

**§ 606.100**

(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]**

**21 CFR Ch. I (4–1–23 Edition)**

**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) Establishments must establish, maintain, and follow written standard operating procedures for all steps in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for allogeneic transfusion, autologous transfusion, and further manufacturing purposes; for all steps in the investigation of product deviations related to § 606.171; and for all steps in record-keeping related to current good manufacturing practice and other applicable requirements and standards. Such procedures must be available to the personnel for use in the areas where the procedures are performed. The written standard operating procedures must include, but are not limited to, descriptions of the following, when applicable:

(1) Criteria used to determine donor eligibility, 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 under §§ 610.46 and 610.47 of this chapter:

(i) To identify previously donated blood and blood components from a donor who later tests reactive for evidence of human immunodeficiency virus (HIV) infection or hepatitis C virus (HCV) infection when tested under § 610.40 of this chapter, or when a blood establishment is made aware of other reliable test results or information indicating evidence of HIV or HCV infection;

(ii) To quarantine in-date blood and blood components previously donated

by such a donor that are intended for use in another person or further manufacture into injectable products, except pooled components intended solely for further manufacturing into products that are manufactured using validated viral clearance procedures;

(iii) To notify consignees to quarantine in-date blood and blood components previously donated by such a donor intended for use in another person or for further manufacture into injectable products, except pooled components intended solely for further manufacturing into products that are manufactured using validated viral clearance procedures;

(iv) To determine the suitability for release, destruction, or relabeling of quarantined in-date blood and blood components;

(v) To notify consignees of the results of the HIV or HCV testing performed on the donors of such blood and blood components;

(vi) To notify the transfusion recipient, the recipient's physician of record, or the recipient's legal representative that the recipient received blood or blood components at increased risk of transmitting HIV or HCV, respectively.

(20) Procedures for donor deferral as prescribed in § 610.41 of this chapter.

(21) Procedures for donor notification and notification of the referring physician of an autologous donor, including procedures for the appropriate followup if the initial attempt at notification fails, as prescribed in § 630.40 of this chapter.

(22) Procedures to control the risks of bacterial contamination of platelets, including all steps required under § 606.145.

(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.

## § 606.110

(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; 66 FR 31176, June 11, 2001; 72 FR 48798, Aug. 24, 2007; 80 FR 80651, Dec. 28, 2015; 80 FR 29895, May 22, 2015]

## § 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 responsible physician who is aware of the health status of the donor, and the physician has determined and documented that the donor's health permits plateletpheresis or leukapheresis.

(b) Plasmapheresis of donors who do not meet the donor requirements of §§ 630.10, 630.15, 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; 80 FR 29895, May 22, 2015]

## 21 CFR Ch. I (4–1–23 Edition)

### Subpart G—Additional Labeling Standards for Blood and Blood Components

#### § 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 intended for use in transfusion or further manufacture by all blood establishments.

(b) The label provided by the collecting facility and the initial processing facility must not be removed, altered, or obscured, except that the label may be altered to indicate the proper name of the product, with any appropriate modifiers and attributes, and other information required to identify accurately the contents of a container after blood components considered finished products have been prepared.

(c) The container label must 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, with any appropriate modifiers and attributes.