

postmarketing study should be categorized using one of the following terms that describes the study's status on the anniversary date of U.S. approval of the application or other agreed upon date:

(i) *Pending*. The study has not been initiated, but does not meet the criterion for delayed.

(ii) *Ongoing*. The study is proceeding according to or ahead of the original schedule described under paragraph (b)(7) of this section.

(iii) *Delayed*. The study is behind the original schedule described under paragraph (b)(7) of this section.

(iv) *Terminated*. The study was ended before completion but a final study report has not been submitted to FDA.

(v) *Submitted*. The study has been completed or terminated and a final study report has been submitted to FDA.

(9) *Explanation of the study's status*. Provide a brief description of the status of the study, including the patient accrual rate (expressed by providing the number of patients or subjects enrolled to date, and the total planned enrollment), and an explanation of the study's status identified under paragraph (b)(8) of this section. If the study has been completed, include the date the study was completed and the date the final study report was submitted to FDA, as applicable. Provide a revised schedule, as well as the reason(s) for the revision, if the schedule under paragraph (b)(7) of this section has changed since the previous report.

(c) *When to report*. Annual progress reports for postmarketing study commitments entered into by applicants shall be reported to FDA within 60 days of the anniversary date of the U.S. approval of the application for the product.

(d) *Where to report*. Submit two copies of the annual progress report of postmarketing studies to the Food and Drug Administration, Center for Biologics Evaluations and Research, Document Control Center (HFM-99), 1401 Rockville Pike, Rockville, MD 20852-1448.

(e) *Public disclosure of information*. Except for the information described in this paragraph, FDA may publicly disclose any information concerning a

postmarketing study, within the meaning of this section, if the agency determines that the information is necessary to identify an applicant or to establish the status of the study including the reasons, if any, for failure to conduct, complete, and report the study. Under this section, FDA will not publicly disclose trade secrets, as defined in §20.61 of this chapter, or information, described in §20.63 of this chapter, the disclosure of which would constitute an unwarranted invasion of personal privacy.

[65 FR 64618, Oct. 30, 2000]

PART 606—CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS

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Subpart A—General Provisions

§ 606.3 Definitions.

As used in this part:

(a) *Blood* means whole blood collected from a single donor and processed either for transfusion or further manufacturing.

(b) *Unit* means the volume of blood or one of its components in a suitable volume of anticoagulant obtained from a single collection of blood from one donor.

(c) *Component* means that part of a single-donor's blood separated by physical or mechanical means.

(d) *Plasma for further manufacturing* means that liquid portion of blood separated and used as material to prepare another product.

(e) *Plasmapheresis* means the procedure in which blood is removed from the donor, the plasma is separated from the formed elements and at least the red blood cells are returned to the donor.

(f) *Plateletpheresis* means the procedure in which blood is removed from a donor, a platelet concentrate is separated, and the remaining formed elements are returned to the donor along with a portion of the residual plasma.

(g) *Leukapheresis* means the procedure in which blood is removed from the donor, a leukocyte concentrate is separated, and the remaining formed elements and residual plasma are returned to the donor.

(h) *Facilities* means any area used for the collection, processing, compatibility testing, storage or distribution of blood and blood components.

(i) *Processing* means any procedure employed after collection and before compatibility testing of blood and includes the identification of a unit of donor blood, the preparation of components from such unit of donor blood, serological testing, labeling and associated recordkeeping.

(j) *Compatibility testing* means the in vitro serological tests performed on donor and recipient blood samples to establish the serological matching of a donor's blood or blood components with that of a potential recipient.

[40 FR 53532, Nov. 18, 1975, as amended at 64 FR 45370, Aug. 19, 1999; 66 FR 1835, Jan. 10, 2001]

EFFECTIVE DATE NOTE: At 65 FR 66635, Nov. 7, 2000, §606.3 was amended by adding paragraphs (k) and (l), effective May 7, 2000. At 65 FR 67477, Nov. 9, 2000, the effective date was corrected to read May 7, 2001. For the convenience of the user, the added text is set forth as follows:

§ 606.3 Definitions.

* * * * *

(k) *Distributed* means:

(1) The blood or blood components have left the control of the licensed manufacturer, unlicensed registered blood establishment, or transfusion service; or

(2) The licensed manufacturer has provided Source Plasma or any other blood component for use in the manufacture of a licensed biological product.

(l) *Control* means having responsibility for maintaining the continued safety, purity, and potency of the product and for compliance with applicable product and establishment standards, and for compliance with current good manufacturing practices.

Subpart B—Organization and Personnel

§ 606.20 Personnel.

(a) [Reserved]

(b) The personnel responsible for the collection, processing, compatibility testing, storage or distribution of blood or blood components shall be adequate in number, educational background, training and experience, including professional training as necessary, or combination thereof, to assure competent performance of their assigned functions, and to ensure that the final product has the safety, purity, potency, identity and effectiveness it purports or is represented to possess. All personnel shall have capabilities commensurate with their assigned functions, a thorough understanding of the procedures or control operations they perform, the necessary training or experience, and adequate information

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concerning the application of pertinent provisions of this part to their respective functions.

