Circular of Information October 2017 revisions to create December 2021

- **Yellow Highlighted Text** – denotes text revised or removed in the October 2017 *Circular*
- **Red Text** – denotes new text in the December 2021 *Circular*

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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	**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 or prescribing health care professionals should be familiar with alternatives to 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 instructions for use should be reviewed for information pertaining to the use of	• "package insert" has been updated to "manufacturer's

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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 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.	transfusion devices (e.g., 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 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.	instructions for use" throughout the *Circular*
General Information for Whole Blood and All Blood Components	**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~~ 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.	**Donors** Blood and blood components described in this *Circular* are collected from blood donors for use in patients (allogeneic transfusions) or from patients donating for themselves (autologous transfusions). Most allogeneic donations are from volunteer blood donors and are labeled "volunteer donor". If donors receive monetary payment for a blood donation, the components must be labeled as "paid donor." All blood donors have satisfactorily completed a health assessment that includes a questionnaire on past and present illnesses and have satisfied minimum physiologic criteria. 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. Autologous donations 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."	• For consistency with the "Blood and Component Labeling" section, language on "Paid Donor" labeling was added here. • Information has been moved from the Red Blood Cell Components Available section. The remainder is captured under Required Testing of Blood Donations.

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	The unit must be labeled "FOR AUTOLOGOUS USE ONLY" if the donor fails to meet donor eligibility requirements or has reactive or positive test results for evidence of infection.	(below)
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~~	**Required Testing of Blood Donations** 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: 1. Nonreactive for antibodies to • human immunodeficiency virus (anti-HIV-1/2), • hepatitis C virus (anti-HCV), • human T lymphotropic virus (anti-HTLV-I/II), • hepatitis B core antigen (anti-HBc), and • *Trypanosoma cruzi* either on the current donation or at least one previous donation. 2. Nonreactive for hepatitis B surface antigen (HBsAg). 3. Nonreactive when tested using licensed nucleic acid tests (NAT) for: • hepatitis B virus (HBV) deoxyribonucleic acid (DNA), • hepatitis C virus (HCV) ribonucleic acid (RNA), • human immunodeficiency virus (HIV-1) RNA, • West Nile virus (WNV) RNA 4. Nonreactive when tested using a licensed NAT for *Babesia* (RNA and DNA) for blood collected in states where *Babesia* testing is required by FDA. 5. Nonreactive when tested using a licensed serologic test for *Treponema pallidum* (syphilis). A blood collector may perform additional testing for pathogens; such additional testing may be performed under an FDA approved investigational new drug (IND)	• Updated and converted to a numbered list. • The word "cell" was deleted to align with FDA language for licensed testing and EID Fact sheets. • Requirements for Babesia testing have been added. • This language was revised to

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~~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 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*.	application, using language for component labeling and/or revisions to the *Circular*, as required in the approved IND and provided 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 for evidence of infection as listed above. Subsequent units that are not tested will be labeled as "DONOR TESTED WITHIN THE LAST 30 DAYS." A biohazard label is required if these units have a reactive relevant transfusion-transmitted infection test result within the last 30 days. In addition, if these units are untested, they must be labeled as "DONOR UNTESTED." 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 donor eligibility and donation suitability requirements and test requirements as allogeneic donors and units. Tests for unexpected antibodies against red blood cell antigens (red cell) 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	reflect that the labeling and *Circular* language is provided by the IND sponsor. • Revised for clarity. • Information moved from the Red Blood Cells, Components Available.

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	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*.	
	Bacterial Risk Control Strategies for Platelets Consistent with the December 2020 FDA recommendations to control the risk of bacterial contamination, platelet components stored at room temperature have been: 1. tested and found negative for bacterial contamination using FDA recommended bacterial risk control strategies and FDA-cleared or approved devices, or 2. treated using FDA approved pathogen reduction technology. Note: Certain bacterial testing strategies include secondary or rapid testing performed prior to transfusion.	• New Section added to incorporate the requirements of the December 2020 Guidance, Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion; Guidance for Industry.
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, ~~w~~hole ~~b~~lood 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	**Blood and Component Labeling** All **Components Available** identified in this *Circular* are listed using the International Society of Blood Transfusion 128 (ISBT 128) product name. 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	• "Other recognized component names" have been removed throughout the *Circular*.

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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.	license number (if applicable) of the collection and processing location. 8. The expiration date, including the day, month, and year, and, if the dating period for the product is 72 hours or less, including any product prepared in a system that might compromise sterility, the hour of expiration. 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 proper recipient identification, this *Circular*, infectious disease risk, and prescription requirement. 14. Any sedimenting agent used during cytapheresis, if applicable.	• This language was revised to align with the language of the regulation. [21 CFR 606.121(c)(4)(i)]
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).	**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).	

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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. 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	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, United States Pharmacopeia (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. 10. Life-threatening reactions may 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. 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	• This was revised because warming devices may be used with products other than RBCs where hemolysis would not be applicable.

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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.	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 after entering the container. 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. Refer to the Section on **Further Processing** for additional information on: • Pathogen Reduction Technology • Leukocyte Reduction • Irradiation • Washing and Volume Reduction. Refer to the Section on **Additional Testing** for additional information on: • Identification of CMV-Seronegative Blood • Identification of Low Titer anti-A and/or anti-B Blood Products.	• The phrase “after entering the container” was added for clarity. • Section added
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	**Side Effects and Hazards for Whole Blood and All Blood Components** Transfusion-related adverse events may be voluntarily reported to the National Healthcare Safety Network (NHSN) hemovigilance program (https://www.cdc.gov/nhsn/index.html) unless there is a state requirement to report. The NHSN Biovigilance Component Hemovigilance Module Surveillance Protocol	• Link updated.

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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.	(https://www.cdc.gov/nhsn/pdfs/biovigilance/bv-hv-protocol-current.pdf) provides case classification criteria for Centers for Disease Control and Prevention-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. 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	**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 human leukocyte antigen (HLA) or platelet-specific antigens on transfused platelets. This is described in more detail in the section on platelets. 3. *Febrile nonhemolytic reaction* is typically manifested by a temperature elevation of ≥1 C or 1.8 F occurring during or within 4 hours after a transfusion and in the absence of any other pyretic 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	• Revised to 1.8 F for accuracy.

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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 react*ions, 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	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 (i.e., 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	

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circulatory overload. Various stimuli in blood components, most commonly white ~~blood~~ cell ~~(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.	circulatory overload. Various stimuli in blood components, most commonly white cell 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 anti-leukocyte 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 anti-leukocyte 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 or female donors who have tested negative for the presence of HLA Class I and/or II antibodies 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.	• Language added
Immunologic Complications, Delayed 1. *Delayed hemolytic reaction* is described in detail in the section on components containing red cells.	**Immunologic Complications, Delayed** 1. *Delayed hemolytic reaction* is described in detail in the section on components containing red cells.	

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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* is a rare syndrome characterized by the development of dramatic, sudden, and self-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	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* is a rare syndrome characterized by the development of dramatic, sudden, and self-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	

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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.	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 (e.g., 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 (e.g., fludarabine, cladribine) or certain other biological immunomodulators (e.g., 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 reduction technology may also be used as an alternative to irradiation to prevent TA-GVHD if the pathogen reduction technology has been shown to inactivate residual lymphocytes.	• Language updated to reflect current terminology.
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	**Nonimmunologic Complications** *Because Whole Blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents [e.g., viruses, bacteria, parasites, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease agent (CJD)].* Also, septic and toxic reactions can result from transfusion of bacterially contaminated blood and blood components. Careful donor selection, available laboratory tests, and pathogen reduction technology do not totally eliminate these hazards. Such complications are infrequent but may be life-threatening. Infectious disease transmission may	• Language consistent with the Aug 2020 CJD guidance • Sentence moved up.

