma is indicated for the initial treatment of patients who are undergoing massive transfusion because of life-threatening trauma/hemorrhages and who have clinically significant coagulation deficiencies.

Contraindications

See Fresh Frozen Plasma. Do not use Liquid Plasma as the treatment for coagulation factor deficiencies where other products are available with higher factor concentrations.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Cryoprecipitated Components

Overview

Description

Cryoprecipitated Antihemophilic Factor (AHF) is prepared by thawing whole-blood-derived or apheresis FFP between 1 and 6 C and recovering the precipitate. The cold-insoluble precipitate is placed in the freezer within 1 hour after removal from the refrigerated centrifuge. Cryoprecipitated AHF contains fibrinogen, Factor VIII, Factor XIII, vWF, and fibronectin. Each unit of Cryoprecipitated AHF should contain ≥80 IU of Factor VIII and ≥150 mg of fibrinogen in approximately 5 to 20 mL of plasma.

If the label indicates “Pooled Cryoprecipitated AHF,” several units of Cryoprecipitated AHF have been pooled. The volume of the pool is indicated on the label and, if used, the volume of 0.9% Sodium Chloride, Injection (USP) may be separately listed. To determine the minimum potency of this component, assume 80 IU of Factor VIII and 150 mg of fibrinogen for each unit of Cryoprecipitated AHF indicated on the label.

Action

Cryoprecipitate serves as a source of fibrinogen, Factor VIII, Factor XIII, vWF, and fibronectin.

Indications

This component is used in the control of bleeding associated with fibrinogen deficiency, and when recombinant and/or

DO NOT COPY

virally inactivated preparations of Factor VIII, Factor XIII, or vWF are not available. It is also indicated as second-line therapy for von Willebrand disease and hemophilia A (Factor VIII deficiency). Coagulation factor preparations other than cryoprecipitate are preferred when blood component therapy is needed for management of von Willebrand disease, Factor VIII deficiency, and Factor XIII deficiency. Every effort must be made to obtain preferred factor concentrates for hemophilia A patients before resorting to the use of cryoprecipitate. Use of this component may be considered for control of uremic bleeding after other modalities have failed. Indications for use as a source of fibronectin are not clear.

Contraindications

Do not use this component unless results of laboratory studies indicate a specific hemostatic defect for which this product is indicated. Cryoprecipitate should not be used if virus-inactivated specific factor concentrates or recombinant factor preparations are available for management of patients with von Willebrand disease, hemophilia A, or Factor XIII deficiency.

Dosage and Administration

Compatibility testing is unnecessary. ABO-compatible material is preferred. Rh type need not be considered when using this component.

The frozen component is thawed in a protective plastic overwrap in a waterbath at 30 to 37 C up to 15 minutes (thawing time may be extended if product is pooled before freezing). This component should not be given if there is evidence of container breakage or of thawing during storage. Do not refreeze after thawing. Thawed Cryoprecipitated AHF should be kept at room temperature and transfused as soon as possible after thawing, within 6 hours if it is a single unit (from an individual donor, or products pooled before freezing or prior to administration using an FDA-cleared sterile connecting device), and within 4 hours after entering the container (eg, to attach an administration set or to pool) without using an FDA-cleared sterile connecting device.

Cryoprecipitated AHF may be transfused as individual units or pooled. For pooling, the precipitate in one or more concentrates should be mixed well with 10 to 15 mL of diluent to ensure complete removal of all material from the container. The preferred diluent is 0.9% Sodium Chloride, Injection (USP). Serial use of each bag's contents to resuspend the precipitate into subsequent bags may be used to efficiently pool cryoprecipitate into a single bag.

The recovery of transfused fibrinogen is 50% to 60%. When used to correct hypofibrinogenemia, Cryoprecipitated AHF may be dosed at one bag per 7 to 10 kg body weight to raise plasma fibrinogen by approximately 50 to 75 mg/dL. Thrombosis alters

DO NOT COPY

fibrinogen kinetics; therefore, patients receiving cryoprecipitate as fibrinogen replacement in conditions associated with increased fibrinogen turnover should be monitored with fibrinogen assays.

For treatment of bleeding in patients with hemophilia A when Factor VIII concentrates are not available, rapid infusion of a loading dose expected to produce the desired level of Factor VIII is usually followed by a smaller maintenance dose every 8 to 12 hours. To maintain hemostasis after surgery, a regimen of therapy for 10 days or longer may be required. If circulating antibodies to Factor VIII are present, the use of larger doses, activated concentrates, porcine-derived concentrates, or other special measures may be indicated. To calculate cryoprecipitate dosage as a source of Factor VIII, the following formula is helpful: Number of bags = (Desired increase in Factor VIII level in % × 40 × body weight in kg) / average units of Factor VIII per bag. Good patient management requires that the Cryoprecipitated AHF treatment responses of Factor VIII-deficient recipients be monitored with periodic plasma Factor VIII assays.

For treatment of von Willebrand disease, smaller amounts of Cryoprecipitated AHF will correct the bleeding time. Because the vWF content of Cryoprecipitated AHF is not usually known, an empiric dose of 1 bag per 10 kg of body weight has been recommended. These patients should be monitored by appropriate laboratory studies to determine the frequency of Cryoprecipitated AHF administration.

See Table 3 for pediatric dosage information.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the earlier section on Side Effects and Hazards for Whole Blood and All Blood Components.

If a large volume of ABO-incompatible cryoprecipitate is used, the recipient may develop a positive DAT and, very rarely, mild hemolysis.

Components Available

1. **CRYOPRECIPITATED AHF (CRYOPRECIPITATED AHF)**
2. **APHERESIS CRYOPRECIPITATED AHF (Cryoprecipitated AHF PHERESIS)**
3. **POOLED CRYOPRECIPITATED AHF (CRYOPRECIPITATED AHF, POOLED)**

DO NOT COPY

Platelet Components

Overview

Description

Platelet therapy may be achieved by infusion of either Apheresis Platelets or Platelets (whole-blood-derived platelet concentrates). In either component, platelets are suspended in an appropriate volume of the original plasma, which contains near-normal levels of stable coagulation factors that are stored at room temperature. Apheresis Platelets may be stored in an additive solution. One unit of Platelets derived from a whole blood collection usually contains $\geq 5.5 \times 10^{10}$ platelets suspended in 40 to 70 mL of plasma. Platelets may be provided either singly or as a pool. One unit of Apheresis Platelets usually contains $\geq 3.0 \times 10^{11}$ platelets and is the therapeutic equivalent of 4 to 6 units of Platelets. Platelet components may contain a varying number of leukocytes depending upon the technique used in preparation. Some units may contain more than the trace amounts of red cells usually present and will appear pink to salmon in color. This occurs more frequently with whole-blood-derived platelets than apheresis platelets.

Actions

Platelets are essential for normal hemostasis. Complex reactions occur between platelets, vWF, collagen in the walls of disturbed vasculature, phospholipids, and soluble coagulation factors, including thrombin. These changes induce platelet adherence to vessel walls and platelet activation, which leads to platelet aggregation and formation of a primary hemostatic plug. The therapeutic goal of platelet transfusion is to provide adequate numbers of normally functioning platelets for the prevention or cessation of bleeding.

Indications

Platelet transfusions may be given to patients with thrombocytopenia, dysfunctional platelet disorders (congenital, metabolic, or medication-induced), or active platelet-related bleeding, or patients at serious risk of bleeding (ie, prophylactic use). Patients with the following medical conditions may require platelet transfusion: leukemia, myelodysplasia, aplastic anemia, solid tumors, congenital or acquired platelet dysfunction, and central nervous system trauma. Patients undergoing extracorporeal membrane oxygenation or cardiopulmonary bypass may also need platelet transfusion, and platelets may be indicated in massive transfusion protocols. Thrombocytopenia is unlikely to be the cause of bleeding in patients with platelet counts of at

DO NOT COPY

least 50,000/μL. Higher transfusion thresholds may be appropriate for patients with platelet dysfunction. For the clinically stable patient with an intact vascular system and normal platelet function, prophylactic platelet transfusions may be appropriate at <5000 to 10,000/μL.

Prophylactic platelet transfusion may not be of therapeutic benefit when thrombocytopenia is related to destruction of circulating platelets secondary to autoimmune disorders [eg, immune thrombocytopenic purpura (ITP)]; however, transfusion may be indicated for active bleeding in these patients.

Platelets Leukocytes Reduced or Apheresis Platelets Leukocytes Reduced are indicated to decrease the frequency of recurrent febrile nonhemolytic transfusion reaction, HLA alloimmunization, and transfusion-transmitted CMV infection (see section on Further Processing).

