

§ 640.66

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]

§ 640.66 Immunization of donors.

If specific immunization of a donor is to be performed, the selection and scheduling of the injection of the antigen, and the evaluation of each donor's clinical response, shall be by a qualified licensed physician or physicians. The administration of the antigen may be performed by a licensed physician or a trained person under his supervision. 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]

§ 640.67 Laboratory tests.

(a) *Hepatitis B surface antigen.* Each unit of Source Plasma shall be non-reactive to a test for hepatitis B sur-

21 CFR Ch. I (4-1-01 Edition)

face antigen as prescribed in §§610.40 and 610.41 of this chapter, except insofar as permitted in §610.40(d)(1) and (d)(2) of this chapter.

(b) *Antibody to HIV.* Each unit of Source Plasma shall be negative by a test for antibody to HIV as prescribed in §610.45 of this chapter, except as provided in §610.45(c) of this chapter.

[53 FR 117, Jan. 5, 1988, as amended at 57 FR 10814, Mar. 31, 1992]

§ 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 products, gives maximum assurance of a sterile container of plasma.

(1) The pooling of plasma from two or more donors is not permitted in the manufacture of Source Plasma intended for manufacturing into injectable products.

(2) The pooling of plasma from two or more donors by the manufacturer of Source Plasma intended for manufacturing into noninjectable products is permitted: *Provided*, That the plasma from two or more donors is pooled after the plasma has been removed from the red blood cells, and after the red blood cell containers are sealed.

(b) *Storage*. Immediately after filling, plasma intended for manufacturing into injectable products shall be stored at a temperature not warmer than -20°C , except for plasma collected as provided in § 640.74. Plasma intended for manufacturing into noninjectable products may be stored at temperatures appropriate for the intended use of the final product, provided these temperatures are included in the Source Plasma license application.

(c) *Inspection*. Source Plasma intended for manufacturing into injectable products shall be inspected for evidence of thawing at the time of issuance, except that inspection of individual plasma containers need not be made if the records of continuous monitoring of the storage temperature establish that the temperature remained at -20°C or colder. If there is evidence that the storage temperature has not been maintained at -20°C or colder, the plasma may be relabeled and issued as provided in § 640.76(a).

(d) *Samples*. If samples are provided, they shall meet the following standards:

(1) Prior to filling, all samples shall be marked or identified so as to relate them directly to the donor of that unit of plasma.

(2) All samples shall be filled at the time the final product is prepared by the person who prepares the final product.

(3) All samples shall be representative of the contents of the final product or be collected from the donor at the time of filling the collection container.

(4) All samples shall be collected in a manner that does not contaminate the contents of the final container.

[38 FR 32089, Nov. 20, 1973, as amended at 41 FR 10769, Mar. 12, 1976; 41 FR 14367, Apr. 5, 1976; 50 FR 4140, Jan. 29, 1985; 63 FR 16685, Apr. 6, 1998; 64 FR 45374, Aug. 19, 1999]

§ 640.70 Labeling.

(a) In addition to the labeling requirements of § 610.62 of this chapter, and in lieu of the requirements in §§ 606.121, 610.60, and 610.61 of this chapter, the following information shall appear on the label affixed to each container of Source Plasma:

(1) The proper name of the product.

(2) The statement "Caution: For Manufacturing Use Only" for products intended for further manufacturing into injectable products, or the statement, "Caution: For Use In Manufacturing Noninjectable Products Only", for products intended for further manufacturing into noninjectable products. The statement shall follow the proper name in the same size and type of print as the proper name.

(3) The statement "Store at -20°C or colder": *Provided*, That where plasma is intended for manufacturing into noninjectable products, this statement may be omitted if replaced by a statement of the temperature appropriate for the final product to be prepared from the plasma.

(4) The total volume or weight of plasma and total quantity and type of anticoagulant used.

(5) The donor number or individual bleed number, or both. If plasma is pooled from two or more donors, either all donor numbers, all bleed numbers, or a pool number that is traceable to