(c) Persons whose presence can adversely affect the safety and purity of the products shall be excluded from areas where the collection, processing, compatibility testing, storage or distribution of blood or blood components is conducted.

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 55 FR 11014, Mar. 26, 1990; 62 FR 53538, Oct. 15, 1997]

Subpart C—Plant and Facilities

§ 606.40 Facilities.

Facilities shall be maintained in a clean and orderly manner, and shall be of suitable size, construction and location to facilitate adequate cleaning, maintenance and proper operations. The facilities shall:

(a) Provide adequate space for the following when applicable:

(1) Private and accurate examinations of individuals to determine their suitability as blood donors.

(2) The withdrawal of blood from donors with minimal risk of contamination, or exposure to activities and equipment unrelated to blood collection.

(3) The storage of blood or blood components pending completion of tests.

(4) The quarantine storage of blood or blood components in a designated location pending repetition of those tests that initially gave questionable serological results.

(5) The storage of finished products prior to distribution.

(6) The quarantine storage, handling and disposition of products and reagents not suitable for use.

(7) The orderly collection, processing, compatibility testing, storage and distribution of blood and blood components to prevent contamination.

(8) The adequate and proper performance of all steps in plasmapheresis, plateletpheresis and leukapheresis procedures.

(9) The orderly conduction of all packaging, labeling and other finishing operations.

(b) Provide adequate lighting, ventilation and screening of open windows and doors.

(c) Provide adequate, clean, and convenient handwashing facilities for personnel, and adequate, clean, and convenient toilet facilities for donors and personnel. Drains shall be of adequate size and, where connected directly to a sewer, shall be equipped with traps to prevent back-siphonage.

(d) Provide for safe and sanitary disposal for the following:

(1) Trash and items used during the collection, processing and compatibility testing of blood and blood components.

(2) Blood and blood components not suitable for use or distribution.

Subpart D—Equipment

§ 606.60 Equipment.

(a) Equipment used in the collection, processing, compatibility testing, storage and distribution of blood and blood components shall be maintained in a clean and orderly manner and located so as to facilitate cleaning and maintenance. The equipment shall be observed, standardized and calibrated on a regularly scheduled basis as prescribed in the Standard Operating Procedures Manual and shall perform in the manner for which it was designed so as to assure compliance with the official requirements prescribed in this chapter for blood and blood products.

(b) Equipment that shall be observed, standardized and calibrated with at least the following frequency, include but are not limited to:

Equipment	Performance check	Frequency	Frequency of calibration
Temperature recorder ...	Compare against thermometer	Daily	As necessary.
Refrigerated centrifuge ..	Observe speed and temperature	Each day of use	Do.
Hematocrit centrifuge	Standardize before initial use, after repairs or adjustments, and annually. Timer every 3 mo.
General lab centrifuge	Tachometer every 6 mo.
Automated blood-typing machine.	Observe controls for correct results	Each day of use.	

Equipment	Performance check	Frequency	Frequency of calibration
Hemoglobinometer	Standardize against cyanmethemoglobin standard.do	
Refractometer	Standardize against distilled waterdo	
Blood container scale	Standardize against container of known weight.do	As necessary.
Water bath	Observe temperaturedo	Do.
Rh view boxdodo	Do.
Autoclavedo	Each time of use	Do.
Serologic rotators	Observe controls for correct results	Each day of use	Speed as necessary.
Laboratory thermometers.dodo	Before initial use.
Electronic thermometersdodo	Monthly.
Vacuum blood agitator ..	Observe weight of the first container of blood filled for correct results.	Each day of use	Standardize with container of known mass or volume before initial use, and after repairs or adjustments.

(c) Equipment employed in the sterilization of materials used in blood collection or for disposition of contaminated products shall be designed, maintained and utilized to ensure the destruction of contaminating microorganisms. The effectiveness of the sterilization procedure shall be no less than that achieved by an attained temperature of 121.5 °C (251 °F) maintained for 20 minutes by saturated steam or by an attained temperature of 170 °C (338 °F) maintained for 2 hours with dry heat.

[40 FR 53532, Nov. 18, 1975; 40 FR 55849, Dec. 2, 1975, as amended at 45 FR 9261, Feb. 12, 1980; 57 FR 11263, Apr. 2, 1992; 57 FR 12862, Apr. 13, 1992]

§ 606.65 Supplies and reagents.

All supplies and reagents used in the collection, processing, compatibility testing, storage and distribution of blood and blood components shall be stored in a safe, sanitary and orderly manner.

(a) All surfaces coming in contact with blood and blood components intended for transfusion shall be sterile, pyrogen-free, and shall not interact with the product in such a manner as to have an adverse effect upon the safety, purity, potency or effectiveness of the product. All final containers and closures for blood and blood components not intended for transfusion shall be clean and free of surface solids and other contaminants.