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of blood. Donor selection 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 (≥2C or ≥3.5 F increase in temperature),	occur despite careful selection of donors and testing of blood. Donor selection 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 Required Testing of Blood Donations). For *other infectious agents* (e.g., *Plasmodia* spp.) there are no licensed tests available for donor testing; however, other screening measures for possible exposure or history of malaria, or use of pathogen reduction technology may mitigate the risk of transfusion-transmitted infections. 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. 1. *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 grams (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. 2. *Bacterial sepsis* occurs rarely but can cause acute, severe, sometimes life-threatening effects. Onset of high fever (≥2C or ≥3.5 F increase in temperature),	• This language was revised and moved up. • *Babesia* spp removed from the list of infectious agents for which there is no test and added to the "Testing of Donor Blood" section. • *Leishmania* spp removed and section revised per FDA's recommendation.

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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 posttransfusion 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*	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. Platelet components are controlled for bacterial contamination, however 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 (e.g., *Yersinia enterocolitica*) and those using citrate as a nutrient have been associated with components containing red cells. A variety of pathogens, as well as skin contaminants, have been found in platelet components. Multiplication of gram-negative bacteria in blood components has also caused endotoxemia in recipients. 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 posttransfusion 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.	• FDA: Skin contaminants are the most common contamination in red cells; *Yersinia* is rare.

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(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 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,	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 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	

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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.	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.~~	FDA's webpage, Transfusion/Donation Fatalities: Reporting requirements can be found on the FDA's webpage, Transfusion/Donation Fatalities: "Section 606.170(b) of Title 21, Code of Federal Regulations (21 CFR 606.170(b)), requires that facilities notify the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ), as soon as possible after confirming a complication of blood collection or transfusion to be fatal. The collecting facility is to report donor fatalities, and the compatibility testing facility is to report recipient fatalities. The regulation also requires the reporting facility to submit a report of the investigation within 7 days after the fatality." FDA's August 2021 Guidance, Notifying FDA of Fatalities Related to Blood Collection or Transfusion; Guidance for Industry, provides recommendations and additional information, including this clarification: "We recommend that you submit the initial notification by email, if possible, and if you do so, you will receive an email	• This section was reformatted to reflect information in the Aug 2021 Guidance, Notifying FDA of Fatalities Related to Blood Collection or Transfusion.

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	confirmation receipt from us. If email is not feasible, please notify us by telephone or facsimile. We cannot access notification outside of customary working hours unless you use email or telephone." When reporting a fatality during or outside of regular business hours, the reporting facility may submit initial notification by leaving a voice message, sending an email, or facsimile to the Division of Inspections and Surveillance. • Email: fatalities2@cber.fda.gov • Telephone/voice-mail number: 240-402-9160 • Fax number: 301-837-6256, Attn: CBER Fatality Program Manager • Express mail address: See below FDA will contact you as soon as possible to obtain more detailed information. This does not replace the 7-day written report regarding the fatality and all related information as described in 21 CFR 606.170(b). The 7-day follow up report may be submitted by email, facsimile, or express mail. Express mail address for 7-day follow up reports: U.S. Food and Drug Administration Office of Compliance and Biologics Quality/CBER Attn: Fatality Program Manager 10903 New Hampshire Ave. Bldg. 71, Rm. 3128 Silver Spring, MD 20993-0002 Refer to FDA's website for information (https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities) and August 2021 Guidance for Industry, Notifying FDA of Fatalities Related to Blood Collection or Transfusion.	

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	Whole Blood **Overview** Whole Blood is transfused to increase oxygen-carrying capacity in patients whom physiologic compensatory mechanisms are inadequate to maintain normal tissue oxygenation. Whole Blood may be transfused in an emergency situation or other clinical setting that necessitates delivery of multiple blood components simultaneously. *Description* 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), drawn in a sterile container that includes an anticoagulant solution licensed for this component. Whole Blood is prepared in an aseptic manner in a ratio of 14 milliliters (mL) of anticoagulant-preservative solution per 100 mL of whole blood targeted for collection. Whole blood contains approximately 5.5 x 10^{10} platelets. The volume of plasma in Whole Blood is about 170 ml or greater and contains non-labile clotting factors. Whole Blood must be stored at 1-6 C for an interval (“shelf life”) determined by the properties of the anticoagulant-preservative solution (see Table 1). Refer to the Section on **Further Processing** for additional information on: • Leukocyte Reduction Refer to the Section on **Additional Testing** for additional information on: • Identification of CMV-Seronegative Blood • Identification of Low Titer anti-A and/or anti-B Blood Products	• New Section for Whole Blood was added.

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	Actions Whole Blood increases the recipient's oxygen-carrying capacity by increasing the mass of circulating Red Blood Cells. In addition to Red Blood Cells, Whole Blood provides plasma, and platelets which provide volume expansion and may contribute to hemostasis. *Indications* Whole Blood may be indicated in life-threatening hemorrhage where oxygen carrying capacity, non-labile coagulation factors, platelets and volume expansion are needed. *Contraindications* Whole Blood should not be used solely for volume expansion or to increase oncotic pressure of circulating blood. *Dosage and Administration* Whole Blood contains enough hemoglobin to increase the hemoglobin concentration in an average-sized adult by approximately 1 gram/deciliter (g/dL) (increase hematocrit by 3%). Whole Blood must be ABO group-specific with the recipient. In life-threatening situations, group Whole Blood may be administered to non-O patients provided facilities have policies and procedures to define low titer cut-off for anti-A and anti-B titers. The transfusing facility must have policies and procedures in place addressing specific indications for use, product	

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	specifications, administration instructions and a defined maximum number of units to be transfused to each patient. 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. *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 4 below for discussion of nonimmunologic hemolysis). The most common cause of severe, acute hemolytic reactions is 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, 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	

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	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 (i.e., complete hemolysis of incompatible red cells). Treatment includes measures to maintain or correct arterial blood pressure; correct coagulopathy, if present; and promote or maintain renal function. 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 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, serologic 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	

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	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 Red Blood Cell components (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. **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 when using warming devices not cleared or approved by FDA, mixture of blood with hypotonic solutions, or transfusion under high pressure through small-gauge or defective needles. **Components Available** **WHOLE BLOOD** is prepared from 400-550 mL of blood collected into the appropriate volume of anticoagulant solution. **WHOLE BLOOD LEUKOCYTES REDUCED is** prepared from Whole Blood by a method resulting in a final product containing $<5.0 \times 10^6$ leukocytes and ≥85% of the	

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	original whole blood content. Leukocyte-reduced Whole Blood may be prepared using a platelet-sparing leukocyte reduction filter.	
Red Blood Cell Components	**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 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.~~	**Overview** RBCs are transfused to increase oxygen-carrying capacity in patients whom physiologic compensatory mechanisms are inadequate to maintain normal tissue oxygenation. Red cells contain hemoglobin and serve as the primary agent for transport of oxygen to tissues. The primary red-cell-containing transfusion component is RBCs. This component is prepared by centrifugation or sedimentation of Whole Blood to remove much of the plasma. RBC components can also be prepared by apheresis methods. *Description* 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 at 1-6 C 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 milliliters (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. After plasma is removed, the resulting component is RBCs,	• Information on Whole Blood was relocated to the new Whole Blood section throughout the Red Blood Cell Component section. • This section was revised and reformatted. • Storage temperature added. • Deleted because it relates to manufacturing.

