

detecting known *Mycoplasma* and each test shall include control cultures of at least two known strains of *Mycoplasma*, one of which must be *M. pneumoniae*. One half of the plates and two tubes of broth shall be incubated aerobically at 36 °C. ±1 °C. and the remaining plates and tubes shall be incubated anaerobically at 36 °C. ±1 °C. in an environment of 5–10 percent CO<sub>2</sub> in N<sub>2</sub>. Aerobic incubation shall be for a period of no less than 14 days and the broth in the two tubes shall be tested after 3 days and 14 days, at which times 0.5 ml. of broth from each of the two tubes shall be combined and subinoculated on to no less than 4 additional plates and incubated aerobically. Anaerobic incubation shall be for no less than 14 days and the broth in the two tubes shall be tested after 3 days and 14 days, at which times 0.5 ml. of broth from each of the two tubes shall be combined and subinoculated onto no less than four additional plates and incubated anaerobically. All inoculated plates shall be incubated for no less than 14 days, at which time observation for growth of *Mycoplasma* shall be made at a magnification of no less than 300x. If the Dienes Methylene Blue-Azure dye or an equivalent staining procedure is used, no less than a one square cm. plug of the agar shall be excised from the inoculated area and examined for the presence of *Mycoplasma*. The presence of the *Mycoplasma* shall be determined by comparison of the growth obtained from the test samples with that of the control cultures, with respect to typical colonial and microscopic morphology. The virus pool is satisfactory for vaccine manufacture if none of the tests on the samples show evidence of the presence of *Mycoplasma*.

### Subpart E—Hepatitis Requirements

#### § 610.40 Test for hepatitis B surface antigen.

(a) *Test sensitivity.* Each donation of blood, plasma, or serum to be used in preparing a biological product shall be tested for the presence of hepatitis B surface antigen by a method of sufficient sensitivity to detect all sera labeled A, (A), B, (B), and C in the Reference Hepatitis B Surface Antigen Panel distributed by the Center for Biologics Evaluation and Research; except that, in emergency situations, a test method of sufficient sensitivity to detect all sera labeled A, (A), and B in the Reference Hepatitis B Surface Antigen Panel may be used and, in dire emergency situations, blood and blood products may be issued without any HB<sub>s</sub> Ag testing, provided that a test

otherwise required by this paragraph is performed as soon as possible after issuance of the blood and blood product.

(b) *Procedures.* Only Antibody to Hepatitis B Surface Antigen licensed under this subchapter shall be used in performing the test and the test method(s) used shall be that for which the antibody product is specifically designed to be effective as recommended by the manufacturer in the package insert. The sample of blood, plasma, or serum to be tested shall have been taken from the donor at the time of donation of that unit. The test need not be performed on the day of the withdrawal of the sample. If the radioimmunoassay method is used, it must be performed in one of the following ways:

(1) The complete test is performed at the collection facility.

(2) The test is performed at the collection facility up to the point of counting the radioactivity of the samples, which counting, thereafter, is performed at another facility by personnel from the collection facility or by personnel from the counting facility.

(3) The complete test is performed by the personnel at an establishment licensed to manufacture blood or blood derivatives under section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)), or by a clinical laboratory which meets the standards of the Clinical Laboratories Improvement Act of 1967 (CLIA) (42 U.S.C. 263a), provided the establishment or the clinical laboratory is qualified to perform radioimmunoassay testing for the presence of hepatitis B surface antigen.

(4) Except as provided in this paragraph (b)(4), a collection facility shall not ship any blood product as a biological product or ship such a blood product where it is intended for use in manufacturing a biological product until the test for hepatitis B surface antigen is completed and the written test results are received by the collection facility. Notwithstanding the provisions of § 610.1 of this chapter, in the case of an emergency, or as otherwise approved in writing by the Director, Center for Biologics Evaluation and Research, a collection facility may ship a blood product before the test for hepatitis B surface antigen is completed. To

obtain approval for such shipments, the collection facility shall submit a description of the control procedures to be used by both the collection facility and the manufacturing facility to the Director, Center for Biologics Evaluation and Research (HFB-1), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892. The control procedures to be used by the collection facility and the manufacturing facility shall include, but may not be limited to, a system of communicating the test results to the manufacturing facility, use of specific labeling warnings for the product to ensure that persons handling the shipment know that it may be infectious, procedures for quarantine of the untested or incompletely tested product both at the collection facility and at the manufacturing facility, and a procedure at the manufacturing facility to identify, preclude use of, and dispose of any blood product that is received and later found to be reactive for hepatitis B surface antigen.

(c) *Materials in storage.* All blood, plasma, or serum in storage which has not been tested for the presence of the hepatitis B surface antigen shall be tested as required in paragraphs (a) and (b) of this section before use as a biological product, or before use in the manufacture of a biological product. All blood, plasma, or serum in storage which has been tested for the presence of the hepatitis B surface antigen by a method of second generation sensitivity may be used as a biological product or in manufacture of a biological product, provided it is used on or before March 15, 1976.