Contraindications

Do not use this component if bleeding is unrelated to decreased numbers of, or abnormally functioning, platelets. Platelets should not be transfused when the platelet count is greater than 100,000/μL, unless there is documented or suspected abnormal function. Prophylactic transfusion is generally not indicated in nonbleeding patients on antiplatelet medications, or when platelet dysfunction is extrinsic to the platelet, such as in uremia, certain types of von Willebrand disease, and hyperglobulinemia. Patients with congenital surface glycoprotein defects should be transfused conservatively to reduce the possibility for alloimmunization to the missing protein(s).

Do not use in patients with activation or autoimmune destruction of endogenous platelets, such as in heparin-induced thrombocytopenia (HIT), TTP, or ITP, unless the patient has a life-threatening hemorrhage.

Dosage and Administration

Compatibility testing is not necessary in routine platelet transfusion. Except in unusual circumstances, the donor plasma should be ABO compatible with the recipient's red cells when this component is to be transfused to infants, or when large volumes are to be transfused. The number of platelet units to be administered depends on the clinical situation of each patient. One unit of Platelets would be expected to increase the platelet count of a 70-kg adult by 5000 to 10,000/μL and increase the count of an 18-kg child by 20,000/μL. The therapeutic adult dose is 1 unit of Apheresis Platelets or 4 to 6 units of whole-blood-derived platelets, either of which usually contains $\geq 3.0 \times 10^{11}$ platelets. For prophylaxis, this dose may need to be repeated in 1 to 3 days because of the short life span of transfused platelets (3 to 4 days). Platelet components must be examined for abnormal appearance before administration. Units with excessive aggre-

DO NOT COPY

gates should not be administered. Transfusion may proceed as quickly as tolerated, but must take less than 4 hours. Do not refrigerate platelets.

The corrected count increment (CCI) is a calculated measure of patient response to platelet transfusion that adjusts for the number of platelets infused and the size of the recipient, based upon body surface area (BSA)

$$\text{CCI} = (\text{postcount} - \text{precount}) \times \text{BSA} / \text{platelets transfused}$$

where postcount and precount are platelet counts (/μL) after and before transfusion, respectively; BSA is the patient body surface area (meter^2); and platelets transfused is the number of administered platelets ($\times 10^{11}$). The CCI is usually determined 10 to 60 minutes after transfusion. For example:

A patient with acute myelogenous leukemia with a nomogram-derived BSA of 1.40 m^2 is transfused with a unit of Apheresis Platelets (a platelet dose of 4.5×10^{11}). The pretransfusion platelet count is 2000/μL. The patient's platelet count from a sample of blood collected 15 minutes after platelet transfusion is 29,000/μL. The CCI is calculated as $(29{,}000 - 2000) \times 1.4 / 4.5 = 8{,}400$/μL per 10^{11} per m^2.

In the clinically stable patient, the CCI is typically greater than 7500 at 10 minutes to 1 hour after transfusion and remains above 4500 at 24 hours. The CCI may be lower following transfusion with platelet components that have been further processed. Both immune and nonimmune mechanisms may contribute to reduced platelet recovery and survival. Along with supportive serologic test results, a CCI of less than 5000 at 10 minutes to 1 hour after transfusion may indicate an immune-mediated refractory state to platelet therapy (refer to Platelet Alloimmunization, below). With nonimmune mechanisms, platelet recovery within 1 hour may be adequate, although survival at 24 hours is reduced.

See Table 3 for pediatric dosage information.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the section on Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are **additional** hazards that apply specifically to components that contain platelets.

1. **Bacterial Contamination:** Although methods to limit and detect bacterial contamination have been implemented for most platelet components, they remain the most likely blood components to be contaminated with bacteria. Gram-positive skin flora are the most commonly recovered bacteria. Symptoms may include high fever (≥2.0 C or ≥3.5 F increase in temperature), severe chills, hypotension, or circulatory collapse during or immediately after transfusion. In some instances, symptoms, especially when associated with

DO NOT COPY

contamination by gram-positive organisms, may be delayed for several hours following transfusion. Prompt management should include broad-spectrum antibiotic therapy along with cultures from the patient, suspected blood component(s), and administration set. A Gram stain of the suspected contaminated unit(s) should be performed whenever possible.

2. **Platelet Alloimmunization:** Platelets bear a variety of antigens, including HLA and platelet-specific antigens. Patients transfused with platelets often develop HLA antibodies. The patient may become refractory to incompatible platelets. When platelets are transfused to a patient with an antibody specific for an expressed antigen, the survival time of the transfused platelets may be markedly shortened. Nonimmune events may also contribute to reduced platelet survival. It may be possible to distinguish between immune and nonimmune platelet refractoriness by assessing platelet recovery soon after infusion (ie, a 10- to 60-minute postinfusion platelet increment). In immune refractory states secondary to serologic incompatibility, there is poor recovery in the early postinfusion interval. In nonimmune mechanisms (eg, splenomegaly, sepsis, fever, intravascular devices, and DIC), platelet recovery within 1 hour of infusion may be adequate while longer-term survival (ie, 24-hour survival) is reduced. Serologic tests may confirm the presence of alloimmunization. Laboratory tests (HLA typing and antibody identification, HPA antibody identification, or a platelet crossmatch) may also be helpful in selecting platelets with acceptable survival.
3. **Red Blood Cell Alloimmunization:** Immunization to red cell antigens may occur because of the presence of residual red cells in Platelets. Red cell compatibility testing is necessary only if the platelet component is prepared by a method that results in the component containing 2 mL or more of red cells, making the unit appear pink to salmon in color. This occurs more frequently with whole-blood-derived platelets than apheresis platelets. When platelet components from Rh-positive donors must be given to Rh-negative females of childbearing potential because Rh-negative platelets are not available, prevention of Rh (D) immunization by use of Rh Immune Globulin should be considered.
4. **Hemolysis:** Platelet components that are not ABO identical with the recipient's blood group may contain incompatible plasma and when transfused may cause a positive DAT and possibly hemolysis. Platelet transfusions from group O donors with high-titer isohemagglutinins (anti-A or anti-B) may cause acute hemolytic reactions in susceptible patients.

DO NOT COPY

Components Available

1. **PLATELETS (PLATELETS)** are a concentrate of platelets separated from a single unit of Whole Blood. One unit of Platelets should contain $\geq 5.5 \times 10^{10}$ platelets suspended in 40 to 70 mL of plasma. This component is usually provided as a pool. See below.
2. **POOLED PLATELETS (PLATELETS POOLED)** are composed of individual platelet units combined by aseptic technique and have an allowable shelf life as specified in the directions for use for the blood collection, processing, and storage system. The number of units of Platelets in the pool will be indicated on the label. To determine the minimum potency of this component, assume 5.5×10^{10} platelets per unit of Platelets indicated on the label. See the label for the approximate volume.
3. **PLATELETS LEUKOCYTES REDUCED (PLATELETS LEUKOCYTES REDUCED)** may be prepared using an open or closed system. One unit of Platelets Leukocytes Reduced should contain $\geq 5.5 \times 10^{10}$ platelets and $<8.3 \times 10^{5}$ leukocytes. Components prepared using an open system will expire 4 hours after preparation. Components prepared using a closed system will have a shelf life as specified in the directions for use for the blood collection, processing, and storage system. This component is usually provided as a pool. See below.
4. **POOLED PLATELETS LEUKOCYTES REDUCED (PLATELETS LEUKOCYTES REDUCED, POOLED)** may be prepared by pooling and filtering Platelets or pooling Platelets Leukocytes Reduced in an open system that will have a 4-hour shelf life. The number of units in the pool will be indicated on the label. To determine the minimum potency of this component, assume 5.5×10^{10} platelets per unit of Platelets Leukocytes Reduced indicated on the label and $<5 \times 10^{6}$ leukocytes in the pool. See the label for the approximate volume. This component can also be prepared and pooled using an FDA-cleared system to provide a product with a 5-day shelf life.
5. **APHERESIS PLATELETS (PLATELETS PHERESIS)** are an effective way to collect a therapeutic adult dose of platelets from a single donor. Apheresis Platelets should contain $\geq 3.0 \times 10^{11}$ platelets. One unit of Apheresis Platelets may be equivalent to 4 to 6 units of Platelets. The product volume is variable and indicated on the label. The number of leukocytes contained in this component varies depending upon the blood cell separator and protocol used for collection. Apheresis Platelets are supplied in one or more connected bags to improve platelet viability during storage by providing more surface area for gas exchange.

DO NOT COPY

ACD-A is the anticoagulant solution currently used for the collection and preservation of Apheresis Platelets.