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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.	which has a hematocrit between 65% to 80% and a usual volume between 225 mL and 350 mL. Red Blood Cells Additive Solution (AS) may be mixed with the red cells remaining after removal of nearly all of the plasma to extend the shelf life (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. Refer to the Section on **Further Processing** for additional information on: • Pathogen Reduction Technology • Leukocyte Reduction • Irradiation • Washing and Volume Reduction Refer to the Section on **Additional Testing** for additional information on: • Identification of CMV-Seronegative Blood • Identification of Low Titer anti-A and/or anti-B Blood Products	
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.	*Actions* RBC components 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; however, 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 AS are the most used red cell product and have limited residual plasma.	
Indications	*Indications*	

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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.	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.	
Contraindications Red-cell-containing components should not be used to treat anemias that can be corrected with specific hematinic medications such as iron, vitamin B12, folic acid, or erythropoietin. RBCs ~~or Whole Blood~~ should not be used solely for volume expansion or to increase oncotic pressure of circulating blood.	*Contraindications* Red-cell-containing components should not be used to treat anemias that can be corrected with specific hematinic medications such as iron, vitamin B12, folic acid, or erythropoietin. RBCs 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.	*Dosage and Administration* Each unit of RBCs contains enough hemoglobin to increase the hemoglobin concentration in an average-sized adult by approximately 1 gram/deciliter (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. 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	The sentence, "RBCs, which contain a reduced volume of antibody-containing plasma, need only be ABO compatible." Was removed.

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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.	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 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	*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 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, associated forms and labels must be reviewed promptly to detect possible errors. A postreaction blood sample, preferably drawn from a site other than the	

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along with the implicated unit of blood and administration set. 2. *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.	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 (i.e., complete hemolysis of incompatible red cells). Treatment includes measures to maintain or correct arterial blood pressure; correct coagulopathy, if present; and promote or maintain renal function. 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 or bilirubin may be noted. Most delayed hemolytic reactions have a benign course and require no	

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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, serologic 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. 3. 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. 4. **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. 5. **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	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, serologic 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. 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 milligrams (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,	

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applicable. 6. **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.	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 when using warming devices not cleared or approved by FDA, mixture of blood with hypotonic solutions, or transfusion under high pressure through small-gauge or defective needles.	• Language was revised to reflect that FDA approves the device not the "method".
Components Available	**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. Separation 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.	**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. Separation may be done at any time during the allowable shelf life. RBCs 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	**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 AS 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%. RBCs in an AS have lower viscosity than RBCs, and flow through administration systems in a manner more comparable to that of Whole Blood. RBCs stored with an AS have an extended shelf life.	

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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.	**RED BLOOD CELLS LEUKOCYTES REDUCED and 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.	**APHERESIS RED BLOOD CELLS** 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)~~**	**APHERESIS RED BLOOD CELLS LEUKOCYTES REDUCED and APHERESIS RED BLOOD CELLS ADENINE SALINE ADDED LEUKOCYTES REDUCED**	

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and APHERESIS RED BLOOD CELLS ADENINE SALINE ADDED LEUKOCYTES 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.	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.	**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.	**FROZEN RED BLOOD CELLS and FROZEN REJUVENATED RED BLOOD CELLS** are prepared by adding glycerol to red cells as a cryoprotective agent before freezing at -65 C or colder. The glycerol must be removed from the thawed component before it is infused. Frozen RBCs stored for up to 10 years. Some rare units may be stored frozen beyond 10 years, provided there is an exceptional medical need for the units. Frozen storage is especially suitable for red cells with unusual antigenic phenotypes.	• Temperature added. • Revised for clarity.

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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. 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.	**DEGLYCEROLIZED RED BLOOD CELLS** is the form in which cryopreserved red cells (Frozen RBCs) 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. 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 stored at 1-6 C and infused within a 2-week interval after thawing and as directed by the manufacturer's instructions for use.	• Storage temperature added and sentence to follow manufacturer's instructions for use.
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.	**REJUVENATED RED BLOOD CELLS** may be prepared from red cells stored at 1-6 C and prepared with citrate-phosphate-dextrose (CPD) and CPD Adenine Solution (CPDA-1) up to 3 days after expiration. RBCs stored in	• Temperature added and modified to reflect language in package insert.

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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.	CPD/AS-1 or CP2D/AS-3 may be rejuvenated up to, but not exceeding 42 days of uninterrupted storage at 1-6 C. 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.	**DEGLYCEROLIZED REJUVENATED RED BLOOD CELLS** is the form in which rejuvenated, cryopreserved red cells (Frozen Rejuvenated RBCs) 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 donor eligibility requirements and test requirements as allogeneic donors and units.~~		This information was revised and moved to: • General Information for Whole Blood • All Blood Components and Required Testing of Blood Donations
~~13. See section on Further Processing.~~		• Moved to *Description*.

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Plasma Components	**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).	**Overview** Plasma is the fluid 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). Refer to the Section on **Further Processing** for additional information on: • Pathogen Reduction Technology and Components Available Refer to the Section on **Additional Testing** for additional information on: • Identification of Low Titer anti-A and/or anti-B Blood Products	
Fresh Frozen Plasma	**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	*Description* FFP is prepared from a whole blood or apheresis collection and frozen at –18 C or colder within the time frame as specified in the manufacturer's instructions for use of 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. FFP contains plasma proteins, including all coagulation factors. FFP contains normal levels of the labile	

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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.~~	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).	
Action FFP serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins.	*Actions* FFP serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins.	
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.	*Indications* FFP is indicated in the following conditions: 1. Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors (e.g., 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~~	*Contraindications* 1. When coagulopathy can be corrected more effectively with specific therapy, such as vitamin K and Prothrombin complex concentrate (PCC) for	• *Contraindications* section was revised.

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~~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.~~	urgent Vitamin K Antagonist (VKA) reversal, Cryoprecipitated AHF or Pathogen Reduced Cryoprecipitated Fibrinogen Complex for hypofibrinogenemia, or specific coagulation factor concentrates when available. Specific reversal agents should be used for non-VKA anticoagulants (e.g., Idarucizumab for Dabigatran or Andexanet for Factor Xa inhibitors such as rivaroxaban and apixaban related life-threatening bleeding). 2. When blood volume can be safely and adequately replaced with other volume expanders.	
	Relative contraindications To correct a minimally elevated international normalized ratio (INR). An INR value between 1.5 - 1.7 represents at least 30% of coagulation factor levels, which should allow for normal hemostasis. Transfusion of a standard dose of plasma (~15 mL/kilogram (kg)) to a patient with an INR of 1.7 may not normalize the INR.	• New *Relative Contraindications* section added.
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.	*Dosage and Administration* Compatibility tests prior to transfusion are not necessary. Plasma must be ABO compatible with the recipient's red cells. Compatibility with RhD is not necessary in plasma transfusion. The volume transfused depends on the clinical situation and patient size and may be guided by laboratory assays of coagulation function. 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.	• Language "Compatibility with RhD is not necessary" added. • Moved to *Side Effects and Hazards*.
Side Effects and Hazards	*Side Effects and Hazards* Do not use FFP if there is evidence of container breakage or of thawing during storage.	• Moved from *Dosage and Administration*.

