

antibody test (§640.104(b) (2) and (3)) whichever date is earlier.

(e) *Labeling.* In addition to complying with all applicable labeling required in this subchapter, labeling shall indicate that:

(1) There is no prescribed potency for viral hepatitis antibodies.

(2) The product is not recommended for intravenous administration.

(3) The lot is or is not suitable for use with Measles Virus Vaccine Live.

(4) The lot is or is not recommended for poliomyelitis.

(f) *Samples and protocols.* For each lot of Immune Globulin (Human) the following material shall be submitted to the Director, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892:

(1) A 50 ml. sample of the final product.

(2) All protocols relating to the history of each lot and all results of all tests prescribed in these additional standards.

[38 FR 32089, Nov. 20, 1973; 48 FR 13026, Mar. 29, 1983, as amended at 49 FR 23834, June 8, 1984; 50 FR 4140, Jan. 29, 1985; 51 FR 15611, Apr. 25, 1986; 55 FR 11013, Mar. 26, 1990]

#### §640.102 Manufacture of Immune Globulin (Human).

(a) *Processing method.* The processing method shall be one that has been shown: (1) To be capable of concentrating tenfold from source material at least two different antibodies; (2) not to affect the integrity of the globulins; (3) to consistently yield a product which is safe for subcutaneous and intramuscular injection and (4) not to transmit viral hepatitis.

(b) *Microbial contamination.* Low temperatures or aseptic techniques shall be used to minimize contamination by microorganisms. Preservatives to inhibit growth of microorganisms shall not be used during processing.

(c) *Bulk storage.* The globulin fraction may be stored in bulk prior to further processing provided it is stored in clearly identified hermetically closed vessels. Globulin as either a liquid concentrate or a solid and containing alcohol or more than 5 percent moisture shall be stored at a temperature of  $-10^{\circ}\text{C}$ . or lower. Globulin as a solid free

from alcohol and containing less than 5 percent moisture, shall be stored at a temperature of  $0^{\circ}\text{C}$ . or lower.

(d) *Determination of the lot.* Each lot of Immune Globulin (Human) shall represent a pooling of approximately equal amounts of material from not less than 1,000 donors.

(e) *Sterilization and heating.* The final product shall be sterilized promptly after solution. At no time during processing shall the product be exposed to temperatures above  $45^{\circ}\text{C}$ . and after sterilization the product shall not be exposed to temperatures above 30 to  $32^{\circ}\text{C}$ . for more than 72 hours.

[38 FR 32089, Nov. 20, 1973, as amended at 50 FR 4140, Jan. 29, 1985]

#### §640.103 The final product.

(a) *Final solution.* The final product shall be a  $16.5\pm 1.5$  percent solution of globulin containing 0.3 molar glycine and a preservative.

(b) *Protein composition.* At least 90 percent of the globulin shall have an electrophoretic mobility not faster than  $-2.8\times 10^{-5}$  centimeters<sup>2</sup> per volt per second, when measured at a 1 percent protein concentration in sodium diethylbarbiturate buffer at pH 8.6 and 0.1 ionic strength.

#### §640.104 Potency.

(a) *Antibody levels and tests.* Each lot of final product shall contain at least the minimum levels of antibodies for diphtheria, measles, and for at least one type of poliomyelitis. In the event the final bulk solution is stored at a temperature above  $5^{\circ}\text{C}$ . the antibody level tests shall be performed after such storage with a sample of the stored material.

(b) *Minimum levels.* The minimum antibody levels are as follows:

(1) No less than 2 units of diphtheria antitoxin per ml.

(2) A measles neutralizing antibody level of no less than 0.50 times the level of the Reference Immune Serum Globulin, except that when recommended for use with Measles Virus Vaccine Live, the measles antibody level shall be as prescribed in §640.114.

(3) A poliomyelitis neutralizing antibody level of no less than 1.0 for Type 1, 1.0 for Type 2, and 2.5 for Type 3,

§ 640.120

times the antibody level of the Reference Immune Serum Globulin.

(c) *Reference materials.* The following reference materials shall be obtained from the Center for Biologics Evaluation and Research:

(1) Reference Immune Serum Globulin for correlation of measles antibody titers.

(2) Reference Immune Serum Globulin for correlation of poliomyelitis antibody titers, Types 1, 2, and 3.

[38 FR 32089, Nov. 20, 1973, as amended at 39 FR 9661, Mar. 13, 1974; 49 FR 23834, June 8, 1984; 50 FR 4140, Jan. 29, 1985; 55 FR 11013, Mar. 26, 1990]

**Subpart K [Reserved]**

**Subpart L—Alternative Procedures**

**§ 640.120 Alternative procedures.**

(a) The Director, Center for Biologics Evaluation and Research, may approve an exception or alternative to any requirement in subchapter F of chapter I of title 21 of the Code of Federal Regulations regarding blood, blood components, or blood products. Requests for such exceptions or alternatives shall ordinarily be in writing. Licensed establishments shall submit such requests in accordance with §601.12 of this chapter. However, in limited circumstances, such requests may be made orally and permission may be given orally by the Director. Oral requests and approvals must be promptly followed by written requests and written approvals.

(b) FDA will publish a list of approved alternative procedures and exceptions periodically in the FEDERAL REGISTER.

[55 FR 10423, Mar. 21, 1990, as amended at 62 FR 39903, July 24, 1997]

**PART 660—ADDITIONAL STANDARDS FOR DIAGNOSTIC SUBSTANCES FOR LABORATORY TESTS**

**Subpart A—Antibody to Hepatitis B Surface Antigen**

Sec.

660.1 Antibody to Hepatitis B Surface Antigen.

660.2 General requirements.

**21 CFR Ch. I (4–1–98 Edition)**

660.3 Reference panel.

660.4 Potency test.

660.5 Specificity.

660.6 Samples; protocols; official release.

**Subpart B [Reserved]**

**Subpart C—Blood Grouping Reagent**

660.20 Blood Grouping Reagent.

660.21 Processing.

660.22 Potency requirements with reference preparations.

660.25 Potency tests without reference preparations.

660.26 Specificity tests and avidity tests.

660.28 Labeling.

**Subpart D—Reagent Red Blood Cells**

660.30 Reagent Red Blood Cells.

660.31 Suitability of the donor.

660.32 Collection of source material.

660.33 Testing of source material.

660.34 Processing.

660.35 Labeling.

660.36 Samples and protocols.

**Subpart E—Hepatitis B Surface Antigen**

660.40 Hepatitis B Surface Antigen.

660.41 Processing.

660.42 Reference panel.

660.43 Potency test.

660.44 Specificity.

660.45 Labeling.

660.46 Samples; protocols; official release.

**Subpart F—Anti-Human Globulin**

660.50 Anti-Human Globulin.

660.51 Processing.

660.52 Reference preparations.

660.53 Controls for serological procedures.

660.54 Potency tests, specificity tests, tests for heterospecific antibodies, and additional tests for nonspecific properties.

660.55 Labeling.

AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371; 42 U.S.C. 216, 262, 263, 263a, 264.

CROSS REFERENCES: For U.S. Customs Service regulations relating to viruses, serums, and toxins, see 19 CFR 12.21–12.23. For U.S. Postal Service regulations relating to the admissibility to the United States mails see parts 124 and 125 of the Domestic Mail Manual, that is incorporated by reference in 39 CFR part 111.

**Subpart A—Antibody to Hepatitis B Surface Antigen**

**§ 660.1 Antibody to Hepatitis B Surface Antigen.**

(a) *Proper name and definition.* The proper name of this product shall be