6. **APHERESIS PLATELETS LEUKOCYTES REDUCED (PLATELETS PHERESIS LEUKOCYTES REDUCED)** can be leukocyte reduced during the collection process or may be prepared by further processing using leukocyte-reduction filters. Apheresis Platelets Leukocytes Reduced should contain $\geq 3.0 \times 10^{11}$ platelets and $<5.0 \times 10^{6}$ leukocytes. When Apheresis Platelets Leukocytes Reduced are prepared by further processing, these may be labeled Apheresis Platelets Leukocytes Reduced provided the requirement for residual leukocyte count is met and the platelet recovery is at least 85% of the prefiltration content. The volume, anticoagulant-preservative, and storage conditions for Apheresis Platelets Leukocytes Reduced are the same as those for Apheresis Platelets.
7. **APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED** (**PLATELETS PHERESIS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED**) are platelets collected by apheresis and suspended in variable amounts of plasma and an approved platelet additive solution (PAS). See Table 6. One unit of platelets should contain $\geq 3 \times 10^{11}$ platelets and $<5.0 \times 10^{6}$ leukocytes. The volume in the product is variable and indicated on the label. Plasma proteins, including coagulation factors present in the plasma, are diluted in proportion to the PAS added. This component has a shelf life of 5 days, and may be further processed (eg, irradiated, divided).
8. See section on Further Processing.

Granulocyte Components

Description

APHERESIS GRANULOCYTES Ω (GRANULOCYTES PHERESIS) contain numerous leukocytes and platelets as well as 20 to 50 mL of red cells. The number of granulocytes in each concentrate is usually $>1.0 \times 10^{10}$. The number of platelets varies in each product. Various modalities may be used to improve granulocyte collection, including donor administration of granulocyte colony-stimulating factor and/or corticosteroids. The final volume of the product is 200 to 300 mL including anticoagulant and plasma as indicated on the label.

Red cell sedimenting agents approved by the FDA, such as hydroxyethyl starch (HES), are typically used in the collection of granulocytes. Residual sedimenting agents will be present in the final component and are described on the label. Apheresis

DO NOT COPY

DO NOT COPY

Table 6. Contents of Platelet Additive Solutions

Additive Solution (mg/100 mL)	Sodium Chloride	Sodium Citrate	Sodium Gluconate	Sodium Acetate	Dibasic Sodium Phosphate	Monobasic Sodium Phosphate	Monobasic Potassium Phosphate	Potassium Chloride	Magnesium Chloride	Shelf Life
PAS-C (Intersol)	452	318 (dihydrate)		442 (trihydrate)	305 (anhydrous)	93 (monohydrate)				5 days
PAS-F (Isoplate)	530		500	370 (trihy-drate)	12 (heptahy-drate)		0.82	37	30 (hexahy-drate)	5 days

PAS = platelet additive solution.

Granulocytes should be administered as soon after collection as possible because of well-documented deterioration of granulocyte function during short-term storage. If stored, maintain at 20 to 24 C without agitation, for no more than 24 hours.

Actions

Granulocytes migrate toward, phagocytize, and kill bacteria and fungi. A quantitative relationship exists between the level of circulating granulocytes and the prevalence of bacterial and fungal infection in neutropenic patients. The ultimate goal is to provide the patient with the ability to fight infection. The infusion of a granulocyte component may not be associated with a significant increase in the patient's granulocyte count and is dependent on multiple factors, including the patient's clinical condition.

Indications

Granulocyte transfusion therapy is controversial. Apheresis Granulocytes are typically used in the treatment of patients with documented infections (especially gram-negative bacteria and fungi) unresponsive to antimicrobial therapy in the setting of neutropenia [absolute granulocyte count $<0.5 \times 10^9$/L (500/μL)] with expected eventual marrow recovery. A trial of broad-spectrum antimicrobial agents should be used before granulocyte transfusion therapy is initiated. If the intended recipient is CMV seronegative and severely immunosuppressed (eg, a marrow transplant recipient), serious consideration should be given before administration of CMV-seropositive granulocytes. In addition to neutropenic patients, patients with hereditary neutrophil function defects (such as chronic granulomatous disease) may be candidates for granulocyte transfusion therapy.

Contraindications

Prophylactic use of granulocytes in noninfected patients is not routinely recommended. Patients with HLA and/or human neutrophil antigen (HNA) antibodies may not derive full benefit from granulocyte transfusion and may have a higher risk of complications. Antigen-matched or HLA-matched components, if available, may be considered in these patients.

Dosage and Administration

Transfuse as soon as possible. A standard blood infusion set is to be used for the administration of Apheresis Granulocytes. Do not administer using leukocyte-reduction filters. Depth-type microaggregate filters and leukocyte-reduction filters remove granulocytes.

The red cells in Apheresis Granulocytes must be ABO compatible. Once granulocyte transfusion therapy is initiated, support should continue at least daily until infection is cured,

DO NOT COPY

defervescence occurs, the absolute granulocyte count returns to at least 0.5×10^9/L (500/μL), or the physician in charge decides to halt the therapy.

Because most patients receiving these products are severely immunosuppressed, Apheresis Granulocytes are usually irradiated to prevent TA-GVHD (see section on Further Processing).

See Table 3 for pediatric dosage information.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the section on Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are hazards that apply specifically to Apheresis Granulocytes.

1. **Febrile Nonhemolytic Reactions:** These reactions are frequently noted in patients receiving granulocyte transfusions. Fever and chills in patients receiving granulocyte components may be avoided or mitigated by slow administration and recipient premedication.
2. **Allergic Reactions:** Allergic reactions to HES and other red cell sedimenting solutions may occur during granulocyte transfusion.
3. **Pulmonary Reactions:** Granulocyte transfusion can cause worsening of pulmonary function in patients with pneumonia, and rarely severe pulmonary reactions, especially in patients receiving concomitant amphotericin B. Patients who have pulmonary reactions should be tested for HLA and HNA antibodies.
4. **Alloimmunization:** Immunization to HLA antigens frequently occurs with granulocyte transfusion and can cause refractoriness to platelet transfusion.

Further Processing

This section addresses further processing of previously described blood components. The processes described in this section are: pathogen reduction, leukocyte reduction, identification of CMV-seronegative components, irradiation, and washing. A component may undergo one or more of these processes.

Pathogen Reduction

Description

Pathogen reduction is a postcollection manufacturing process intended to reduce the risk of certain transfusion-transmitted infections (TTI). Pathogen reduction technology employs a combination of ultraviolet (UV) irradiation and photosensitizers

DO NOT COPY

to damage pathogen nucleic acids, preventing replication and growth.

Psoralen treatment is a specific pathogen reduction technology used to prepare pathogen-reduced whole-blood-derived pooled plasma, apheresis plasma, or apheresis platelets. The platelet source and suspension medium must be in accordance with the pathogen reduction system package insert. Psoralen treatment inactivates a broad spectrum of viruses, as well as gram-positive and gram-negative bacteria, spirochetes, and parasites. In addition, leukocyte activity is reduced. It does not completely inactivate all pathogens; eg, hepatitis A (HAV), hepatitis E (HEV), human parvovirus B19 (B19V), poliovirus, and *Bacillus cereus* spores have shown resistance to the process.

In brief, the inactivation procedure is as follows: A psoralen (eg, amotosalen) is added to the plasma or platelet product and then transferred into a container that is placed inside an illumination device for UVA treatment. Unreacted psoralen and free photoproducts are subsequently removed with a compound adsorption device.

Following treatment, the plasma product is distributed among two or three plasma bags for use or storage at or below –18 C. Treated pooled whole-blood-derived plasma must be placed at –18 C or colder within 24 hours of blood collection. Treated apheresis plasma must be placed at –18 C or colder within 8 hours of collection. The plasma products must be transfused within 24 hours of thawing.

Treated platelets are transferred to storage container(s) for use or storage at 20 to 24 C with continuous agitation for up to 5 days from the time of collection.

Indications

Pathogen-reduced blood components have reduced risk for certain types of TTIs and may also be used to prevent TA-GVHD if the pathogen reduction technology has been shown to inactivate residual lymphocytes. These components may be used similarly to other products as indicated in the Plasma Components and Platelet Components sections.

Contraindications

These components are contraindicated for patients with a history of hypersensitivity reaction to amotosalen or other psoralens.

They are also contraindicated for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth less than 375 nm, due to the potential for erythema resulting from the interaction between UV light and amotosalen.

DO NOT COPY

Side Effects and Hazards

Psoralen-treated platelets may have an increased risk of causing acute respiratory distress syndrome (ARDS) compared to conventional platelet components.

In patients with TTP who are being treated with therapeutic plasma exchange (TPE), amotosalen-treated plasma may cause adverse cardiac events. Patients should be monitored for signs and symptoms of cardiac events during TPE for TTP.

Specific Pathogen-Reduced Components

The list of blood components that can be further processed using pathogen reduction technology may change as device manufacturers receive additional approvals from the FDA. A list will be maintained on the AABB website, and additions will be announced in AABB newsletters.