(b) Each blood collecting container and its satellite container(s), if any, shall be examined visually for damage or evidence of contamination prior to

its use and immediately after filling. Such examination shall include inspection for breakage of seals, when indicated, and abnormal discoloration. Where any defect is observed, the container shall not be used, or, if detected after filling, shall be properly discarded.

(c) Representative samples of each lot of the following reagents or solutions shall be tested on a regularly scheduled basis by methods described in the Standard Operating Procedures Manual to determine their capacity to perform as required:

Reagent or solution	Frequency of testing
Anti-human globulin	Each day of use.
Blood grouping reagents	Do.
Lectins	Do.
Antibody screening and reverse grouping cells.	Do.
Hepatitis test reagents	Each run.
Syphilis serology reagents	Do.
Enzymes	Each day of use.

(d) Supplies and reagents that do not bear an expiration date shall be stored in such a manner that the oldest is used first.

(e) Supplies and reagents shall be used in a manner consistent with instructions provided by the manufacturer.

(f) Items that are required to be sterile and come into contact with blood should be disposable whenever possible.

[40 FR 53532, Nov. 18, 1975, as amended at 59 FR 23636, May 6, 1994]

Subpart E [Reserved]

Subpart F—Production and Process Controls

§ 606.100 Standard operating procedures.

(a) In all instances, except clinical investigations, standard operating procedures shall comply with published additional standards in part 640 of this chapter for the products being processed; except that, references in part 640 relating to licenses, licensed establishments and submission of material or data to or approval by the Director, Center for Biologics Evaluation and Research, are not applicable to establishments not subject to licensure under section 351 of the Public Health Service Act.

(b) Written standard operating procedures shall be maintained and shall include all steps to be followed in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for transfusion and further manufacturing purposes. Such procedures shall be available to the personnel for use in the areas where the procedures are performed. The written standard operating procedures shall include, but are not limited to, descriptions of the following, when applicable:

(1) Criteria used to determine donor suitability, including acceptable medical history criteria.

(2) Methods of performing donor qualifying tests and measurements, including minimum and maximum values for a test or procedure when a factor in determining acceptability.

(3) Solutions and methods used to prepare the site of phlebotomy to give maximum assurance of a sterile container of blood.

(4) Method of accurately relating the product(s) to the donor.

(5) Blood collection procedure, including in-process precautions taken to measure accurately the quantity of blood removed from the donor.

(6) Methods of component preparation, including any time restrictions for specific steps in processing.

(7) All tests and repeat tests performed on blood and blood components during manufacturing.

(8) Pretransfusion testing, where applicable, including precautions to be

taken to identify accurately the recipient blood samples and crossmatched donor units.

(9) Procedures for investigating adverse donor and recipient reactions.

(10) Storage temperatures and methods of controlling storage temperatures for all blood products and reagents as prescribed in §§ 600.15 and 610.53 of this chapter.

(11) Length of expiration dates, if any, assigned for all final products as prescribed in § 610.53 of this chapter.

(12) Criteria for determining whether returned blood is suitable for reissue.

(13) Procedures used for relating a unit of blood or blood component from the donor to its final disposition.

(14) Quality control procedures for supplies and reagents employed in blood collection, processing and pretransfusion testing.

(15) Schedules and procedures for equipment maintenance and calibration.

(16) Labeling procedures, including safeguards to avoid labeling mixups.

(17) Procedures of plasmapheresis, plateletpheresis, and leukapheresis, if performed, including precautions to be taken to ensure reinfusion of a donor's own cells.

(18) Procedures for preparing recovered plasma, if performed, including details of separation, pooling, labeling, storage, and distribution.

(19) Procedures in accordance with § 610.46 of this chapter to look at prior donations of Whole Blood, blood components, Source Plasma and Source Leukocytes from a donor who has donated blood and subsequently tests repeatedly reactive for antibody to human immunodeficiency virus (HIV) or otherwise is determined to be unsuitable when tested in accordance with § 610.45 of this chapter. Procedures to quarantine in-house Whole Blood, blood components, Source Plasma and Source Leukocytes intended for further manufacture into injectable products that were obtained from such donors; procedures to notify consignees regarding the need to quarantine such products; procedures to determine the suitability for release of such products from quarantine; procedures to notify consignees of Whole Blood, blood components, Source Plasma and Source

Leukocytes from such donors of the results of the antibody testing of such donors; and procedures in accordance with §610.47 of this chapter to notify attending physicians so that transfusion recipients are informed that they may have received Whole Blood and, blood components at increased risk for transmitting human immunodeficiency virus.

(c) All records pertinent to the lot or unit maintained pursuant to these regulations shall be reviewed before the release or distribution of a lot or unit of final product. The review or portions of the review may be performed at appropriate periods during or after blood collecting, processing, compatibility testing and storing. A thorough investigation, including the conclusions and followup, of any unexplained discrepancy or the failure of a lot or unit to meet any of its specifications shall be made and recorded.