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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.	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.	
	Components Available **FRESH FROZEN PLASMA** **APHERESIS FRESH FROZEN PLASMA**	
Plasma Frozen Within 24 Hours After Phlebotomy	**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).	*Description* Plasma Frozen Within 24 Hours After Phlebotomy (PF24) is prepared from a Whole Blood or apheresis collection. The anticoagulant solution used, and the component volume are indicated on the label. On average, PF24 contains 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; a disintegrin and metalloprotease with thrombospondin type 1 motifs 13 (ADAMTS13); fibrinogen; and Factors II, VII, IX, X, and XI remain at 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. 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.	*Actions* PF24 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	*Indications*	

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See Fresh Frozen Plasma.	For Plasma Frozen Within 24 Hours After Phlebotomy *Indications* see Fresh Frozen Plasma *Indications*, page 20.	
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.	*Contraindications* For Plasma Frozen Within 24 Hours After Phlebotomy *Contraindications* see Fresh Frozen Plasma *Contraindications* and *Relative Contraindications*, page 20. 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.	*Dosage and Administration* For Plasma Frozen Within 24 Hours After Phlebotomy *Dosage and Administration* see Fresh Frozen Plasma *Dosage and Administration*, page 23.	
Side Effects and Hazards See Fresh Frozen Plasma.	*Side Effects and Hazards* For Plasma Frozen Within 24 Hours After Phlebotomy *Side Effects and Hazards* see Fresh Frozen Plasma *Side Effects and Hazards*, page 23.	
Components Available 1. **PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY (~~PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY~~)** is prepared from a whole blood 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.~~	**Components Available** **PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY** is prepared from a Whole Blood collection and must be separated and placed at –18 C or colder within 24 hours from whole blood collection. **APHERESIS PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY** 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.	
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**	
Description	*Description*	

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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.~~	Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy (PF24RT24) 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, PF24RT24 contains 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. 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).	
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.	*Actions* 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.~~	*Indications* For Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy *Indications* see Fresh Frozen Plasma *Indications*.	
Contraindications	*Contraindications*	

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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.	For Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy *Contraindications* see Fresh Frozen Plasma *Contraindications* and *Relative Contraindications*. 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.~~	*Dosage and Administration* For Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy *Dosage and Administration* see Fresh Frozen Plasma *Dosage and Administration.*	
Side Effects and Hazards ~~See Fresh Frozen Plasma.~~	*Side Effects and Hazards* For Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy *Side Effects and Hazards* see Fresh Frozen Plasma *Side Effects and Hazards.*	
	Components Available **PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY HELD AT ROOM TEMPERATURE UP TO 24 HOURS AFTER PHLEBOTOMY** **APHERESIS PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY HELD AT ROOM TEMPERATURE UP TO 24 HOURS AFTER PHLEBOTOMY**	
Plasma Cryoprecipitate Reduced	**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	*Description* Plasma Cryoprecipitate Reduced is prepared from Whole Blood-dervived or apheresis-collected FFP (frozen at –18 C or colder within 8 hours of collection) after thawing and centrifugation and removal of the cryoprecipitate. The remaining product is plasma that is reduced in fibrinogen, Factor VIII, Factor XIII, vWF and cryoglobulin. This supernatant plasma must be refrozen within 24 hours of	• Temperature and time added. • The word “deficient” was replaced by “reduced.” • “fibronectin” was removed.

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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.	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 4 days after the initial 24-hour post-thaw period has elapsed 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.	*Actions* 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.	*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 for transfusion support of patients with appropriate clinical indications when specific plasma concentrates and/or other plasma products are not available.	• Language added.
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.	*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, PF24RT24 or Thawed Plasma.	• PF24/RT24 added.
Dosage and Administration ~~See Fresh Frozen Plasma~~.	*Dosage and Administration* For Plasma Cryoprecipitate Reduced *Dosage and Administration* see Fresh Frozen Plasma *Dosage and Administration*, page 23.	
Side Effects and Hazards ~~See Fresh Frozen Plasma.~~	*Side Effects and Hazards* For Plasma Cryoprecipitate Reduced *Side Effects and Hazards* see Fresh Frozen Plasma *Side Effects and Hazards*, page 24.	
	Component Available	

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	PLASMA CRYOPRECIPITATE REDUCED **APHERESIS PLASMA CRYOPRECIPITATE REDUCED**	
~~**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.~~		• The Header "Liquid Plasma" and *Description* were removed.
	Thawed Plasma Ω	• Component header added
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).	*Description* 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 post-thaw 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.	*Actions* 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~~	*Indications* For Thawed Plasma *Indications* see Fresh Frozen Plasma *Indications*, page 20.	• Revised

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~~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.	*Contraindications* For Thawed Plasma *Contraindications* see Fresh Frozen Plasma *Contraindications* and *Relative Contraindications*. 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.	
Dosage and Administration ~~See Fresh Frozen Plasma.~~	*Dosage and Administration* For Thawed Plasma *Dosage and Administration*, see Fresh Frozen Plasma *Dosage and Administration*, page 23.	
Side Effects and Hazards ~~See Fresh Frozen Plasma.~~	*Side Effects and Hazards* For Thawed Plasma *Side Effects and Hazards*, see Fresh Frozen Plasma *Side Effects and Hazards*, page 23.	
	Components Available **THAWED PLASMA Ω**	
	Thawed Plasma Cryoprecipitate Reduced Ω	• Component header added
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.	*Description* 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 post-thaw period has elapsed. The volume is indicated on the label. Thawed Plasma Cryoprecipitate Reduced is deficient in fibrinogen, Factor VIII, Factor XIII, vWF, and cryoglobulin, and contains variable levels of albumin, ADAMTS13, and Factors II, V, VII, IX, X, and XI.	• "fibronectin" removed.
Action	*Action* For Thawed Plasma Cryoprecipitate Reduced *Actions*, see	

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~~See Plasma Cryoprecipitate Reduced.~~	Plasma Cryoprecipitate Reduced *Actions*, page 25.	
Indications ~~See Plasma Cryoprecipitate Reduced.~~	*Indications* For Thawed Plasma Cryoprecipitate Reduced *Indications*, see Plasma Cryoprecipitate Reduced *Indications* page 25.	
Contraindications ~~See Plasma Cryoprecipitate Reduced.~~	*Contraindications* For Thawed Plasma Cryoprecipitate Reduced *Contraindications*, see Plasma Cryoprecipitate Reduced *Contraindications*, page 25.	
Dosage and Administration ~~See Fresh Frozen Plasma.~~	*Dosage and Administration* For Thawed Plasma Cryoprecipitate Reduced *Dosage and Administration*, see Fresh Frozen Plasma *Dosage and Administration* page 23.	
Side Effects and Hazards ~~See Fresh Frozen Plasma.~~	*Side Effects and Hazards* For Thawed Plasma Cryoprecipitate Reduced *Side Effects and Hazards*, see Fresh Frozen Plasma *Side Effects and Hazards*, page 23.	
	Components Available **THAWED PLASMA CRYOPRECIPITATE REDUCED Ω**	
	Liquid Plasma	• Component header added
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.	*Description* Liquid plasma is prepared from Whole Blood and stored at 1-6 C. Liquid Plasma expires 5 days from end of Whole Blood dating period. The profile and activity of plasma proteins involved in coagulation of 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.	