All components resulting from psoralen-based pathogen reduction treatment will bear the labeling attribute "psoralen-treated." Downstream components manufactured at a later time also will bear the labeling attribute "psoralen-treated."

Leukocyte Reduction

Description

A unit of whole blood generally contains ≥ 1 to 10×10^9 white cells. Leukocyte reduction may be achieved by in-process collection or filtration: 1) soon after collection (prestorage), 2) after varying periods of storage in the laboratory, or 3) at the bedside. The method used in the laboratory for leukocyte reduction is subject to quality control testing; leukocyte-reduced components prepared at the bedside are not routinely subjected to quality control testing. Leukocyte reduction will decrease the cellular content and volume of blood according to characteristics of the filter system used. Red Blood Cells Leukocytes Reduced, Apheresis Red Blood Cells Leukocytes Reduced, and Apheresis Platelets Leukocytes Reduced must have a residual content of leukocytes $<5.0 \times 10^6$, and Platelets Leukocytes Reduced must have $<8.3 \times 10^5$ residual leukocytes. Leukocyte-reduction filters variably remove other cellular elements in addition to white cells. Washing is not a substitute for leukocyte reduction. Leukocyte reduction is not a substitute for irradiation.

Indications

Leukocyte-reduced components are indicated to decrease the frequency of recurrent febrile nonhemolytic transfusion reaction. They have also been shown to reduce the risk of transfusion-transmitted CMV and to reduce the incidence of HLA alloimmunization.

DO NOT COPY

Contraindications

Leukocyte-reduced components do not prevent TA-GVHD. Leukocyte-reduction filters are not to be used in the administration of Apheresis Granulocytes.

Side Effects and Hazards

The use of blood components that are leukocyte reduced at the bedside may cause unexpected severe hypotension in some recipients, particularly those taking angiotensin-converting enzyme inhibitor medication.

Specific Leukocyte-Reduced Components

All components resulting from the leukocyte reduction process will bear the labeling attribute "leukocytes reduced."

Irradiation

Description

Blood components that contain viable lymphocytes may be irradiated to prevent proliferation of T lymphocytes, which is the immediate cause of TA-GVHD. Irradiated blood is prepared by exposing the component to a radiation source. The standard dose of gamma irradiation is 2500 cGy targeted to the central portion of the container with a minimum dose of 1500 cGy delivered to any part of the component.

Indications

Irradiated cellular components are indicated for use in patient groups that are at risk for TA-GVHD. At-risk groups include: fetal and neonatal recipients of intrauterine transfusions, selected immunocompromised recipients, recipients of cellular components known to be from a blood relative, recipients who have undergone marrow or peripheral blood progenitor cell transplantation, and recipients of cellular components whose donor is selected for HLA compatibility. Transfused patients receiving purine analogues (eg, fludarabine, cladribine) or certain other biological immunmodulators (eg, alemtuzumab, antithymocyte globulin) may be at risk for TA-GVHD, depending on clinical factors and the source of the biological agent.

Side Effects and Hazards

Irradiation induces erythrocyte membrane damage. Irradiated red cells have been shown to have higher supernatant potassium levels than nonirradiated red cells. Removal of residual supernatant plasma before transfusion may reduce the risks associated with elevated plasma potassium. The expiration date of irradiated red cells is changed to 28 days after irradiation if remaining shelf life exceeds 28 days. There are no known adverse effects

DO NOT COPY

following irradiation of platelets; the expiration date is unchanged.

Specific Irradiated Components

All components that have been irradiated will bear the labeling attribute “irradiated.”

Washing

Description

Washed components are typically prepared using 0.9% Sodium Chloride, Injection (USP) with or without small amounts of dextrose. Washing removes unwanted plasma proteins, including antibodies and glycerol from previously frozen units. There will also be some loss of red cells and platelets, as well as a loss of platelet function through platelet activation. The shelf life of washed components is no more than 24 hours at 1 to 6 C or 4 hours at 20 to 24 C. Washing is not a substitute for leukocyte reduction, and only cellular components should be washed.

Indications

Washing may be used to reduce exposure to plasma proteins, acellular constituents or additives (such as mannitol). It is indicated to reduce exposure to antibodies targeting known recipient antigens (such as an Apheresis Platelet unit containing incompatible plasma collected from a mother for the treatment of neonatal alloimmune thrombocytopenia), or to remove constituents that predispose patients to significant or repeated transfusion reactions (eg, the removal of IgA-containing plasma in providing transfusion support for an IgA-deficient recipient or in rare recipients experiencing anaphylactoid/anaphylactic reactions to other plasma components).

Specific Washed Components

WASHED RED BLOOD CELLS (Red Blood Cells Washed)
WASHED APHERESIS RED BLOOD CELLS (Red Blood Cells Pheresis Washed)
WASHED PLATELETS Ω (Platelets Washed)
WASHED APHERESIS PLATELETS Ω (Platelets Pheresis Washed)
WASHED APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED Ω (Platelets Pheresis Platelet Additive Solution Added Leukocytes Reduced)

DO NOT COPY

Volume Reduction

Description

Volume reduction is a special manipulation of cellular blood products using centrifugation. The process involves the aseptic removal of a portion of the supernatant, containing plasma and storage medium. Volume reduction removes excess plasma, thereby reducing unwanted plasma proteins, including antibodies. It is more commonly used in pediatric and in-utero transfusions. There will be some loss of platelet function through platelet activation as a result of volume reduction. The shelf life of volume-reduced components is no more than 24 hours at 1 to 6 C or 4 hours at 20 to 24 C.

Indications

Reducing the plasma volume of cellular components is indicated in cases where the volume status of a patient is being aggressively managed, such as in infants with compromised cardiac function. Component volume reduction is also used to mitigate adverse transfusion reactions such as TACO and allergic reactions, and ABO incompatibilities.

Contraindications

Volume reduction is not a substitute for washing or for dosing with small aliquots.

Specific Volume-Reduced Components

RED BLOOD CELLS PLASMA REDUCED Ω (Volume Reduced Red Blood Cells)
RED BLOOD CELLS SUPERNATANT REDUCED Ω (Volume Reduced Red Blood Cells)
APHERESIS RED BLOOD CELLS PLASMA REDUCED Ω (Volume Reduced Red Blood Cells Pheresis)
APHERESIS RED BLOOD CELLS SUPERNATANT REDUCED Ω (Volume Reduced Red Blood Cells Pheresis)
PLATELETS PLASMA REDUCED Ω (Volume Reduced Platelets)
APHERESIS PLATELETS PLASMA REDUCED Ω (Volume Reduced Platelets Pheresis)
APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED SUPERNATANT REDUCED Ω (Volume Reduced Platelets Pheresis Platelet Additive Solution Added Leukocytes Reduced)

DO NOT COPY

Further Testing to Identify CMV-Seronegative Blood

Description

CMV-seronegative blood is selected by performing testing for antibodies to CMV. Transmission of CMV disease is associated with cellular blood components. Plasma, cryoprecipitate, and other plasma-derived blood components do not transmit CMV; therefore, CMV testing is not required for these components.

Indications

Transfusion of CMV-negative blood is indicated in CMV-seronegative recipients who are at risk for severe CMV infections. These at-risk groups include pregnant women and their fetuses, low-birthweight infants, hematopoietic progenitor cell transplant recipients, solid-organ transplant recipients, severely immunosuppressed recipients, and HIV-infected patients.

Leukocyte-reduced components are considered an alternative to CMV-seronegative transfusion.

DO NOT COPY

DO NOT COPY

Table 7. Summary Chart of Blood Components

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Red Blood Cells	Symptomatic anemia; red cell exchange transfusion.	Increases oxygen-carrying capacity.	Pharmacologically treatable anemia. Volume expansion.	Must be ABO compatible.	Infectious diseases. Hemolytic, septic/toxic, allergic, febrile reactions. Iron overload. TACO. TRALI. TA-GVHD.	As fast as patient can tolerate but less than 4 hours.
Deglycerolized Red Blood Cells	See Red Blood Cells. IgA deficiency with anaphylactoid/anaphylactic reaction.	See Red Blood Cells. Deglycerolization removes plasma proteins. Risk of allergic and febrile reactions reduced.	See Red Blood Cells.	See Red Blood Cells.	See Red Blood Cells. Hemolysis due to incomplete deglycerolization can occur.	See Red Blood Cells.