(d) In addition to the requirements of this subpart and in conformity with this section, any facility may utilize current standard operating procedures such as the manuals of the organizations, as long as such specific procedures are consistent with, and at least as stringent as, the requirements contained in this part.

(1) American Association of Blood Banks.

(2) American National Red Cross.

(3) Other organizations or individual blood banks, subject to approval by the Director, Center for Biologics Evaluation and Research.

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990; 61 FR 47422, Sept. 9, 1996; 64 FR 45370, Aug. 19, 1999]

§ 606.110 Plateletpheresis, leukapheresis, and plasmapheresis.

(a) The use of plateletpheresis and leukapheresis procedures to obtain a product for a specific recipient may be at variance with the additional standards for specific products prescribed in this part provided that: (1) A physician has determined that the recipient must be transfused with the leukocytes or platelets from a specific donor, and (2) the procedure is performed under the supervision of a qualified licensed physician who is aware of the health sta-

tus of the donor, and the physician has certified in writing that the donor's health permits plateletpheresis or leukapheresis.

(b) Plasmapheresis of donors who do not meet the donor requirements of §§ 640.63, 640.64 and 640.65 of this chapter for the collection of plasma containing rare antibodies shall be permitted only with the prior approval of the Director, Center for Biologics Evaluation and Research.

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990]

Subpart G—Finished Product Control

§ 606.120 Labeling, general requirements.

(a) Labeling operations shall be separated physically or spatially from other operations in a manner adequate to prevent mixups.

(b) The labeling operation shall include the following labeling controls:

(1) Labels shall be held upon receipt, pending review and proofing against an approved final copy, to ensure accuracy regarding identity, content, and conformity with the approved copy.

(2) Each type of label representing different products shall be stored and maintained in a manner to prevent mixups, and stocks of obsolete labels shall be destroyed.

(3) All necessary checks in labeling procedures shall be utilized to prevent errors in translating test results to container labels.

(c) All labeling shall be clear and legible.

[50 FR 35469, Aug. 30, 1985]

§ 606.121 Container label.

(a) The container label requirements are designed to facilitate the use of a uniform container label for blood and blood components (except Source Plasma) by all blood establishments.

(b) The label provided by the collecting facility and the initial processing facility shall not be removed, altered, or obscured, except that the label may be altered to indicate the

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proper name and other information required to identify accurately the contents of a container after blood components have been prepared.

(c) The container label shall include the following information, as well as other specialized information as required in this section for specific products:

(1) The proper name of the product in a prominent position, and modifier(s), if appropriate.

(2) The name, address, registration number, and, if a licensed product, the license number of each manufacturer.

(3) The donor, pool, or lot number relating the unit to the donor.

(4) The expiration date, including the day, month, and year, and, if the dating period for the product is 72 hours or less, the hour of expiration.

(5) If the product is intended for transfusion, the appropriate donor classification statement, i.e., "paid donor" or "volunteer donor", in no less prominence than the proper name of the product.

(i) A paid donor is a person who receives monetary payment for a blood donation.

(ii) A volunteer donor is a person who does not receive monetary payment for a blood donation.

(iii) Benefits, such as time off from work, membership in blood assurance programs, and cancellation of non-replacement fees that are not readily convertible to cash, do not constitute monetary payment within the meaning of this paragraph.

(6) For Whole Blood, Plasma, Platelets, and partial units of Red Blood Cells, the volume of the product, accurate to within ± 10 percent; or optionally for Platelets, the volume range within reasonable limits.

(7) The recommended storage temperature (in degrees Celsius).

(8) If the product is intended for transfusion, the statements:

(i) "Caution: Federal law prohibits dispensing without prescription."

(ii) "See circular of information for indications, contraindications, cautions, and methods of infusion."

(iii) "Properly identify intended recipient."

(9) The statement: "This product may transmit infectious agents."

(10) Where applicable, the name and volume of source material.

(11) The statement: "Caution: For Manufacturing Use Only", when applicable.

(12) If the product is intended for transfusion, the ABO and Rh groups of the donor shall be designated conspicuously. For Cryoprecipitated AHF, the Rh group may be omitted. The Rh group shall be designated as follows:

(i) If the test using Anti-D Blood Grouping Reagent is positive, the product shall be labeled: "Rh positive."

(ii) If the test using Anti-D Blood Grouping Reagent is negative but the test for D^u is positive, the product shall be labeled: "Rh positive."

(iii) If the test using Anti-D Blood Grouping Reagent is negative and the test for D^u is negative, the product shall be labeled: "Rh negative."

(13) The container label may bear encoded information in the form of machine-readable symbols approved for use by the Director, Center for Biologics Evaluation and Research (HFB-1).

(d) Except for recovered plasma intended for manufacturing use or as otherwise approved by the Director, Center for Biologics Evaluation and Research (HFB-1), the paper of the container label shall be white and print shall be solid black, with the following additional exceptions:

(1) The Rh blood group shall be printed as follows:

(i) Rh positive: Use black print on white background.