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~~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.	*Actions* This component serves as a source of plasma proteins. Levels and activation state of coagulation proteins are variable and change over time.	
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.	*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.	*Contraindications* For Liquid Plasma *Contraindications*, see Fresh Frozen Plasma *Contraindications*. 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.~~	*Dosage and Administration* For Liquid Plasma *Dosage and Administration*, see Fresh Frozen Plasma *Dosage and Administration*, page 23.	
Side Effects and Hazards ~~See Fresh Frozen Plasma.~~	*Side Effects and Hazards* For Liquid Plasma *Side Effects and Hazards*, see Fresh Frozen Plasma *Side Effects and Hazards*, page 23.	
	Components Available **LIQUID PLASMA**	
Cryoprecipitated Components	**Cryoprecipitated Antihemophilic Factor**	
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~~	*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 at -18 C or colder within 1 hour after removal from the refrigerated centrifuge. Cryoprecipitated AHF contains fibrinogen, Factor VIII,	• Temperature added. • "fibronectin" removed.

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~~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.	Factor XIII, and vWF. Each unit of Cryoprecipitated AHF should contain ≥80 International Units (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~~.	*Actions* Cryoprecipitate serves as a source of fibrinogen, Factor VIII, Factor XIII, and vWF.	• "fibronectin" removed.
Indications This component is used in the control of bleeding associated with fibrinogen deficiency, and when recombinant and/or 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.~~	*Indications* This component is used in the control of bleeding associated with fibrinogen deficiency, and when recombinant and/or virally inactivated preparations of fibrinogen, Factor VIII, Factor XIII, or vWF are not readily available. It is also indicated as second-line therapy for von Willebrand Disease (vWD) and hemophilia A (Factor VIII deficiency). Coagulation factor preparations other than Cryoprecipitated AHF are preferred for management of vWD, 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 Cryoprecipitated AHF. Use of this component may be considered for control of uremic bleeding after other modalities have failed.	• "fibrinogen" added. • "fibronectin" removed.
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	*Contraindications* Do not use this component unless results of laboratory studies indicate a specific hemostatic defect for which this product is indicated. Cryoprecipitated AHF should not be used if virus-inactivated specific factor concentrates or	

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preparations are available for management of patients with ~~von Willebrand disease~~, hemophilia A, or Factor XIII deficiency.	recombinant factor preparations are available for management of patients with vWD, 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 fibrinogen kinetics; therefore, patients receiving cryoprecipitate as fibrinogen replacement in conditions associated with increased fibrinogen turnover should be monitored with fibrinogen assays.	*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 water bath 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 (e.g., 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 fibrinogen kinetics; therefore, patients receiving cryoprecipitate as fibrinogen replacement in conditions associated with increased fibrinogen turnover should be monitored with fibrinogen assays.	

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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.	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 vWD, 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. Patients receiving this treatment 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.~~	*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 Cryoprecipitated AHF is used, the recipient may develop a positive DAT.	
Components Available **1. CRYOPRECIPITATED AHF ~~(CRYOPRECIPITATED AHF)~~**	**Components Available** **CRYOPRECIPITATED AHF**	

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2. APHERESIS CRYOPRECIPITATED AHF ~~(Cryoprecipitated AHF PHERESIS)~~ **3. POOLED CRYOPRECIPITATED AHF ~~(CRYOPRECIPITATED AHF, POOLED)~~**	**APHERESIS CRYOPRECIPITATED AHF** **POOLED CRYOPRECIPITATED AHF**	
Platelet Components	**Platelet Components**	
Overview	**Overview** Platelet transfusions are administered to treat patients with thrombocytopenia, dysfunctional platelet disorders, active platelet-related bleeding, or administered prophylactically to patients at serious risk of bleeding. This section applies to all platelet components stored at room temperature 20-24 C, in plasma or platelet additive solution (PAS), including platelets manufactured by automated methods (apheresis platelets), as well as WBD single and pooled (pre-storage and post-storage) platelet components. Refer to the Section on **Further Processing** for additional information on • Pathogen Reduction Technology and Components Available • Leukocyte Reduction • Irradiation • Washing and Volume Reduction Refer to the Section on **Additional Testing** for additional information on: • Identification of CMV-Seronegative Blood • Identification of Low Titer anti-A and/or anti-B Blood Products	• Overview language added.
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~~	***Description*** Platelets for transfusion are manufactured using automated collection by apheresis ("Apheresis Platelets") or from whole blood collections ("WBD Platelets"). One unit of WBD platelets typically contains $\geq 5.5 \times 10^{10}$ platelets suspended in 40 to 70 mL of plasma. WBD platelets may be transfused as single units or as a pool. WBD platelets may be pooled pre-	• This section was revised for clarity.

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~~blood collection usually contains ≥5.5 × 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 ≥3.0 × 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.	storage using a closed system or post-storage using an open system. A pool of approximately 6 units of WBD platelets is considered the therapeutic equivalent of one unit of apheresis platelets which usually contains ≥3.0 × 10^{11} platelets. Platelet components may contain a varying number of leukocytes depending upon the manufacturing method. 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 WBD platelets than with apheresis platelets. Platelet products are stored at room temperature, 20-24 C with continuous gentle agitation. Platelet products stored in plasma at room temperatures contain near-normal levels of stable coagulation factors. To control the risk of bacterial contamination, platelets are either pathogen reduced or tested for bacteria. FDA has provided recommendations for bacterial risk control strategies in the December 2020 Final Guidance, "Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion." Based on the strategy used, platelets may either have a 5-, 6-, or 7-day expiration. Note that certain testing strategies may require secondary testing prior to transfusion. For more information on bacterial contamination risk refer to *Side Effects and Hazards* section below and FDA Guidance titled "*Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion."*	• Language was added to describe that one unit of apheresis platelets is the therapeutic equivalent of 6 units of WBD platelets. • Added to address labeling requirements of the December 2020 *Bacterial Risk Control Strategies for Blood Collection Establishments and transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion*.
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	*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	

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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.	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 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).	*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 (i.e., 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 least 50,000/microliter (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 [e.g., 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	

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	infection. See sections on **Further Processing** and **Additional Testing.**	
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.	*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 vWD, 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 5,000 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 ≥3.0 × 10^{11} platelets. For prophylaxis, this dose may need to be	*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. An apheresis platelet unit, transfused to an average-sized relatively healthy recipient, would be expected to result in a 1-hour posttransfusion increase in platelet count of approximately 30,000 to 60,000/uL. One unit of WBD platelets would be expected to increase the platelet count of a 70-kg adult by 5,000 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 6 units of WBD platelets, either of which usually contains ≥ 3.0 × 10^{11} platelets. For prophylaxis, this dose may	• This section was revised to include information on the 1-hour post transfusion increase for an apheresis platelet.