Continued

Table 7. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Red Blood Cells Leukocytes Reduced	See Red Blood Cells. Reduction of febrile reactions, HLA allo-immunization and CMV infection.	See Red Blood Cells.	See Red Blood Cells. Leukocyte reduction should not be used to prevent TA-GVHD.	See Red Blood Cells.	See Red Blood Cells. Hypotensive reaction may occur if bedside leukocyte-reduction filter is used.	See Red Blood Cells.
Washed Red Blood Cells	See Red Blood Cells. IgA deficiency with anaphylactoid/anaphylactic reaction. Recurrent severe allergic reactions to unwashed red cell products.	See Red Blood Cells. Washing reduces plasma proteins. Risk of allergic reactions is reduced.	See Red Blood Cells. Washing is not a substitute for leukocyte reduction.	See Red Blood Cells.	See Red Blood Cells.	See Red Blood Cells.

DO NOT COPY

Whole Blood	Symptomatic anemia with large volume deficit.	Increases oxygen-carrying capacity. Increases blood volume.	Condition responsive to specific component. Treatment of coagulopathy.	Must be ABO identical.	See Red Blood Cells.	As fast as patient can tolerate but less than 4 hours.
Fresh Frozen Plasma (FFP)	Clinically significant plasma protein deficiencies when no specific coagulation factor concentrates are available. TTP.	Source of plasma proteins, including all coagulation factors.	Volume expansion. Coagulopathy that can be more effectively treated with specific therapy.	Must be ABO compatible.	Infectious diseases. Allergic, febrile reactions. TACO. TRALI.	Less than 4 hours.
Plasma Frozen Within 24 Hours After Phlebotomy (PF24)	Clinically significant deficiency of stable coagulation factors when no specific coagulation factor concentrates are available. TTP.	Source of nonlabile plasma proteins. Levels of Factor VIII are significantly reduced and levels of Factor V and other labile plasma proteins are variable compared to FFP.	Volume expansion. Deficiencies of labile coagulation factors including Factors V and VIII and Protein C.	Must be ABO compatible.	See FFP.	Less than 4 hours.

DO NOT COPY

Continued

DO NOT COPY

Table 7. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy (PF24RT24)	Clinically significant deficiency of stable coagulation factors when no specific coagulation factor concentrates are available. TTP.	Source of nonlabile plasma proteins. Levels of Factor V, Factor VIII, and Protein S are significantly reduced, and levels of other labile plasma proteins are variable compared with FFP.	Volume expansion. Deficiencies of labile coagulation factors including Factors V and VIII and Protein S.	Must be ABO compatible.	See FFP.	Less than 4 hours.

Plasma Cryoprecipitate Reduced	TTP.	Plasma protein replacement for plasma exchange in TTP. Deficient in fibrinogen, vWF, Factors VIII and XIII. Deficient in high-molecular-weight vWF multimers as compared to FFP.	Volume expansion. Deficiency of coagulation factors known to be depleted in this product: fibrinogen, vWF, Factors VIII and XIII.	Must be ABO compatible.	See FFP.	Less than 4 hours.
Thawed Plasma Ω	Clinically significant deficiency of stable coagulation factors when no specific coagulation factor concentrates are available. TTP.	Source of plasma proteins. Levels and activation state of co-agulation proteins in thawed plasma are variable and change over time.	Not indicated as treatment for isolated coagulation factor deficiencies or specific plasma protein deficiencies.	Must be ABO compatible.	See FFP.	Less than 4 hours.

Continued

DO NOT COPY

Table 7. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Thawed Plasma Cryoprecipitate Reduced Ω	TTP.	Plasma protein replacement for plasma exchange in TTP. Deficient in fibrinogen, vWF, Factors VIII and XIII.	Volume expansion. Deficiency of coagulation factors known to be depleted in this product: fibrinogen, vWF, Factors VIII and XIII.	Must be ABO compatible.	See FFP.	Less than 4 hours.
Liquid Plasma	Initial treatment of patients undergoing massive transfusion.	Coagulation support for life-threatening trauma/ hemorrhages.	Not indicated as treatment for coagulation factor deficiencies where other products are available with higher factor concentrations.	Must be ABO compatible.	See FFP.	Less than 4 hours.

DO NOT COPY

		The profile of plasma proteins in Liquid Plasma is not completely characterized. Levels and activation state of coagulation proteins are dependent upon production methods and storage.				
Cryoprecipitated AHF; Pooled Cryoprecipitated AHF	Hypofibrinogenemia. Factor XIII deficiency. Second-line therapy of von Willebrand disease, hemophilia A, and uremic bleeding.	Provides fibrinogen, vWF, Factors VIII and XIII.	Not indicated if specific concentrates are available. Deficiency of any plasma protein other than those enriched in Cryoprecipitated AHF.		Infectious diseases. Allergic, febrile reactions.	Less than 4 hours.

Continued

DO NOT COPY

Table 7. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Platelets/Apheresis Platelets	Bleeding due to thrombocytopenia or platelet function abnormality including antiplatelet drugs. Prevention of bleeding from marrow hypoplasia.	Improves hemostasis. Apheresis platelets may be HLA (or other antigen) selected.	Plasma coagulation deficits. Some conditions with rapid platelet destruction (eg, ITP, TTP) unless life-threatening hemorrhage.	Should only use platelet-compatible filters (check manufacturer's instructions).	Infectious diseases. Septic/toxic, allergic, febrile reactions. TACO. TRALI. TA-GVHD.	Less than 4 hours.
Platelets Leukocytes Reduced/ Apheresis Platelets Leukocytes Reduced	See Platelets. Reduction of febrile reactions, HLA alloimmunization and CMV infection.	See Platelets.	See Platelets. Leukocyte reduction should not be used to prevent TA-GVHD.	See Platelets.	See Platelets.	See Platelets.

DO NOT COPY

Apheresis Platelets Platelet Additive Solution Added Leukocytes Reduced	See Platelets Leukocytes Reduced.	See Platelets.	See Platelets Leukocytes Reduced.	See Platelets.	See Platelets.	See Platelets.
Apheresis Granulocytes Ω	Neutropenia with infection, unresponsive to appropriate antibiotics.	Provides granulocytes and platelets.	Infection responsive to antibiotics, eventual marrow recovery not expected.	Must be ABO compatible. Use only filters specifically approved by a manufacturer for granulocyte transfusions (check manufacturer's instructions).	Infectious diseases. Hemolytic, allergic, febrile reactions. TACO. TRALI. TA-GVHD. Maintain caution. Pulmonary reactions may occur in patients receiving concomitant amphotericin B.	One unit over 2-4 hours. Closely observe for reactions.

Continued

DO NOT COPY

DO NOT COPY

*For all cellular components there is a risk the recipient may become alloimmunized and experience rapid destruction of certain types of blood products. Red-cell-containing components and thawed plasma (thawed FFP, thawed PF24, thawed PF24RT24, or Thawed Plasma) should be stored at 1-6 C. Platelets, Granulocytes, and thawed Cryoprecipitate should be stored at 20-24 C. Disclaimer: Please check the corresponding section of the *Circular* for more detailed information. TACO = transfusion-associated circulatory overload; TRALI = transfusion-related acute lung injury; TA-GVHD = transfusion-associated graft-vs-host disease; CMV = cytomegalovirus; TTP = thrombotic thrombocytopenic purpura; AHF = antihemophilic factor; ITP = immune thrombocytopenic purpura; vWF = von Willebrand factor; HLA = Human Leukocyte Antigen; IUT = intrauterine transfusion.

References

General

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: An updated report. Anesthesiology 2006;105:198-208.

Desmet L, Lacroix J. Transfusion in pediatrics. Crit Care Clin 2004;20:299-311.

Expert Working Group. Guidelines for red blood cell and plasma transfusion for adults and children. *CMAJ* 1997;156(11 Suppl):S1-S24.

Ferraris VA, Brown JB, Despotis GJ, et al. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg 2011;91:944-82.

Fung MK, Eder AF, Spitalnik SL, Westhoff CM, eds. Technical manual. 19th ed. Bethesda, MD: AABB, 2017.

Gajewski JL, Johnson VV, Sandler SG, et al. A review of transfusion practice before, during and after hematopoietic progenitor cell transplantation. Blood 2008;112:3036-47.

Gibson BE, Todd A, Roberts I, et al for the British Committee for Standards in Haematology Transfusion Task Force. Transfusion guidelines for neonates and older children. Br J Haematol 2004;124:433-53.

Harvey AR, Basavaraju SV, Chung KW, Kuehnert MJ. Transfusion-related adverse reactions reported to the National Healthcare Safety Network Hemovigilance Module, United States, 2010 to 2012. Transfusion 2015;55:709-18.

Herman JH, Manno CS, eds. Pediatric transfusion therapy. Bethesda, MD: AABB Press, 2002.

Kleinman S, Chan P, Robillard P. Risks associated with transfusion of cellular blood components in Canada. Transfus Med Rev 2003;17:120-62.

McFarland JG. Perioperative blood transfusions. Chest 1999;115:113S-21S.