(d) *Restrictions on use.* Blood, plasma, or serum that is reactive when tested for hepatitis B surface antigen or that was collected from a donor known to be reactive for hepatitis B surface antigen shall not be used in manufacturing biological products except as provided in paragraphs (d) (1) and (2) of this section.

(1) *Injectable biological products and licensed in vitro diagnostic biological products.* Blood, plasma, or serum that is reactive when tested for hepatitis B surface antigen or that was collected from a donor known to be reactive for hepatitis B surface antigen may be

used in manufacturing hepatitis B vaccine and licensed in vitro diagnostic biological products if all of the following conditions are met:

(i) The final product cannot be prepared from blood, plasma, or serum that is nonreactive when tested for hepatitis B surface antigen, due either to the nature or to the scarcity of the final product.

(ii) The label of the source blood, plasma, or serum conspicuously states either that it is reactive when tested for hepatitis B surface antigen and it may transmit viral hepatitis; or that the source blood, plasma, or serum was collected from a donor known to be reactive for hepatitis B surface antigen and it may transmit viral hepatitis, although confirmatory hepatitis testing has not been done.

(iii) The package label of the licensed in vitro diagnostic biological product prepared from such blood, plasma, or serum states conspicuously that either the product was prepared from source material that was reactive when tested for hepatitis B surface antigen and it may transmit viral hepatitis; or that the source material was collected from a donor known to be reactive for hepatitis B surface antigen and it may transmit viral hepatitis, although confirmatory hepatitis testing has not been done.

(iv) The package label of the licensed injectable biological product prepared from such blood, plasma, or serum states that the product has been inactivated.

(v) The Director, Center for Biologics Evaluation and Research (HFB-1), Food and Drug Administration, 8800 Rockville Pike, Bethesda MD 20892, is notified in writing at the time of the shipment, or in the case of repetitive shipments, or April 1 and October 1 of each year, of each shipment of source blood, plasma, or serum for manufacture into hepatitis B vaccine or into a licensed in vitro diagnostic biological product. Such shipments shall not be subject to the requirements of paragraph (b)(3) of this section. Each notification shall identify the kind and amount of source material shipped, the name and address of the consignee, the date of shipment, and the manner in which the source material is labeled.

(2) *Unlicensed in vitro diagnostic biological products.* Blood, plasma, or serum that is reactive when tested for hepatitis B surface antigen or that was collected from a donor known to be reactive for hepatitis B surface antigen may be used in manufacturing unlicensed in vitro diagnostic biological products including clinical chemistry control reagents if all of the following conditions are met:

(i) The final product cannot be prepared from blood, plasma, or serum that is nonreactive when tested for hepatitis B surface antigen, due either to the nature or to the scarcity of the final product.

(ii) The label of the source blood, plasma, or serum states conspicuously that either it is reactive when tested for hepatitis B surface antigen and it may transmit viral hepatitis; or that the source blood, plasma, or serum was collected from a donor known to be reactive for hepatitis B surface antigen and it may transmit viral hepatitis, although confirmatory hepatitis testing has not been done.

(iii) The manufacturer of the source blood, plasma, or serum obtains written assurance from the manufacturer(s) of the final unlicensed product that package labels of all unlicensed products will conspicuously state, as required by §809.10(a)(4) of this chapter, that the product was prepared from blood, plasma, or serum that was reactive when tested for hepatitis B surface antigen and it may transmit viral hepatitis; or that the source material was collected from a donor known to be reactive for hepatitis B surface antigen and it may transmit viral hepatitis, although confirmatory hepatitis testing has not been done.

(iv) At the time of shipment, the Director, Center for Biologics Evaluation and Research (HFB-1), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892, is notified in writing of each shipment of source blood, plasma, or serum signifying the kind and the amount of source material shipped, the name and address of the consignee, the date of shipment, and the manner in which such source material was labeled. Such shipments shall not be subject to the requirements of paragraph (b)(3) of this section.

(e) *Manufacturing responsibility.* When the radioimmunoassay method for hepatitis B surface antigen testing is performed by personnel other than those of the facility collecting the blood, plasma, or serum, as provided in paragraph (b) of this section, it shall not be considered as divided manufacturing as described in §610.63, provided the following conditions are met:

(1) The collecting facility has obtained a written agreement that the testing laboratory will permit authorized representatives 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.

(f) The information collection requirements in paragraph (d) of this section were approved by the Office of Management and Budget and assigned OMB control number 0910-0136.

(Information collection requirements contained in paragraph (b)(4) were approved by the Office of Management and Budget under control number 0910-0168)

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#### **§610.41 History of hepatitis B surface antigen.**

A person known to have previously tested positive for hepatitis B surface antigen, testing positive, or both, may not serve as a donor of human blood, plasma, or serum, except that under §640.120 of this chapter, such a donor may serve as a source of hepatitis B surface antigen for the manufacture of hepatitis B vaccine or the preparation of a diagnostic product for laboratory tests, or a person known to have previously tested positive for hepatitis B surface antigen may serve as a source of antibody to hepatitis B surface antigen for the preparation of a biological product or a diagnostic product for laboratory tests.

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