

and Drug Administration. Such testing shall not be considered as divided manufacturing, as described in §610.63 of this chapter, provided the following conditions are met:

(1) The establishment licensed for Cryoprecipitated AHF has obtained a written agreement that the testing laboratory will permit an authorized representative of the Food and Drug Administration to inspect its testing procedures and facilities during reasonable business hours.

(2) The testing laboratory will participate in any proficiency testing programs undertaken by the Center for Biologics Evaluation and Research, Food and Drug Administration.

(d) If the average potency level of antihemophilic factor in the containers tested is less than 80 units of antihemophilic factor per container, immediate corrective actions shall be taken and a record maintained of such action.

[42 FR 21774, Apr. 29, 1977, as amended at 49 FR 23834, June 8, 1984; 50 FR 4140, Jan. 29, 1985; 55 FR 11013, Mar. 26, 1990; 64 FR 45373, Aug. 19, 1999; 66 FR 1837, Jan. 10, 2001]

Subpart G—Source Plasma

§ 640.60 Source Plasma.

The proper name of the product shall be Source Plasma. The product is defined as the fluid portion of human blood collected by plasmapheresis and intended as source material for further manufacturing use. The definition excludes single donor plasma products intended for intravenous use.

[41 FR 10768, Mar. 12, 1976, as amended at 50 FR 4140, Jan. 29, 1985]

§ 640.64 Collection of blood for Source Plasma.

(a) [Reserved]

(b) *Blood containers.* Blood containers and donor sets must be pyrogen-free, sterile, and identified by lot number.

(c) *The anticoagulant solution.* The anticoagulant solution must be sterile and pyrogen-free. Anticoagulant solutions must be compounded and used according to a formula that has been approved for the applicant by the Director, Center for Biologics Evaluation and Research.

(d) *Donor identification.* Each unit of blood and plasma shall be so marked or identified by number or other symbol so as to relate it directly to the donor.

(e) *Prevention of contamination of the blood and plasma.* The skin of the donor at the site of phlebotomy shall be prepared thoroughly and carefully by a method that gives maximum assurance of a sterile container of blood. The blood shall be collected, the plasma separated, and the cells returned to the donor by aseptic methods in a sterile system which may be closed, or may be vented if the vent protects the blood cells and plasma against contamination.

[38 FR 32089, Nov. 20, 1973; 39 FR 13632, Apr. 16, 1974, as amended at 41 FR 10768, Mar. 12, 1976; 49 FR 23834, June 8, 1984; 50 FR 4140, Jan. 29, 1985; 55 FR 11013, Mar. 26, 1990; 59 FR 49351, Sept. 28, 1994; 63 FR 16685, Apr. 6, 1998; 64 FR 56453, Oct. 20, 1999; 72 FR 45888, Aug. 16, 2007; 80 FR 29905, May 22, 2015]

§ 640.65 Plasmapheresis.

(a) *Procedure-general.* The plasmapheresis procedure is a procedure in which, during a single visit to the establishment, blood is removed from a donor, the plasma separated from the formed elements, and at least the red blood cells returned to the donor. This procedure shall be described in detail in the biologics license application.

(b) *Procedures-specific requirements.* The plasmapheresis procedure shall meet the following requirements:

(1)(i) Except as provided under § 630.25 of this chapter, the responsible physician must draw a sample of blood from each donor on the day of the initial physical examination or plasmapheresis, whichever comes first, and at least every 4 months thereafter. A serologic test for syphilis, a total plasma or serum protein determination, and a plasma or serum protein electrophoresis or quantitative immuno-diffusion test or an equivalent test to determine immunoglobulin composition of the plasma or serum shall be performed on the sample.

(ii) A repeat donor who does not return for plasmapheresis at the time the 4-month sample is due to be collected may be plasmapheresed on the day he appears: *Provided*, That no longer than 6 months has elapsed since the last

sample was collected, and the responsible physician approves the plasmapheresis procedure and so indicates by signing the donor's record before such procedure is performed. The sample for the 4-month tests shall be collected on the day of the donor's return.

(iii) A repeat donor from whom the plasmapheresis center is unable to obtain a sample for testing as prescribed in paragraph (b)(1)(i) of this section for a total period exceeding 6 months shall be processed as a new donor.

(2)(i) Except as provided under § 630.25 of this chapter, the responsible physician must review the accumulated laboratory data, including any tracings of the plasma or serum protein electrophoresis pattern, the calculated values of the protein composition of each component, and the collection records within 14 calendar days after the sample is drawn to determine whether or not the donor should be deferred from further donation. If a determination is not made within 14 calendar days, the donor must be deferred pending such a determination. The responsible physician must sign the review. If the protein composition is not within normal limits established by the testing laboratory, or if the total protein level is less than 6.0 grams per deciliter or more than 9.0 grams per deciliter in a plasma sample or serum sample, the donor must be deferred from donation until the protein composition returns to acceptable levels. Reinstatement of the donor into the plasmapheresis program when the donor's protein composition values have returned to an acceptable level must first be approved by the responsible physician.

(ii) A donor with a reactive serologic test for syphilis shall not be plasmapheresed again until the donor's serum is tested and found to be non-reactive to a serologic test for syphilis, except as provided in paragraph (b)(2)(iii) and (iv) of this section.