Murdock J, Watson D, Doree CJ, et al. Drugs and blood transfusions: Dogma or evidence-based practice? Transfus Med 2009;19:6-15.

DO NOT COPY

Ooley PW, ed. Standards for blood banks and transfusion services. 30th ed. Bethesda, MD: AABB, 2016.

Popovsky MA, ed. Transfusion reactions. 4th ed. Bethesda, MD: AABB Press, 2012.

Roseff SD, Luban NL, Manno CS. Guidelines for assessing appropriateness of pediatric transfusion. Transfusion 2002;42: 1398-413.

Sazama K, DeChristopher PJ, Dodd R, et al. Practice parameter for the recognition, management, and prevention of adverse consequences of blood transfusion. Arch Pathol Lab Med 2000;124:61-70.

Wortham ST, Ortolano GA, Wenz B. A brief history of blood filtration: Clot screens, microaggregate removal and leukocyte reduction. Transfus Med Rev 2003;17:216-22.

Zou S, Notari EP 4th, Musavi F, et al. Current impact of the confidential unit exclusion option. Transfusion 2004;44:651-7.

Infectious Complications

AABB, Clinical Transfusion Medicine Committee, Heddle NM, et al. AABB committee report: Reducing transfusion-transmitted cytomegalovirus infections. Transfusion 2016;56: 1581-7.

Alter HJ, Stramer SL, Dodd RY. Emerging infectious diseases that threaten the blood supply. Semin Hematol 2007;44:32-41.

Benjamin RJ, Kline L, Dy BA, et al. Bacterial contamination of whole blood-derived platelets: The introduction of sample diversion and prestorage pooling with culture testing in the American Red Cross. Transfusion 2008;48:2348-55.

Dorsey K, Zou S, Schonberger LB, et al. Lack of evidence of transfusion transmission of Creutzfeldt-Jakob disease in a US surveillance study. Transfusion 2009;49:977-84.

Eder AF, Chambers LA. Noninfectious complications of blood transfusion. Arch Pathol Lab Med 2007;131:708-18.

Eder AF, Kennedy JM, Dy BA, et al. Limiting and detecting bacterial contamination of apheresis platelets: Inlet-line diversion and increased culture volume improve component safety. Transfusion 2009;49:1154-63.

Herwaldt B, Linden JV, Bosserman E, et al. Transfusion-associated babesiosis in the United States: A description of cases. Ann Intern Med 2011;155:509-19.

DO NOT COPY

Llewelyn CA, Hewitt PE, Knight RSG, et al. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet 2004;364:527-9.

MacGregor I. Prion protein and developments in its detection. Transfus Med 2001;11:3-14.

Montgomery SP, Brown JA, Kuehnert M, et al. Transfusion-associated transmission of West Nile virus, United States 2003 through 2005. Transfusion 2006;46:2038-46.

Petersen LR, Busch MP. Transfusion-transmitted arboviruses. Vox Sang 2010;98:495-503.

Stramer SL. Reacting to an emerging safety threat: West Nile virus in North America. Dev Biol (Basel) 2007;127:43-58.

Stramer SL, Glynn SA, Kleinman SH, et al. Detection of HIV-1 and HCV infections among antibody-negative blood donors by nucleic-acid amplification testing. N Engl J Med 2004;351: 760-8.

Stramer SL, Hollinger B, Katz LM, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion 2009;49(Suppl 2):1S-29S.

Vamvakas EC. Is white blood cell reduction equivalent to antibody screening in preventing transmission of cytomegalovirus by transfusion? A review of the literature and meta-analysis. Transfus Med Rev 2005;19:181-99.

Wilson K, Ricketts MN. A third episode of transfusion-derived vCJD (editorial). Lancet 2006;368:2037-9.

Wroe SJ, Pal S, Siddique D. Clinical presentation and pre-mortem diagnosis of variant Creutzfeldt-Jakob disease associated with blood transfusion: A case report. Lancet 2006;368:2061-7.

Zou S, Stramer SL, Dodd RY. Donor testing and risk: Current prevalence, incidence and residual risk of transfusion-transmissible agents in US allogeneic donations. Transfus Med Rev 2012;26:119-28.

Malaria

Kitchen AD, Chiodini PL. Malaria and blood transfusion. Vox Sang 2006;90:77-84.

Kopolovic I, Ostro J, Tsubota H, et al. A systematic review of transfusion-associated graft-versus-host disease. Blood 2015; 126:406-14.

DO NOT COPY

Mungai M, Tegtmeier G, Chamberland M, et al. Transfusion-transmitted malaria in the United States from 1963 through 1999. N Engl J Med 2001;344:1973-8.

TA-GVHD/Irradiation

Dwyre DM, Holland PV. Transfusion-associated graft-versus-host disease. Vox Sang 2008;95:85-93.

Leitman SF, Tisdale JF, Bolan CD, et al. Transfusion-associated GVHD after fludarabine therapy in a patient with systemic lupus erythematosus. Transfusion 2003;43:1667-71.

Moroff G, Luban NLC. The irradiation of blood and blood components to prevent graft-versus-host disease: Technical issues and guidelines. Transfus Med Rev 1997;11:15-26.

Przepiorka D, LeParc GF, Stovall MA, et al. Use of irradiated blood components. Practice parameter. Am J Clin Pathol 1996; 106:6-11.

Ruhl H, Bein G, Sachs UJH. Transfusion-associated graft-versus-host disease. Transfus Med Rev 2009;23:62-71.

TRALI

Bux J, Sachs UJH. The pathogenesis of transfusion-related acute lung injury (TRALI). Br J Haematol 2007;136:788-99.

Chapman CL, Stainsby D, Jones H, et al. Ten years of hemovigilance reports of transfusion-related acute lung injury in the United Kingdom and the impact of preferential use of male donor plasma. Transfusion 2009;49:440-52.

Eder AF, Herron RM Jr, Strupp A, et al. Effective reduction of transfusion-related acute lung injury risk with male-predominant plasma strategy in the American Red Cross (2006-2008). Transfusion 2010;50:1732-42.

Goldman M, Webert KE, Arnold DM, et al. Proceedings of a consensus conference: Towards an understanding of TRALI. Transfus Med Rev 2005;19:2-31.

Kleinman S, Caulfield T, Chan P, et al. Toward an understanding of transfusion-related acute lung injury: Statement of a consensus panel. Transfusion 2004;44:1774-89.

Kopko PM, Marshall CS, MacKenzie MR, et al. Transfusion-related acute lung injury: Report of a clinical look-back investigation. JAMA 2002;287:1968-71.

Rana R, Fernandez-Perez ER, Khan SA, et al. Transfusion-related acute lung injury and pulmonary edema in critically ill patients: A retrospective study. Transfusion 2006;46:1478-83.

DO NOT COPY

Sanchez R, Toy P. Transfusion-related acute lung injury: A pediatric perspective. Pediatr Blood Cancer 2005;45:248-55.

Silliman C, Ambruso D, Boshkov L. Transfusion-related acute lung injury. Blood 2005;105:2266-73.

Circulatory Overload

Andrzejewski C Jr, Casey MA, Popovsky MA. How we view and approach transfusion-associated circulatory overload: Pathogenesis, diagnosis, management, mitigation, and prevention. Transfusion 2013;53:3037-47.

Gajic O, Gropper MA, Hubmayr RD. Pulmonary edema after transfusion: How to differentiate transfusion-associated circulatory overload from transfusion-related acute lung injury. Crit Care Med 2006;34(5 Suppl):S109-13.

Popovsky MA. Transfusion and the lung: Circulatory overload and acute lung injury. Vox Sang 2004;87(Suppl 2):62-5.

Febrile Nonhemolytic Transfusion Reactions

Geiger TL, Howard SC. Acetaminophen and diphenhydramine premedication for allergic and febrile nonhemolytic transfusion reactions: Good prophylaxis or bad practice? Transfus Med Rev 2007;21:1-12.

King KE, Shirey RS, Thoman SK, et al. Universal leukoreduction decreases the incidence of febrile nonhemolytic transfusion reactions to RBCs. Transfusion 2004;44:25-9.

Paglino JC, Pomper GJ, Fisch GS, et al. Reduction of febrile but not allergic reactions to RBCs and platelets after conversion to universal prestorage leukoreduction. Transfusion 2004; 44:16-24.

Platelet Refractoriness

Blanchette VS, Johnson J, Rand M. The management of alloimmune neonatal thrombocytopenia. Baillieres Best Pract Res Clin Haematol 2000;13:365-90.

Dzik S. How I do it: Platelet support for refractory patients. Transfusion 2007;47:374-8.

Hod E, Schwartz J. Platelet transfusion refractoriness. Br J Haematol 2008;142:348-60.