(ii) Rh negative: Use white print on black background.

(2) The proper name of the product, any appropriate modifier(s), the donor classification statement, and the statement "properly identify intended recipient" shall be printed in solid red or in solid black.

(3) The following color scheme may be used optionally for differentiating ABO Blood groups:

Blood group	Color of label paper
O	Blue
A	Yellow
B	Pink
AB	White

(4) Ink colors used for the optional color coding system described in paragraph (d)(3) of this section shall be a visual match to specific color samples designated by the Director, Center for Biologics Evaluation and Research (HFB-1).

(5) Special labels, such as those described in paragraphs (h) and (i) of this section, may be color coded using the colors recommended in the guideline (see paragraph (a) of this section), or colors otherwise approved for use by the Director, Center for Biologics Evaluation and Research (HFB-1).

(e) Container label requirements for particular products or groups of products.

(1) Whole Blood labels shall include:

(i) The volume of anticoagulant.

(ii) The name of the applicable anticoagulant immediately preceding and of no less prominence than the proper name approved for use by the Director, Center for Biologics Evaluation and Research.

(iii) If tests for unexpected antibodies are positive, blood intended for transfusion shall be labeled: "Contains (*name of antibody*)."

(2) Except for frozen, deglycerolized, or washed Red Blood Cell products, red blood cell labels shall include:

(i) The volume and kind of Whole Blood, including the type of anticoagulant, from which the product was prepared.

(ii) If tests for unexpected antibodies are positive and the product is intended for transfusion, the statement: "Contains (*name of antibody*)."

(3) Labels for products with a dating period of 72 hours or less, including any product prepared in a system that may compromise sterility, shall bear the hour of expiration.

(4) If tests for unexpected antibodies are positive, Plasma intended for transfusion shall be labeled: "Contains (*name of antibody*)."

(5) Recovered plasma labels shall include:

(i) In lieu of an expiration date, the date of collection of the oldest material in the container.

(ii) The statement: "Caution: For Manufacturing Use Only"; or "Caution: For Use in Manufacturing

Noninjectable Products Only", as applicable.

(iii) For recovered plasma not meeting the requirements for manufacture into licensable products, the statement: "Not for Use in Products Subject to License Under Section 351 of the Public Health Service Act."

(f) Blood and blood components determined to be unsuitable for transfusion shall be prominently labeled: "NOT FOR TRANSFUSION", and the label shall state the reason the unit is considered unsuitable. The provision does not apply to recovered plasma labeled according to paragraph (e)(5) of this section.

(g) As required under §610.40 of this chapter, labels for blood and blood components that are reactive for Hepatitis B Surface Antigen, but that are intended for further manufacturing, shall state conspicuously that the material is reactive when tested for hepatitis B surface antigen and may transmit viral hepatitis or, as applicable, that blood was collected from a donor known to be reactive for hepatitis B surface antigen and is presumed to be infectious, although confirmatory hepatitis testing has not been done.

(h) The following additional information shall appear on the label for blood or blood components shipped in an emergency, prior to completion of required tests, in accordance with §640.2(f) of this chapter:

(1) The statement: "FOR EMERGENCY USE ONLY BY _____."

(2) Results of any tests prescribed under §§610.40, 610.45, and 640.5 (a), (b), or (c) of this chapter completed before shipment.

(3) Indication of any tests prescribed under §§610.40, 610.45, and 640.5 (a), (b), or (c) of this chapter and not completed before shipment.

(i) The following additional information shall appear on the label for Whole Blood or Red Blood Cells intended for autologous infusion:

(1) Information adequately identifying the patient, e.g., name, blood group, hospital, and identification number.

(2) Date of donation.

(3) The statement: "FOR AUTOLOGOUS USE ONLY."

(4) In place of the blood group label, each container of blood intended for autologous use and obtained from a donor who fails to meet any of the donor suitability requirements under § 640.3 of this chapter or who is reactive in the hepatitis tests prescribed under § 610.40 of this chapter shall be prominently and permanently labeled: “FOR AUTOLOGOUS USE ONLY.”

(5) Units of blood originally intended for autologous use, except those labeled as prescribed under paragraph (i)(4) of this section, may be issued for homologous transfusion provided the container label complies with all applicable provisions of paragraphs (b) through (e) of this section. In such case, the special label required under paragraph (i) (1), (2), and (3) of this section shall be removed or otherwise obscured.

(j) A tie-tag attached to the container may be used for providing the information required by paragraph (e) (1)(iii), (2)(ii), and (4), (h), or (i)(1), (2), and (3) of this section.