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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 aggregates should not be administered. Transfusion may proceed as quickly as tolerated, but must take less than 4 hours. ~~Do not refrigerate platelets.~~	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 aggregates should not be administered. Transfusion, using a standard platelet administration set, may proceed as quickly as tolerated, but must take less than 4 hours after entering the container.	• "Do not refrigerate platelets" was removed on the recommendation of FDA. Use of cold stored platelets requires the approval of an exception (also called a variance) under 21 CFR 640.120. Specific information in the approval such as indication, storage temperature and duration etc. should be added to the designated 3 blank pages prior to the Table of Contents of the *Circular*.
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)~~ CCI = (postcount – precount) × BSA / 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 (× 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) × 1.4 / 4.5 = 8,400/μL per 10^{11} per m^2.	The corrected count increment (CCI) is a calculated measure of patient response to platelet transfusion and is not directly correlated with bleeding risk. CCI adjusts for the number of platelets infused and the size of the recipient, based upon body surface area (BSA): CCI = (postcount – precount) × BSA / platelets transfused where postcount and precount are platelet counts (/μL) after and before transfusion, respectively; patient BSA (meter^2); and platelets transfused is the number of administered platelets (× 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) × 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	In an afebrile, non-bleeding patient, the CCI is typically greater than 7500 at 10 minutes to 1 hour after transfusion and remains above 4500 at 24 hours for conventional platelets. A lower CCI may be expected following transfusion with platelet components that have been further manufactured (pathogen reduced, irradiated or washed) or in patients that have been multiply transfused. Both immune and nonimmune mechanisms of platelet destruction may contribute to reduced platelet recovery and lower CCIs.	• Revised for clarity

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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.	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 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~~	*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 more often associated with platelet components. 1. **Bacterial Contamination:** Room temperature stored platelets are associated with a higher risk of sepsis and related fatality than any other transfusable blood component. Platelet products have undergone bacterial detection testing as described above or have undergone treatment using pathogen reduction technology approved/cleared by the FDA. Although methods to limit and detect bacterial contamination have been implemented for platelet components, risk of bacterial contamination remains a hazard of platelet transfusion, and platelets remain the most likely blood components to be contaminated with bacteria. Gram-positive skin flora are the most commonly recovered bacteria. Symptoms may include, but are not limited to, 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 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. Consider	• Added to address labeling requirements of the December 2020 *Bacterial Risk Control Strategies for Blood Collection Establishments and transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion* • Revised for clarity.

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~~be performed whenever possible.~~	gram stain, culture or other rapid detection method of the suspected contaminated unit(s) 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.	2. **Platelet Alloimmunization:** Platelets bear a variety of antigens, including Class I HLA and platelet-specific antigens. In the setting of platelet transfusion, patients may develop Class I HLA and/or human platelet antigen (HPA) antibodies potentially leading to refractoriness to transfused 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. Medication should be considered as a cause of immune or nonimmune thrombocytopenia. 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 (i.e., a 10- to 60- minute CCI). In immune refractory states secondary to serologic incompatibility, there is poor recovery in the early post-infusion interval resulting in a CCI <7500. In nonimmune mechanisms (e.g., splenomegaly, sepsis, fever, intravascular devices, and DIC), platelet recovery within 1 hour of infusion may be adequate while longer-term survival (i.e., 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.	• Revised for clarity.
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~~	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 WBD platelets than apheresis platelets. Rh(D) positive platelet transfusions to Rh (D) negative	• Revised for clarity.

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~~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.	individuals are common. The risk of Rh (D) alloimmunization is higher with WBD platelets and is very low with apheresis platelets. Providers may consider the use of Rh Immune Globulin to mitigate this risk in select patient populations. 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 ABO incompatible donors with high-titer isohemagglutinins (anti-A or anti-B) may cause acute hemolytic reactions in susceptible patients.	
Components Available	**Components Available** **This information is divided into sections by component type:** • Whole Blood-derived platelets • Apheresis platelets	
	Whole Blood-Derived Platelet Components	
1. **PLATELETS ~~(PLATELETS)~~** are a concentrate of platelets separated from a single unit of Whole Blood. One unit of Platelets should contain ≥5.5 × 10^{10} platelets suspended in 40 to 70 mL of plasma. This component is usually provided as a pool. See below.	**PLATELETS** are a concentrate of platelets separated from a single unit of Whole Blood also referred to as WBD. One unit of Platelets should contain ≥5.5 × 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.	**POOLED PLATELETS** may be prepared using aseptic technique as an open or closed 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.	• Revised for clarity. • References to shelf-life (expiration) have been addressed under the OVERVIEW and *Description* section and have been removed here.
3. **PLATELETS LEUKOCYTES REDUCED ~~(PLATELETS LEUKOCYTES REDUCED)~~** may be prepared using an open or closed system. One unit of Platelets Leukocytes Reduced should contain	**PLATELETS LEUKOCYTES REDUCED** may be prepared using an open or closed system. One unit of Platelets Leukocytes Reduced should contain ≥5.5 × 10^{10}	

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≥5.5 × 10^{10} platelets and <8.3 × 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.	platelets and <8.3 × 10^{5} leukocytes. 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 × 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.~~	**POOLED PLATELETS LEUKOCYTES REDUCED**. may be prepared using aseptic technique as an open or closed system by pooling and filtering Platelets or pooling Platelets Leukocytes Reduced. 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 × 10^{6} leukocytes in the pool. See the label for the approximate volume.	
5.	**Apheresis Platelet Components:**	
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 ≥3.0 × 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. ~~ACD-A~~ is the anticoagulant solution currently used for the collection and preservation of Apheresis Platelets.	**APHERESIS PLATELETS** are an effective way to collect a therapeutic adult dose of platelets from a single donor. Apheresis Platelets should contain ≥3.0 × 10^{11} platelets. One unit of Apheresis Platelets may be equivalent to 6 units of WBD 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. Anticoagulant Citrate Dextrose-Solution A is the anticoagulant solution currently used for the collection and preservation of Apheresis Platelets.	• One unit of apheresis platelets is the therapeutic equivalent of 6 units of WBD platelets.

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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.	**APHERESIS PLATELETS 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 during 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).~~	**APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED** are platelets collected by apheresis and suspended in variable amounts of plasma and an approved PAS. See Table 6. One unit of platelets should contain $\geq 3.0 \times 10^{11}$ 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.	• Irradiation and divided components are addressed in the section on Further Processing and Additional Testing.
~~8. See section on Further Processing.~~		Moved to **Overview** section.
Granulocyte Components	**Granulocyte Components**	
Description	**Apheresis Granulocytes Ω** *Description*	

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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 × 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 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.	Apheresis Granulocytes 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 × 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 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.	*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 × 10^9/L (500/μL)] with expected eventual marrow recovery. A trial of	*Indications* Granulocyte transfusion therapy is controversial. Apheresis Granulocytes are typically used in the treatment of patients with documented infections (bacterial and fungal) unresponsive to antimicrobial therapy in the setting of neutropenia [absolute granulocyte count <0.5 × 10^9/L (500/μL)] with expected eventual marrow recovery. A trial of	• Revised for clarity.

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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.	broad-spectrum antimicrobial agents should be used before granulocyte transfusion therapy is initiated. If the intended recipient is CMV seronegative and severely immunosuppressed (e.g., 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.	*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 pulmonary reactions. Antigen-matched or HLA-matched components, if available, may be considered in these patients.	• "Pulmonary reactions" added for clarity.
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, defervescence occurs, the absolute granulocyte count returns to at least 0.5 × 109/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.	*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, 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 and may be at risk for TA-GVHD, Apheresis Granulocytes should be irradiated (see sections on **Further Processing** and **Additional Testing**). See Table 3 for pediatric dosage information.	• Revised for clarity and consistency with Irradiation section.