Kiefel V, Bassler D, Kroll H, et al. Antigen-positive platelet transfusion in neonatal alloimmune thrombocytopenia (NAIT). Blood 2006;107:3761-3.

DO NOT COPY

McVey M, Cserti-Gazdewich CM. Platelet transfusion refractoriness responding preferentially to single donor aphaeresis platelets compatible for both ABO and HLA. Transfus Med 2010;20:346-53.

Refaai M, Phipps R, Spinelli S, et al. Platelet transfusions: Impact on hemostasis, thrombosis, inflammation and clinical outcomes. Thromb Res 2011;10:1012-16.

Sacher RA, Kickler TS, Schiffer CA, et al for the College of American Pathologists Transfusion Medicine Resource Committee. Management of patients refractory to platelet transfusion. Arch Pathol Lab Med 2003;127:409-14.

Slichter SJ, Davis K, Enright H, et al. Factors affecting post transfusion platelet increments, platelet refractoriness and platelet transfusion intervals in thrombocytopenic patients. Blood 2006;105:4106-14.

Citrate Toxicity

Dzik WH, Kirkley SA. Citrate toxicity during massive blood transfusion. Transfus Med Rev 1988;2:76-94.

Sihler KC, Napolitano LM. Complications of massive transfusion. Chest 2010;137:209-20.

Allergic and Anaphylactoid/Anaphylactic Reactions

Koda Y, Watanabe Y, Soejima M, et al. Simple PCR detection of haptoglobin gene deletion in anhaptoglobinemic patients with antihaptoglobin antibody that causes anaphylactic transfusion reactions. Blood 2000;95:1138-43.

Marti-Carvajal AJ, Sola I, Gonzalez LE, et al. Pharmacological interventions for the prevention of allergic and febrile non-haemolytic transfusion reactions. Cochrane Database Syst Rev 2010;6:CD007539.

Sandler SG. How I manage patients suspected of having had an IgA anaphylactic transfusion reaction. Transfusion 2006; 46:10-13.

Sandler SG, Eder A, Goldman M, et al. The entity of immunoglobulin A–related anaphylactic transfusion reactions is not evidence based. Transfusion 2015;55:199-204.

Savage W, Tobian A, Savage J, et al. Scratching the surface of allergic transfusion reactions. Transfusion 2013;53:1361-71.

Savage W, Tobian A, Savage J, et al. Transfusion and component characteristics are not associated with allergic transfusion reactions to apheresis platelets. Transfusion 2015;55:296-300.

DO NOT COPY

Tobian AAR, Savage WJ, Tisch DJ, et al. Prevention of allergic transfusion reactions to platelets and red blood cells through plasma reduction. Transfusion 2011;51:1676-83.

Vassallo RR. Review: IgA anaphylactic transfusion reactions. Part I. Laboratory diagnosis, incidence, and supply of IgA-deficient products. Immunohematol 2004;20:226-33.

Iron Overload

Majhail NS, Lazarus HM, Burns LJ. Iron overload in hematopoietic cell transplantation. Bone Marrow Transplant 2008;41: 997-1003.

Shander A, Sazama K. Clinical consequences of iron overload from chronic red blood cell transfusions, its diagnosis, and its management by chelation therapy. Transfusion 2010;50:1144-55.

Red Blood Cells

Bell EF, Strauss RG, Widness JA, et al. Randomized trial of liberal versus restrictive guidelines for red blood cell transfusion in preterm infants. Pediatrics 2005;115:1685-91.

Carless PA, Henry DA, Carson JL, et al. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion (review). Cochrane Database Syst Rev 2010;10: CD002042.

Carson JL, Grossman BJ, Kleinman S, et al for the AABB Clinical Transfusion Medicine Committee. Red blood cell transfusion: A clinical practice guideline from the AABB. Ann Intern Med 2012;157:49-58.

Carson JL, Terrin ML, Novek H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011;365:2453-62.

D'Alessandro A, Nemkov T, Hansen K, et al. Red blood cell storage in additive solution-7 preserves energy and redox metabolism: A metabolomics approach. Transfusion 2015;55: 2955-66.

Dumont L, Cancelas J, Maes L, et al. Overnight, room temperature hold of whole blood followed by 42-day storage of red blood cells in additive solution-7. Transfusion 2015;55: 485-90.

Gould S, Cimino MJ, Gerber DR. Packed red blood cell transfusion in the intensive care unit: Limitations and consequences. Am J Crit Care 2007;16:39-48.

DO NOT COPY

Hajjar LA, Vincent JL, Galas FR, et al. Transfusion requirements after cardiac surgery: The TRACS randomized controlled trial. JAMA 2010;304:1559-67.

Hébert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999;340:409-17.

Hébert PC, Yetisir E, Martin C. Is a low transfusion threshold safe in critically ill patients with cardiovascular disease? Crit Care Med 2001;29:227-34.

Istaphanous GK, Wheeler DS, Lisco SJ, et al. Red blood cell transfusion in critically ill children: A narrative review. Pediatr Crit Care Med 2011;12:174-83.

Josephson CD, Su LL, Hillyer KL, et al. Transfusion in the patient with sickle cell disease: A critical review of the literature and transfusion guidelines. Transfus Med Rev 2007;21:118-33.

Kirpalani H, Whyte RK, Andersen C, et al. The Premature Infants in Need of Transfusion (PINT) Study: A randomized, controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely low birth weight infants. J Pediatr 2006;149:301-7.

Lacroix J, Hébert PC, Hutchison JS, et al; TRIPICU Investigators; Canadian Critical Care Trials Group; Pediatric Acute Lung Injury and Sepsis Investigators Network. Transfusion strategies for patients in pediatric intensive care units. N Engl J Med 2007;356:1609-19.

Lavoie J. Blood transfusion risks and alternative strategies in pediatric patients. Paediatr Anaesth 2011;21:14-24.

Luban NL. Management of anemia in the newborn. Early Hum Dev 2008;84:493-8.

Napolitano LM, Kurek S, Luchette FA, et al. Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care. Crit Care Med 2009;37:3124-57.

Poole J, Daniels G. Blood group antibodies and their significance in transfusion medicine. Transfus Med Rev 2007;21:58-71.

Shander A, Fink A, Javidroozi M, et al. Appropriateness of allogeneic red blood cell transfusion: The international consensus conference on transfusion outcomes. Transfus Med Rev 2011;25:232-46.

DO NOT COPY

Stainsby D, MacLennan S, Thomas D, et al for the Standards in Haematology Writing Group. Guidelines for the management of massive blood loss. Br J Haematol 2006;135:634-41.

Veale M, Healey G, Sran A, et al. AS-7 improved in vitro quality of red blood cells prepared from whole blood held overnight at room temperature. Transfusion 2015;55:108-14.

Weiskopf RB, Viele MK, Feiner J, et al. Human cardiovascular and metabolic response to acute, severe isovolemic anemia. JAMA 1998;279:217-21.

Plasma, Cryoprecipitate, and Granulocytes

Blackall DP, Uhl L, Spitalnik SL, et al for the Transfusion Practices Committee. Cryoprecipitate-reduced plasma: Rationale for use and efficacy in the treatment of thrombotic thrombocytopenic purpura. Transfusion 2001;41:840-4.

Bostrom F, Sjödahl M, Wehlin L, et al. Coagulation parameters in apheresis and leukodepleted whole-blood plasma during storage. Transfusion 2007;47:460-3.

Burtelow M, Riley E, Druzin M, et al. How we treat: Management of life-threatening primary postpartum hemorrhage with a standardized massive transfusion protocol. Transfusion 2007;47:1564-72.

Callum JL, Karkouti K, Lin Y. Cryoprecipitate: The current state of knowledge. Transfus Med Rev 2009;23:177-88.

Cardigan R, Lawrie A, Mackie IJ, et al. The quality of fresh-frozen plasma produced from whole blood stored at 4 degrees C overnight. Transfusion 2005;45:1342-8.

Caudill JS, Nichols WL, Plumhoff EA, et al. Comparison of coagulation factor XIII content and concentration in cryoprecipitate and fresh-frozen plasma. Transfusion 2009;49:765-70.

Dara SI, Rana R, Afessa B, et al. Fresh frozen plasma transfusion in critically ill medical patients with coagulopathy. Crit Care Med 2005;33:2667-71.

Droubatchevskaia N, Wong MP, Chipperfield KM, et al. Guidelines for cryoprecipitate transfusion. BCMJ 2007;49: 441-5.

Dumont L, Cancelas J, Maes L, et al. The bioequivalence of frozen plasma prepared from whole blood held overnight at room temperature compared to fresh-frozen plasma prepared within eight hours of collection. Transfusion 2015;55:476-84.

Eder AF, Sebok MA. Plasma components: FFP, FP24, and thawed plasma. Immunohematol 2007;23:150-5.