(iii) A donor whose serum is determined to have a biologic false-positive reaction to a serologic test for syphilis may be plasmapheresed: *Provided*, That the donor's file identifies the serologic test for syphilis and results used to confirm the biologic false-positive reaction and indicates that the responsible physician has determined the

false-positive reaction is not the result of an underlying disorder that would disqualify the donor from participation in the plasmapheresis program. If the serologic test for syphilis is performed at a facility other than the plasmapheresis center, all applicable provisions of § 640.71 shall be met.

(iv) A donor with a reactive serologic test for syphilis may be plasmapheresed only to obtain plasma to be used for further manufacturing into control serum for the serologic test for syphilis: *Provided*, That the responsible physician approves the donation, the donor's file contains a signed statement from a physician or clinic establishing that treatment for syphilis has been initiated and that continuance in the plasmapheresis program will not interfere with or jeopardize the treatment of the syphilitic donor.

(3) A donor identification system shall be established that positively identifies each donor and relates such donor directly to his blood and its components as well as to his accumulated records and laboratory data. Such system shall include either a photograph of each donor which shall be used on each visit to confirm the donor's identity, or some other method that provides equal or greater assurance of positively identifying the donor.

(4) The amount of whole blood, not including anticoagulant, removed from a donor during a manual plasmapheresis procedure or in any 2-day period shall not exceed 1,000 milliliters unless the donor's weight is 175 pounds or greater, in which case the amount of whole blood, not including anticoagulant, removed from the donor during a manual plasmapheresis procedure or in any 2-day period shall not exceed 1,200 milliliters.

(5) The amount of whole blood, not including anticoagulant, removed from a donor during a manual plasmapheresis procedure within a 7-day period shall not exceed 2,000 milliliters unless the donor's weight is 175 pounds or greater, in which case the amount of whole blood, not including anticoagulant, removed from a donor during a manual plasmapheresis procedure within a 7-day period shall not exceed 2,400 milliliters.

(6) No more than 500 milliliters of whole blood shall be removed from a donor at one time, unless the donor's weight is 175 pounds or greater, in which case no more than 600 milliliters of whole blood shall be removed from the donor at one time.

(7) The plasma shall be separated from the red blood cells immediately after blood collection. The maximum feasible volume of red blood cells shall be returned to the donor before another unit is collected.

(8) The volume of plasma collected during an automated plasmapheresis collection procedure shall be consistent with the volumes specifically approved by the Director, Center for Biologics Evaluation and Research, and collection shall not occur less than 2 days apart or more frequently than twice in a 7-day period.

[38 FR 32089, Nov. 20, 1973, as amended at 41 FR 10769, Mar. 12, 1976; 64 FR 45373, Aug. 19, 1999; 64 FR 56453, Oct. 20, 1999; 80 FR 29905, May 22, 2015]

§ 640.66 Immunization of donors.

If specific immunization of a donor is to be performed, the selection, scheduling and administration of the antigen, and the evaluation of each donor's clinical response, shall be by the responsible physician. Any material used for immunization shall be either a product licensed under section 351 of the Public Health Service Act for such purpose or one specifically approved by the Director, Center for Biologics Evaluation and Research, Food and Drug Administration. Immunization procedures shall be on file at each plasmapheresis center where immunizations are performed.

[38 FR 32089, Nov. 20, 1973, as amended at 49 FR 23834, June 8, 1984; 55 FR 11013, Mar. 26, 1990; 80 FR 29905, May 22, 2015]

§ 640.67 Laboratory tests.

Each unit of Source Plasma shall be tested for evidence of infection due to relevant transfusion-transmitted infections as required under §610.40 of this chapter.

[66 FR 31165, June 11, 2001, as amended at 80 FR 29905, May 22, 2015]

§ 640.68 Processing.

(a) *Sterile system.* All administration and transfer sets inserted into blood containers used for processing Source Plasma intended for manufacturing into injectable or noninjectable products and all interior surfaces of plasma containers used for processing Source Plasma intended for manufacturing into injectable products shall be sterile, pyrogen-free, nontoxic, and compatible with the contents under normal conditions of use. Only Sodium Chloride Injection USP shall be used as a red blood cell diluent. If the method of separation of the plasma intended for injectable products involves a system in which an airway must be inserted into the plasma container, the airway shall be sterile and constructed so as to exclude microorganisms and maintain a sterile system.

(b) *Final containers.* Final containers used for Source Plasma, whether integrally attached or separated from the original blood container, shall not be entered prior to issuance for any purpose except for filling with the plasma. Such containers shall be uncolored and hermetically sealed, and shall permit clear visibility of the contents. Final containers and their components shall not interact with the plasma contents under conditions of storage and use so as to alter the safety, quality, purity, or potency of the plasma and shall provide adequate protection against external factors that may cause deterioration or contamination. Prior to filling, the final container shall be marked or identified by number or other symbol which will relate it directly to the donor.

(c) *Preservative.* Source Plasma shall not contain a preservative.

[38 FR 32089, Nov. 20, 1973, as amended at 41 FR 10769, Mar. 12, 1976; 50 FR 4140, Jan. 29, 1985]

§ 640.69 General requirements.

(a) *Pooling.* Two units of Source Plasma from the same donor may be pooled if such units are collected during one plasmapheresis procedure: *Provided*, That the pooling is done by a procedure that does not introduce a risk of contamination of the red blood cells and, for plasma intended for injectable