[50 FR 35469, Aug. 30, 1985, as amended at 53 FR 116, Jan. 5, 1988; 55 FR 11014, Mar. 26, 1990; 57 FR 10814, Mar. 31, 1992; 59 FR 23636, May 6, 1994; 63 FR 16685, Apr. 6, 1998; 64 FR 45371, Aug. 19, 1999]

EFFECTIVE DATE NOTE: The information collection requirements contained in § 606.121 will not become effective until OMB approval has been obtained. FDA will publish a notice of OMB approval in the FEDERAL REGISTER.

§ 606.122 Instruction circular.

An instruction circular shall be available for distribution if the product is intended for transfusion. The instruction circular shall provide adequate directions for use, including the following information:

(a) Instructions to mix the product before use.

(b) Instructions to use a filter in the administration equipment.

(c) The statement “Do Not Add Medications” or an explanation concerning allowable additives.

(d) A description of the product, its source, and preparation, including the name and proportion of the anticoagulant used in collecting the Whole Blood from each product is prepared.

(e) Statements that the product was prepared from blood that was negative when tested for antibody to Human Immunodeficiency Virus (HIV) and non-reactive for hepatitis B surface antigen by FDA required tests and nonreactive when tested for syphilis by a serologic test for syphilis (STS).

(f) The statements: “Warning. The risk of transmitting infectious agents is present. Careful donor selection and available laboratory tests do not eliminate the hazard.”

(g) The names of cryoprotective agents and other additives that may still be present in the product.

(h) The names and results of all tests performed when necessary for safe and effective use.

(i) The use of the product, indications, contraindications, side effects and hazards, dosage and administration recommendations.

(j) [Reserved]

(k) For Red Blood Cells, the instruction circular shall contain:

(1) Instructions to administer a suitable plasma volume expander if Red Blood Cells are substituted when Whole Blood is the indicated product.

(2) A warning not to add Lactated Ringer’s Injection U.S.P. solution to Red Blood Cell products.

(1) For Platelets, the instruction circular shall contain:

(1) The approximate volume of plasma from which a sample unit of Platelets is prepared.

(2) Instructions to begin administration as soon as possible, but not more than 4 hours after entering the container.

(m) For Plasma, the instruction circular shall contain:

(1) A warning against further processing of the frozen product if there is evidence of breakage or thawing.

(2) Instructions to thaw the frozen product at a temperature between 30 and 37 °C.

(3) When applicable, instructions to begin administration of the product within 6 hours after thawing.

(4) Instructions to administer to ABO-group-compatible recipients.

(5) A statement that this product has the same hepatitis risk as Whole Blood;

other plasma volume expanders without this risk are available for treating hypovolemia.

(n) For Cryoprecipitated AHF, the instruction circular shall contain:

(1) A statement that the average potency is 80 or more International Units of antihemophilic factor.

(2) The statement: "Usually contains at least 150 milligrams of fibrinogen"; or, alternatively, the average fibrinogen level determined by assay of representative units.

(3) A warning against further processing of the product if there is evidence of breakage or thawing.

(4) Instructions to thaw the product for no more than 15 minutes at a temperature of between 30 and 37 °C.

(5) Instructions to store at room temperature after thawing and to begin administration as soon as possible but no more than 4 hours after entering the container or after pooling and within 6 hours after thawing.

(6) A statement that 0.9 percent Sodium Chloride Injection U.S.P. is the preferred diluent.

(7) Adequate instructions for pooling to ensure complete removal of all concentrated material from each container.

(8) The statement: "Good patient management requires monitoring treatment responses to Cryoprecipitated AHF transfusions with periodic plasma factor VIII or fibrinogen assays in hemophilia A and hypofibrinogenemic recipients, respectively."

[50 FR 35470, Aug. 30, 1985, as amended at 53 FR 116, Jan. 5, 1988; 64 FR 45371, Aug. 19, 1999]

EFFECTIVE DATE NOTE: The information collection requirements contained in §606.122 will not become effective until OMB approval has been obtained. FDA will publish a notice of OMB approval in the FEDERAL REGISTER.

Subpart H—Laboratory Controls

§ 606.140 Laboratory controls.

Laboratory control procedures shall include:

(a) The establishment of scientifically sound and appropriate specifications, standards and test procedures to assure that blood and blood compo-

nents are safe, pure, potent and effective.

(b) Adequate provisions for monitoring the reliability, accuracy, precision and performance of laboratory test procedures and instruments.

(c) Adequate identification and handling of all test samples so that they are accurately related to the specific unit of product being tested, or to its donor, or to the specific recipient, where applicable.

§ 606.151 Compatibility testing.

Standard operating procedures for compatibility testing shall include the following:

(a) A method of collecting and identifying the blood samples of recipients to ensure positive identification.

(b) The use of fresh recipient serum samples less than 48 hours old for all pretransfusion testing.

(c) The testing of the donor's cells with the recipient's serum (major crossmatch) by a method that will demonstrate agglutinating, coating, and hemolytic antibodies, which shall include the antiglobulin method.

(d) A provision that, if the unit of donor's blood has not been screened by a method that will demonstrate agglutinating, coating and hemolytic antibodies, the recipient's cells shall be tested with the donor's serum (minor crossmatch) by a method that will so demonstrate.