DO NOT COPY

Gajic O, Dzik WH, Toy P. Fresh frozen plasma and platelet transfusion for nonbleeding patients in the intensive care unit. Crit Care Med 2006;34(5 Suppl):S170-3.

Galbusera M, Remuzzi G, Boccardo P. Treatment of bleeding in dialysis patients. Semin Dial 2009;22:279-86.

Gerhard GS, Hoffman SM, Williams EC. Coagulation parameters of ABO group-specific cryosupernatant. Am J Clin Pathol 1998;109:379-86.

Goldenberg NA, Manco-Johnson MJ. Pediatric hemostasis and use of plasma components. Best Pract Res Clin Haematol 2006;19:143-55.

Goldstein JN, Refaai MA, Milling TJ Jr, et al. Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal in patients needing urgent surgical or invasive interventions: A phase 3b, open-label, non-inferiority, randomised trial. Lancet 2015;385;2077-87.

Goodnough LT, Shander A. How we treat management of warfarin-associated coagulopathy in patients with intracerebral hemorrhage. Blood 2011;117:6091-9.

Gosselin RC, Marshall C, Dwyre DM, et al. Coagulation profile of liquid-state plasma. Transfusion 2013;53:579-90.

Hardy J-F, de Moerloose P, Samama CM. Massive transfusion and coagulopathy: Pathophysiology and implications of clinical management. Can J Anesth 2006;53:S40-S58.

Heim KF, Flesher TA, Stroncek DF, et al. The relationship between alloimmunization and posttransfusion granulocyte survival: Experience in a chronic granulomatous disease cohort. Transfusion 2011;51:1154-62.

Holland LL, Brooks JP. Toward rational fresh frozen plasma transfusion: The effect of plasma transfusion on coagulation test results. Am J Clin Pathol 2006;126:133-9.

Inbal A, Oldenburg J, Carcao M, et al. Recombinant factor XIII: A safe and novel treatment for congenital factor XIII deficiency. Blood 2012;119:5111-17.

Ketchum L, Hess JR, Hiippala S. Indications for early fresh frozen plasma, cryoprecipitate, and platelet transfusion in trauma. J Trauma 2006;60(6 Suppl):S51-8.

Kor DJ, Stubbs JR, Gajic O. Perioperative coagulation management–fresh frozen plasma. Best Pract Res Clin Anaesthesiol 2010;24:51-64.

Matijevic N, Wang Y-W, Cotton B, et al. Better hemostatic profiles of never-frozen liquid plasma compared with thawed

DO NOT COPY

fresh frozen plasma. J Trauma Acute Care Surg 2013;74:84-90.

Medical and Scientific Advisory Council of the National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. MASAC recommendation #249, May 19, 2017. New York: National Hemophilia Foundation, 2017. [Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-for-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders (accessed June 7, 2017).]

Neisser-Svae A, Trawnicek L, Heger A, et al. Five-day stability of thawed plasma: Solvent/detergent-treated plasma comparable with fresh-frozen plasma and plasma frozen within 24 hours. Transfusion 2016;56:404-9.

Nichols WL, Hultin MB, James AH, et al. von Willebrand disease (VWD): Evidence-based diagnosis, and management guidelines, the National Heart, Lung and Blood Institute (NHLBI) Expert Panel report (USA). Haemophilia 2008;14: 171-232.

Norda R, Andersson T, Edgren G, et al. The impact of plasma preparations and their storage time on short-term posttransfusion mortality: A population-based study using the Scandinavian Donation and Transfusion database. J Trauma Acute Care Surg 2012;72:954-60.

O'Neill EM, Rowley J, Hansson-Wicher M, et al. Effect of 24-hour whole-blood storage on plasma clotting factors. Transfusion 1999;39:488-91.

O'Shaughnessy DF, Atterbury C, Bolton-Maggs P, et al for the British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004;126:11-28. [Amendments and corrections in 2006;136: 514-16.]

Poterjoy BS, Josephson CD. Platelets, frozen plasma, and cryoprecipitate: What is the clinical evidence for their use in the neonatal intensive care unit? Semin Perinatol 2009;33:66-74.

Price TH. Granulocyte transfusion: Current status. Semin Hematol 2007;44:15-23.

Price TH, Boeckh M, Harrison RW, et al, Efficacy of transfusion with granulocytes from G-CSF/dexamethasone-treated

DO NOT COPY

donors in neutropenic patients with infection. Blood 2015;126:2153-61.

Ramsey G. Treating coagulopathy in liver disease with plasma transfusions or recombinant factor VIIa: An evidence-based review. Best Pract Res Clin Haematol 2006;19:113-26.

Roback JD, Caldwell S, Carson J, et al. Evidence-based practice guidelines for plasma transfusion. Transfusion 2010;50: 1227-39.

Scott EA, Puca KE, Bradley C, et al. Comparison and stability of ADAMTS13 activity in therapeutic plasma products. Transfusion 2007;47:120-5.

Scott EA, Puca K, Heraly JC, et al. Evaluation and comparison of coagulation factor activity in fresh-frozen plasma and 24-hour plasma at thaw and after 120 hours of 1 to 6 C storage. Transfusion 2009;49:1584-91.

Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: An evidence-based review. Transfusion 2005;45:1413-25.

Spence RK. Clinical use of plasma and plasma fractions. Best Pract Res Clin Haematol 2006;19:83-96.

Stanworth SJ, Brunskill SJ, Hyde CJ, et al. Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. Br J Haematol 2004;126:139-52.

Triulzi DJ. The art of plasma transfusion therapy. Transfusion 2006;46:1268-70.

Triulzi D, Gottschall J, Murphy E, et al. A multicenter study of plasma use in the United States. Transfusion 2015;55:1313-19; quiz, 1312.

Vamvakas EC, Pineda AA. Meta-analysis of clinical studies of the efficacy of granulocyte transfusions in the treatment of bacterial sepsis. J Clin Apher 1996;11:1-9.

Yazer MH, Cortese-Hassett A, Triulzi DJ. Coagulation factor levels in plasma frozen within 24 hours of phlebotomy over 5 days of storage at 1 to 6^0 C. Transfusion 2008;48:2525-30.

Platelets

Ashford P, Gulliksson H, Georgsen J, Distler P. Standard terminology for platelet additive solutions. Vox Sang 2010;98: 577-8.

DO NOT COPY

Blumberg N, Heal JM, Rowe JM. A randomized trial of washed red blood cell and platelet transfusions in adult leukemia. BMC Blood Disord 2004;4:6.

Brecher M. The platelet prophylactic trigger: When expectations meet reality. Transfusion 2007;47:188-91.

British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of platelet transfusions. Br J Haematol 2003;122:10-23.

British Committee for Standards in Haematology, Blood Transfusion Task Force. Transfusion guidelines for neonates and older children. Br J Haematol 2004;124:433-53.

Heal JM, Blumberg N. Optimizing platelet transfusion therapy. Blood Rev 2004;31:1-14.

Herve F, Tardivel R, Semana G, et al. Large scale use of platelet additive solution (PAS) reduces allergic type transfusion adverse events. Vox Sang 2007;93(Suppl 1):267.

Kerkhoffs JL, Eikenboom JC, Schipperus MS, et al. A multicenter randomized study of the efficacy of transfusion with platelets stored in platelet additive solution II versus plasma. Blood 2006;108:3210-15.

Kerkhoffs JL, van Putten WL, Novotny VM, et al. Clinical effectiveness of leucoreduced, pooled donor platelet concentrates, stored in plasma or additive solution with and without pathogen reduction. Br J Haematol 2010:150:209-17.

McCullough J. Overview of platelet transfusion. Semin Hematol 2010;47:235-42.

Schiffer CA, Anderson KC, Bennett CL. Platelet transfusion for patients with cancer: Clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001;l: 1519-38.

Schoenfeld H, Muhm M, Doepfmer U, et al. The functional integrity of platelets in volume-reduced platelet concentrates. Anesth Analg 2005;100:78-81.

Schoenfeld H, Spies C, Jakob C. Volume-reduced platelet concentrates. Curr Hematol Rep 2006;5:82-8.

Slichter SJ. Relationship between platelet count and bleeding risk in thrombocytopenic patients. Transfus Med Rev 2004; 18:153-67.

Slichter SJ, Kaufman RM, Assmann SF, et al. Dose of prophylactic platelet transfusions and prevention of hemorrhage. N Engl J Med 2010;362:600-13.

DO NOT COPY

Tinmouth A, Semple E, Shehata N, et al. Platelet immunopathology and therapy: A Canadian Blood Services research and development symposium. Transfus Med Rev 2006;20:294-314.

Webert KE, Cook RJ, Sigouin CS, et al. The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. Hematology 2006;91:1530-7.

DO NOT COPY

173011
October 2017