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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.	*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.	
	Components Available **APHERESIS GRANULOCYTES Ω**	
Further Processing	**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.	This section addresses further processing of previously described blood components. The processes described in this section are pathogen reduction technology, leukocyte reduction, irradiation, washing, and volume reduction. A component may undergo one or more of these processes.	• Created a new section, "Additional Testing" to address identification of CMV seronegative components and Low Titer anti-A and/or anti-B Components.
Pathogen Reduction *Description*	**Pathogen Reduction Technology** *Description*	• This section was revised extensively.

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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 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.~~	Pathogen reduction is an ex vivo process intended to reduce the risk of certain transfusion-transmitted infections (TTI). including sepsis and may also be used as an alternative to irradiation to prevent TA-GVHD if the pathogen reduction technology has been shown to inactivate residual lymphocytes. There is no pathogen inactivation process that has been shown to eliminate all pathogens; e.g. hepatitis A (HAV), hepatitis E (HEV), human parvovirus B19, poliovirus, and *Bacillus cereus* spores have shown resistance to some processes. A current pathogen reduction procedure uses a chemical photosensitizer that 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 photosensitizer and free photoproducts are subsequently removed with a compound adsorption device. Products currently approved by FDA for pathogen reduction technology include apheresis platelets and Whole Blood-derived (WBD) plasma or apheresis plasma. Pathogen-reduced plasma may be further manufactured, using a system approved by FDA for this purpose, into Pathogen Reduced, Cryoprecipitated Fibrinogen Complex (PRCFC) and Pathogen Reduced Plasma, Cryoprecipitate Reduced (PR-PCPR). Pathogen reduction technology may apply to other products in the future. Consistent with the **Notice to All Users** section on page 1, refer to the manufacturer's instructions for use of components prepared using a pathogen reduction device for all components listed in this section. • **Refer to the Platelet Section beginning on page 29 or the Plasma Section beginning on page 19** for the corresponding *Description, Actions, Indications, Contraindications, Relative Contraindications, Dosage and Administration* and *Side Effects and Hazards* as applicable to pathogen reduced platelet components, and	• Individual Pathogen Reduced Components have been added.

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~~*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.~~ ~~*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~~	frozen and thawed pathogen reduced plasma components. • NOTE: *Additional Contraindications* for pathogen reduced platelet and plasma components include: 1. Contraindicated for preparation of pathogen reduced components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. 2. Contraindicated for preparation of pathogen reduced components intended 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 <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen. • NOTE: Additional *Warnings and Precautions* for pathogen reduced platelet and plasma components include: **Platelet Components:** Amotosalen-treated platelets may cause the following adverse reaction: *Pulmonary events*: Acute Respiratory Distress Syndrome (ARDS). An increased incidence of ARDS was reported in a randomized trial for recipients of INTERCEPT processed platelets, 5/318 (1.6%), compared to recipients of conventional platelet components (0/327). Monitor patients for signs and symptoms of ARDS. **Plasma Components:** Amotosalen-treated plasma may cause the following adverse reaction: *Cardiac Events* In a randomized controlled trial of therapeutic plasma exchange (TPE) for TTP, five patients treated with INTERCEPT Blood System processed plasma and none with conventional plasma had adverse events in the cardiac system	

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~~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."~~	organ class (SOC) reported.12 These events included angina pectoris (n=3), cardiac arrest (n=1), bradycardia (n=1), tachycardia (n=1) and sinus arrhythmia (n=1). None of these events resulted in documented myocardial infarction or death.13 Monitor patients for signs and symptoms of cardiac events during TPE for TTP.	
	Components Available **APHERESIS PLATELETS LEUKOCYTES REDUCED PSORALEN-TREATED** **APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED PSORALEN-TREATED** **APHERESIS FRESH FROZEN PLASMA PSORALEN-TREATED** **POOLED FRESH FROZEN PLASMA PSORALEN-TREATED** **POOLED PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY PSORALEN-TREATED** **APHERESIS PLASMA CRYOPRECIPITATE REDUCED PSORALEN-TREATED** **POOLED PLASMA CRYOPRECIPITATE REDUCED PSORALEN-TREATED** **THAWED APHERESIS PLASMA PSORALEN-TREATED** **THAWED POOLED PLASMA PSORALEN-TREATED** **THAWED PLASMA CRYOPRECIPITATE REDUCED PSORALEN-TREATED**	

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	Pathogen Reduced Cryoprecipitated Fibrinogen Complex	
	Description Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC) is prepared from plasma that has been processed with an FDA approved pathogen reduction device. The PRCFC process includes thawing pathogen reduced plasma between 1 and 6 C and recovering the precipitate. The cold-insoluble precipitate is placed in the freezer at -18 C or colder.	
	Actions PRCFC serves as an enriched source of fibrinogen, Factor XIII, von Willebrand Factor (vWF), and other constituents. The 5-day post thaw shelf life of PRCFC is based on retention of critical functional activities that have shown a high level of correlation with therapeutic efficacy and the reduced pathogen risk associated with pathogen inactivation. PRCFC is not intended to be used for replacement of Factor VIII.	
	Indications PRCFC is indicated for: 1. Treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency. 2. Control of bleeding when recombinant and/or specific virally inactivated preparations of Factor XIII or vWF are not available. 3. Second-line therapy for vWD. 4. Control of uremic bleeding after other treatment modalities have failed. *Limitations of Use:* PRCFC should not be used for replacement of Factor VIII.	
	Contraindications 1. Contraindicated for preparation of blood	

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	components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. 2. Contraindicated for preparation of blood components intended 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 <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.	
	Warnings and Precautions 1. For management of patients with vWD or Factor XIII deficiency, PRCFC should not be used if recombinant or specific virally-inactivated factor preparations are available. In emergent situations, if recombinant or specific virally-inactivated factor preparations are not available, PRCFC may be administered.	
	Dosage and Administration 1. Compatibility testing is not required. ABO-compatible PRCFC is preferred. Rh type need not be considered when using this product. 2. Thaw according to institutional procedures and manufacturer's instructions for use of PR CFC. If using a waterbath, for thawing PRCFC, place in liquid-impermeable plastic overwrap. Do not allow product to contact water. Do not refreeze post thaw. 3. Do not administer PRCFC if there is evidence of container breakage or of thawing during frozen storage. 4. If PRCFC is pooled or aliquoted post thaw without using an FDA-cleared sterile connection device, transfuse within 4 hours of pooling or aliquoting. PRCFC may be transfused from a single or multiple containers. For in hospital pooling, the precipitate in one or more containers may be mixed well with 10 to 15 mL of	

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	diluent to allow complete removal of all material from the container. The preferred diluent is 0.9% Sodium Chloride, Injection (USP). Serial use of each container's contents to resuspend the precipitate into subsequent containers may be used to efficiently pool PRCFC into a single container. Thrombosis alters fibrinogen kinetics; therefore, patients receiving PRCFC as fibrinogen replacement in conditions associated with increased fibrinogen turnover should be monitored with fibrinogen assays. When used to correct hypofibrinogenemia, PRCFC may be dosed based on the clinical presentation and expected fibrinogen content of the product. For example, a unit of PRCFC prepared from 2 Whole Blood-derived plasma units will contain about 740 ±166 mg fibrinogen immediately post thaw, and 686 ±165 mg fibrinogen after 120 hours.	
	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.	
	Components Available **POOLED FIBRINOGEN COMPLEX CRYOPRECIPITATED PSORALEN-TREATED** **APHERESIS FIBRINOGEN COMPLEX CRYOPRECIPITATED PSORALEN-TREATED** **APHERESIS POOLED FIBRINOGEN COMPLEX CRYOPRECIPITATED PSORALEN-TREATED**	
Leukocyte Reduction	**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	*Description* A unit of whole blood generally contains ≥1 to 10×10^9 white cells. Leukocyte reduction will decrease the cellular content and volume of blood according to characteristics of the technology used. RBCs Leukocytes Reduced, Apheresis	• This section was edited for clarity. Some content has been reordered.