(e) Procedures to expedite transfusion in life-threatening emergencies. Records of all such incidents shall be maintained, including complete documentation justifying the emergency action, which shall be signed by a physician.

[40 FR 53532, Nov. 18, 1975, as amended at 64 FR 45371, Aug. 19, 1999; 66 FR 1835, Jan. 10, 2001]

Subpart I—Records and Reports

§ 606.160 Records.

(a)(1) Records shall be maintained concurrently with the performance of each significant step in the collection, processing, compatibility testing, storage and distribution of each unit of blood and blood components so that all steps can be clearly traced. All records shall be legible and indelible, and shall

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identify the person performing the work, include dates of the various entries, show test results as well as the interpretation of the results, show the expiration date assigned to specific products, and be as detailed as necessary to provide a complete history of the work performed.

(2) Appropriate records shall be available from which to determine lot numbers of supplies and reagents used for specific lots or units of the final product.

(b) Records shall be maintained that include, but are not limited to, the following when applicable:

(1) Donor records:

(i) Donor selection, including medical interview and examination and where applicable, informed consent.

(ii) Permanent and temporary deferrals for health reasons including reason(s) for deferral.

(iii) Donor adverse reaction complaints and reports, including results of all investigations and followup.

(iv) Therapeutic bleedings, including signed requests from attending physicians, the donor's disease and disposition of units.

(v) Immunization, including informed consent, identification of the antigen, dosage and route of administration.

(vi) Blood collection, including identification of the phlebotomist.

(vii) Records to relate the donor with the unit number of each previous donation from that donor.

(viii) Records of quarantine, notification, testing, and disposition performed pursuant to §§ 610.46 and 610.47 of this chapter.

(2) Processing records:

(i) Blood processing, including results and interpretation of all tests and retests.

(ii) Component preparation, including all relevant dates and times.

(iii) Separation and pooling of recovered plasma.

(iv) Centrifugation and pooling of source plasma.

(v) Labeling, including initials of the person(s) performing the procedure.

(3) Storage and distribution records:

(i) Distribution and disposition, as appropriate, of blood and blood products.

(ii) Visual inspection of whole blood and red blood cells during storage and immediately before distribution.

(iii) Storage temperature, including initialed temperature recorder charts.

(iv) Reissue, including records of proper temperature maintenance.

(v) Emergency release of blood, including signature of requesting physician obtained before or after release.

(4) Compatibility test records:

(i) Results of all compatibility tests, including crossmatching, testing of patient samples, antibody screening and identification.

(ii) Results of confirmatory testing.

(5) Quality control records:

(i) Calibration and standardization of equipment.

(ii) Performance checks of equipment and reagents.

(iii) Periodic check on sterile technique.

(iv) Periodic tests of capacity of shipping containers to maintain proper temperature in transit.

(v) Proficiency test results.

(6) Transfusion reaction reports and complaints, including records of investigations and followup.

(7) General records:

(i) Sterilization of supplies and reagents prepared within the facility, including date, time interval, temperature and mode.

(ii) Responsible personnel.

(iii) Errors and accidents.

(iv) Maintenance records for equipment and general physical plant.

(v) Supplies and reagents, including name of manufacturer or supplier, lot numbers, expiration date and date of receipt.

(vi) Disposition of rejected supplies and reagents used in the collection, processing and compatibility testing of blood and blood components.

(c) A donor number shall be assigned to each accepted donor, which relates the unit of blood collected to that donor, to his medical record, to any component or blood product from that donor's unit of blood, and to all records describing the history and ultimate disposition of these products.

(d) Records shall be retained for such interval beyond the expiration date for the blood or blood component as necessary to facilitate the reporting of

any unfavorable clinical reactions. The retention period shall be no less than 5 years after the records of processing have been completed or 6 months after the latest expiration date for the individual product, whichever is a later date. When there is no expiration date, records shall be retained indefinitely.

(e) A record shall be available from which unsuitable donors may be identified so that products from such individuals will not be distributed.

[40 FR 53532, Nov. 18, 1975, as amended at 61 FR 47422, Sept. 9, 1996; 64 FR 45371, Aug. 19, 1999]

EFFECTIVE DATE NOTE: At 65 FR 66635, Nov. 7, 2000, §606.160 was amended by revising paragraph (b)(7)(iii), effective May 7, 2000. At 65 FR 67477, Nov. 9, 2000, the effective date was corrected to read May 7, 2001. For the convenience of the user, the revised text is set forth as follows:

§ 606.160 Records.

- * * * * *
- (b) * * *
- (7) * * *
- (iii) Biological product deviations.
- * * * * *

§ 606.165 Distribution and receipt; procedures and records.

(a) Distribution and receipt procedures shall include a system by which the distribution or receipt of each unit can be readily determined to facilitate its recall, if necessary.

