

the manufacturer of the final blood derivative product who has requested the Source Plasma Liquid.

(3) The label for the Source Plasma Liquid shall be easily distinguished from that of the frozen product. Color coding shall not be used for this purpose.

(4) The label affixed to each container of Source Plasma Liquid shall contain, in addition to the information required by § 640.70(a) but excluding § 640.70(a)(3), the name of the manufacturer of the final blood derivative product for whom it was prepared.

(5) Source Plasma Liquid shall be inspected immediately prior to issuance. If the color or physical appearance is abnormal, or there is any indication or suspicion of microbial contamination, the unit of Source Plasma Liquid shall not be issued.

[38 FR 32089, Nov. 20, 1973. Redesignated and amended at 41 FR 10770, 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]

§ 640.76 Products stored or shipped at unacceptable temperatures.

(a) *Storage temperature.* (1) Except as provided in paragraph (a)(2) of this section, Source Plasma intended for manufacture into injectable products that is inadvertently exposed (i.e., an unforeseen occurrence in spite of compliance with good manufacturing practice) to a storage temperature warmer than -20°C and colder than $+10^{\circ}\text{C}$ may be issued only if labeled as "Source Plasma Salvaged." The label shall be revised before issuance, and appropriate records shall be maintained identifying the units involved, describing their disposition, and explaining fully the conditions that caused the inadvertent temperature exposure.

(2) Source Plasma intended for manufacture into injectable products that is exposed inadvertently (i.e., an unforeseen occurrence in spite of compliance with good manufacturing practice) to one episode of storage temperature fluctuation that is warmer than -20°C and colder than -5°C for not more than 72 hours is exempt from the labeling requirements of paragraph (a)(1) of this section, provided that the plasma has been and remains frozen solid. Appropriate records shall be maintained identifying the units involved, describing their disposition, explaining fully the conditions that caused the inadvertent temperature exposure, and documenting that the episode of temperature elevation did not exceed 72 hours, that the temperature did not rise to warmer than -5°C in storage, and that the plasma remained frozen solid throughout the period of elevated temperature. When requested, copies of the records shall be provided to the plasma derivative manufacturer.

(b) *Shipping temperature.* If Source Plasma for manufacture into injectable products is exposed inadvertently (i.e., an unforeseen occurrence in spite of compliance with good manufacturing practice) to a shipping temperature warmer than -5°C and colder than $+10^{\circ}\text{C}$, the plasma derivative manufacturer shall label it "Source Plasma Salvaged." Appropriate records shall be maintained identifying the units involved, describing their disposition, and explaining fully the conditions that caused the inadvertent temperature exposure.

(c) *Relabeling.* If Source Plasma is required to be relabeled as "Source Plasma Salvaged" under paragraph (a)(1) or (b) of this section, the person responsible for the relabeling shall cover the original label with either (1) a complete new label containing the appropriate information or (2) a partial label affixed to the original label and containing the appropriate new information, which covers the incorrect information regarding storage temperature.

[45 FR 80501, Dec. 5, 1980, as amended at 50 FR 4140, Jan. 29, 1985]

Subpart H—Albumin (Human)

§ 640.80 Albumin (Human).

(a) *Proper name and definition.* The proper name of the product shall be Albumin (Human). The product is defined as a sterile solution of the albumin component of human blood.

(b) *Source material.* The source material of Albumin (Human) shall be blood, plasma, serum or placentas from human donors determined at the time of donation to have been free from disease-causative agents that are not destroyed or removed by the processing

method, as determined by the medical history of the donor and from such physical examination and clinical tests as may appear necessary for each donor at the time the blood was obtained. Where source material is a product for which additional standards are effective, the requirements of those additional standards shall determine the propriety of the source material for use in the production of Albumin (Human). Where no additional standards are effective with respect to source material for the production of Albumin (Human), such source material shall:

(1) Be collected by a procedure which is designed to assure the integrity and to minimize the risk of contamination of the source material. The manufacturer of Albumin (Human) shall ensure that the collection procedure shall be as described in its license.

(2) Be identified to relate it accurately to the individual donor and the dates of collection.

(3) Not contain a preservative.

(4) Be stored and transported in a manner designed to prevent contamination by microorganisms, pyrogens, or other impurities.

(c) *Additives in source material.* Source material shall not contain an additive unless it is shown that the processing method yields a final product free of the additive to such extent that the continued safety, purity, potency, and effectiveness of the final product will not be adversely affected.

[42 FR 27582, May 31, 1977, as amended at 50 FR 4140, Jan. 29, 1985]

§ 640.81 Processing.

(a) *Date of manufacture.* The date of manufacture shall be the date of final sterile filtration of a uniform pool of bulk solution.

(b) *Processing method.* The processing method shall not affect the integrity of the product, and shall have been shown to yield consistently a product which is safe for intravenous injection.

(c) *Microbial contamination.* All processing steps shall be conducted in a manner to minimize the risk of contamination from either microorganisms or other deleterious matter. Preservatives to inhibit growth of microorganisms shall not be used during processing.

(d) *Storage of bulk fraction.* Bulk concentrate to be held more than 1 week prior to further processing shall be stored in clearly identified closed vessels at a temperature of -5°C or colder. Any other bulk form of the product, exclusive of the sterile bulk solution, to be held more than 1 week prior to further processing shall be stored in clearly identified closed vessels at a temperature of 5°C or colder. Any bulk fraction to be held one week or less prior to further processing shall be stored in clearly identified closed vessels at a temperature of 5°C or colder.

(e) *Heat treatment.* Heating of the final containers of Albumin (Human) shall begin within 24 hours after completion of filling. Heat treatment shall be conducted so that the solution is heated for not less than 10 or more than 11 hours at an attained temperature of $60^{\circ}\pm 0.5^{\circ}\text{C}$.

(f) *Stabilizer.* Either 0.16 millimole sodium acetyltryptophanate, or 0.08 millimole sodium acetyltryptophanate and 0.08 millimole sodium caprylate shall be added per gram of albumin as a stabilizer.

(g) *Incubation.* All final containers of Albumin (Human) shall be incubated at 20 to 35°C for at least 14 days following the heat treatment prescribed in paragraph (e) of this section. At the end of this incubation period, each final container shall be examined and all containers showing any indication of turbidity or microbial contamination shall not be issued. The contents of turbid final containers shall be examined microscopically and tested for sterility. If growth occurs, organisms shall be identified as to genus, and the material from such containers shall not be used for further manufacturing.

[42 FR 27582, May 31, 1977, as amended at 50 FR 4140, Jan. 29, 1985]

§ 640.82 Tests on final product.

Tests shall be performed on the final product to determine that it meets the following standards:

(a) *Protein content.* Final product shall conform to one of the following concentrations: 4.0 ± 0.25 percent; 5.0 ± 0.30 percent; 20.0 ± 1.2 percent; and 25.0 ± 1.5 percent solution of protein.

(b) *Protein composition.* At least 96 percent of the total protein in the final