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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.	RBCs Leukocytes Reduced, Apheresis Platelets Leukocytes Reduced and Pooled Platelets Leukocytes Reduced must have $<5.0 \times 10^6$ residual leukocytes per unit., Platelets Leukocytes Reduced (single unit WBD) must have $<8.3 \times 10^5$ residual leukocytes per unit. Leukocyte reduction may be performed using in-process collection methods. Leukocyte reduction may be performed using additional post-collection processing steps to permit labeling as a leukocytes reduced component: 1) soon after collection (prestorage), 2) after varying periods of storage in the laboratory, or 3) at the bedside as directed by manufacturer's instructions. The methods used by the laboratory for leukocyte reduction are subject to quality control testing; leukocyte-reduced components prepared at the bedside are not routinely subjected to quality control testing. Leukocyte-reduction technologies 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.	*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.	
Contraindications Leukocyte-reduced components do not prevent TA-GVHD. Leukocyte-reduction filters are not to be used in the administration of Apheresis Granulocytes.	*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.	*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	*Specific Leukocyte-Reduced Components*	

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All components resulting from the leukocyte reduction process will bear the labeling attribute "leukocytes reduced."	All components resulting from the leukocyte reduction process will bear the labeling attribute "leukocytes reduced."	
Irradiation	**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.	*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 or X-ray irradiation is 2500 centigray (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.	*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 peripheral blood progenitor cell transplantation, recipients of cellular components whose donor is selected for HLA compatibility and recipients of granulocyte transfusions. Transfused patients receiving purine analogues (e.g., fludarabine, cladribine) or certain other biological immunomodulators (e.g., alemtuzumab, antithymocyte globulin) may be at risk for TA-GVHD, depending on clinical factors and the source of the biological agent.	• Edited for clarity. Recipients of granulocyte transfusions added as an indication.
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	*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	

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are no known adverse effects following irradiation of platelets; the expiration date is unchanged.	are no known adverse effects following irradiation of platelets; the expiration date is unchanged.	
Specific Irradiated Components All components that have been irradiated will bear the labeling attribute "irradiated."	*Specific Irradiated Components* All components that have been irradiated will bear the labeling attribute "irradiated."	
Washing	**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.	*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).	*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 (e.g., 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)~~**	*Specific Washed Components* **WASHED RED BLOOD CELLS** **WASHED APHERESIS RED BLOOD CELLS**	

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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)~~**	**WASHED PLATELETS Ω** **WASHED APHERESIS PLATELETS Ω** **WASHED APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED Ω**	
Volume Reduction	**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.	*Description* Volume reduction is a special manipulation of cellular blood products using centrifugation to remove plasma and storage media in order to concentrate the product. It is typically performed immediately prior to issuing the product for patient administration. 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 intrauterine 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.	• Revised for clarity
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.	*Indications* Reducing the plasma volume of cellular components is indicated in cases where consequences of hypervolemia are of concern, (such as in infants with compromised cardiac function). Component volume reduction is also used to mitigate adverse transfusion reactions such as TACO, severe allergic reactions, and ABO incompatibilities.	• Revised for clarity. The qualifier “severe” clarifies between mild allergic reactions where volume-reduction would not be indicated.
Contraindications Volume reduction is not a substitute for washing or for dosing with small aliquots.	*Contraindications* Volume reduction is not a substitute for washing or for dosing with small aliquots.	
Specific Volume-Reduced Components	*Specific Volume-Reduced Components*	

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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)~~**	**RED BLOOD CELLS PLASMA REDUCED Ω** **RED BLOOD CELLS SUPERNATANT REDUCED Ω** **APHERESIS RED BLOOD CELLS PLASMA REDUCED Ω** **APHERESIS RED BLOOD CELLS SUPERNATANT REDUCED Ω** **PLATELETS PLASMA REDUCED Ω** **APHERESIS PLATELETS PLASMA REDUCED Ω** **APHERESIS PLATELETS PLATELET ADDITIVE SOLUTION ADDED LEUKOCYTES REDUCED SUPERNATANT REDUCED Ω**	
	Additional Testing This section addresses additional testing performed on previously described blood components. The testing described in this section includes identification of CMV-seronegative blood, and identification of low titer anti-A and/or anti-B blood products.	• New Section added to differentiate Further Processing and Additional Testing.
~~Further Testing to Identify~~ CMV-Seronegative Blood	**Identification of 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.	*Description* CMV-seronegative blood is selected by testing for antibodies to CMV. Transmission of CMV disease is associated with cellular blood components specifically those containing mononuclear leukocytes from donors with a history of CMV infection. Plasma, cryoprecipitate, and other plasma-derived blood components are not associated with CMV transmission. Therefore, CMV testing is not necessary for these components.	• Revised for clarity.
Indications	*Indications*	

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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.~~	In the latently infected donor, CMV is exclusively associated with mononuclear leukocytes. Current studies indicate that transfusion of prestorage, leukocyte-reduced blood products safely reduce the risk of CMV transmission to levels not significantly different to transfusion with CMV-seronegative blood. Thus prestorage, leukocyte-reduced components are considered a suitable alternative to CMV-seronegative transfusion. Transfusion of prestorage leukocyte-reduced or CMV-seronegative 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.	• Revised and reordered. Additional information added.
	Identification of Low Titer anti-A and/or anti-B Blood Products	• New Section added
	Description Plasma, apheresis platelet and whole blood products containing defined titers of anti-A and/or anti-B may reduce the risk of hemolytic transfusion reactions when transfusing ABO incompatible blood products. Titers considered "low" are not standardized; there is no "safe" titer because hemolytic reactions have been observed at even low titers with no direct correlation of titer and risk of reactions. Facilities must have policies and procedures to define cut-offs for anti-A and/or anti-B titers for ABO incompatible blood components. Refer to the United States Industry Consensus Standard for Uniform Labeling of Blood and Blood Components Using ISBT 128 (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/united-states-industry-consensus-standard-uniform-labeling-blood-and-	

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	blood-components-using-isbt-128) for labeling recommendations. Options include placing the titer value on a tie tag.	
	Indications Group O Whole Blood and group A plasma tested for anti-A and/or anti-B may be used as an initial resuscitation fluid for an acutely bleeding patient prior to determining the recipient blood group. The transfusing facility must have policies and procedures in place addressing specific indications for use, product specifications, administration instructions and a defined maximum number of units to be transfused to each patient.	
	Contraindications ABO incompatible products should not be transfused when an appropriate product that is ABO compatible is readily available, or when the risk of administering ABO incompatible blood components outweighs the potential therapeutic benefit.	
References	**References**	