(b) Distribution records shall contain information to readily facilitate the identification of the name and address of the consignee, the date and quantity delivered, the lot number of the unit(s), the date of expiration or the date of collection, whichever is applicable, or for crossmatched blood and blood components, the name of the recipient.

(c) Receipt records shall contain the name and address of the collecting facility, date received, donor or lot number assigned by the collecting facility and the date of expiration or the date of collection, whichever is applicable.

§ 606.170 Adverse reaction file.

(a) Records shall be maintained of any reports of complaints of adverse reactions regarding each unit of blood

or blood product arising as a result of blood collection or transfusion. A thorough investigation of each reported adverse reaction shall be made. A written report of the investigation of adverse reactions, including conclusions and followup, shall be prepared and maintained as part of the record for that lot or unit of final product by the collecting or transfusing facility. When it is determined that the product was at fault in causing a transfusion reaction, copies of all such written reports shall be forwarded to and maintained by the manufacturer or collecting facility.

(b) When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, shall be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible; a written report of the investigation shall be submitted to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, within 7 days after the fatality by the collecting facility in the event of a donor reaction, or by the facility that performed the compatibility tests in the event of a transfusion reaction.

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0116)

[40 FR 53532, Nov. 18, 1975, as amended at 49 FR 23833, June 8, 1984; 50 FR 35471, Aug. 30, 1985; 55 FR 11014, Mar. 26, 1990; 64 FR 45371, Aug. 19, 1999]

§ 606.171 Reporting of product deviations by licensed manufacturers, unlicensed registered blood establishments, and transfusion services.

(a) *Who must report under this section?* You, a licensed manufacturer of blood and blood components, including Source Plasma; an unlicensed registered blood establishment; or a transfusion service who had control over the product when the deviation occurred, must report under this section. If you arrange for another person to perform a manufacturing, holding, or distribution step, while the product is in your control, that step is performed under your control. You must establish, maintain, and follow a procedure for

receiving information from that person on all deviations, complaints, and adverse events concerning the affected product.

(b) *What do I report under this section?* You must report any event, and information relevant to the event, associated with the manufacturing, to include testing, processing, packing, labeling, or storage, or with the holding or distribution, of both licensed and unlicensed blood or blood components, including Source Plasma, if that event meets all the following criteria:

(1) Either:

(i) Represents a deviation from current good manufacturing practice, applicable regulations, applicable standards, or established specifications that may affect the safety, purity, or potency of that product; or

(ii) Represents an unexpected or unforeseeable event that may affect the safety, purity, or potency of that product; and

(2) Occurs in your facility or another facility under contract with you; and

(3) Involves distributed blood or blood components.

(c) *When do I report under this section?* You should report a biological product deviation as soon as possible but you must report at a date not to exceed 45-calendar days from the date you, your agent, or another person who performs a manufacturing, holding, or distribution step under your control, acquire information reasonably suggesting that a reportable event has occurred.

(d) *How do I report under this section?* You must report on Form FDA-3486.

(e) *Where do I report under this section?* You must send the completed Form FDA-3486 to the Director, Office of Compliance and Biologics Quality (HFM-600), 1401 Rockville Pike, suite 200N, Rockville MD, 20852-1448 by either a paper or electronic filing:

(1) If you make a paper filing, you should identify on the envelope that a BPDR (biological product deviation report) is enclosed; or

(2) If you make an electronic filing, you may submit the completed Form FDA-3486 electronically through CBER's website at www.fda.gov/cber.

(f) *How does this regulation affect other FDA regulations?* This part supplements and does not supersede other provisions

of the regulations in this chapter. All biological product deviations, whether or not they are required to be reported under this section, should be investigated in accordance with the applicable provisions of parts 211, 606, and 820 of this chapter.

EFFECTIVE DATE NOTE: At 65 FR 66635, Nov. 7, 2000, §606.171 was added to subpart I, effective May 7, 2000. At 65 FR 67477, Nov. 9, 2000, the effective date was corrected to May 7, 2001.

PART 607—ESTABLISHMENT REGISTRATION AND PRODUCT LISTING FOR MANUFACTURERS OF HUMAN BLOOD AND BLOOD PRODUCTS

Subpart A—General Provisions

Sec.

607.3 Definitions.

607.7 Establishment registration and product listing of blood banks and other firms manufacturing human blood and blood products.

Subpart B—Procedures for Domestic Blood Product Establishments

607.20 Who must register and submit a blood product list.

607.21 Times for establishment registration and blood product listing.

607.22 How and where to register establishments and list blood products.

607.25 Information required for establishment registration and blood product listing.

607.26 Amendments to establishment registration.

607.30 Updating blood product listing information.

607.31 Additional blood product listing information.

607.35 Notification of registrant; blood product establishment registration number and NDC Labeler Code.

607.37 Inspection of establishment registrations and blood product listings.

607.39 Misbranding by reference to establishment registration or to registration number.

Subpart C—Procedures for Foreign Blood Product Establishments

607.40 Blood product listing requirements for foreign blood product establishments.