Donor Suitability Related to Laboratory Testing (12/22/93)

Date: December 22, 1993

From: Director, Center for Biologics Evaluation and Research

Subject: Donor Suitability Related to Laboratory Testing for Viral Hepatitis and a History of Viral Hepatitis

To: All Registered Blood Establishments

This Memorandum is intended to clarify donor suitability criteria related to medical history and laboratory testing for viral hepatitis enumerated in 21 CFR 610.40 and 21 CFR 640.41 (for blood, plasma or serum), 21 CFR 640.3(c)(1) (for Whole Blood) and 640.63(c)(11) (for Source Plasma).

This clarification augments the Memorandum of April 23, 1992, to all registered blood establishments, "Exemptions to Permit Persons with a History of Viral Hepatitis Before the Age of Eleven Years to Serve as Donors of Whole Blood and Plasma: Alternative Procedures, 21 CFR 640.120." In that Memorandum, the agency noted that the regulations, 21 CFR 640.3(c)(1) and 640.63(c)(11), preclude persons with a history of viral hepatitis, occurring at any age, from donating Whole Blood or Source Plasma. Based on a recommendation of the Blood Products Advisory Committee made on September 27, 1991, and its own evaluation of the data, FDA announced its intention to propose amendments to the regulations to permit persons with a history of viral hepatitis occurring before the age of 11 years to donate Whole Blood and Source Plasma. Until the regulations are amended, the FDA will consider procedures acceptable that permit a person with a history of viral hepatitis before the age of eleven years to serve as a donor of Whole Blood, and Source Plasma, in conformance with 21 CFR 640.120, Alternative Procedures.

On September 24, 1992, after discussion in a public meeting FDA's Blood Products Advisory Committee recommended that FDA clarify the term "history of viral hepatitis", as it appears in the regulations cited above. The Committee concluded that isolated laboratory test results that may be associated with a diagnosis of viral hepatitis, i.e., test results in the absence of a clinical history or medical diagnosis, should not be interpreted as a history of viral hepatitis.

In accordance with the recommendations of the Committee, the FDA is providing the following guidance:

Whole Blood and Blood Components Intended for Transfusion

A. History of Viral Hepatitis at the Age of 11 Years or Later

Donor suitability in regard to a history of viral hepatitis at the age of 11 years or later should be assessed by asking the donor for recollections of experiencing physical signs or symptoms of clinical hepatitis (e.g., "yellow jaundice" or other pertinent physical evidence of clinical hepatitis) or having received a diagnosis of viral hepatitis from a physician. Records of laboratory data (e.g., serology, ALT, AST, bilirubin, prothrombin time), if available, may assist the medical director in making the donor suitability determination in the face of an inconclusive history. However, certain isolated laboratory test results should not be considered equivalent to a history of viral hepatitis. In particular, a history of an elevated alanine aminotransferase (ALT) or a reactive test for anti-HAV or anti-HBs need not be cause to defer a donor. However, persons with a history of a positive (confirmed) test for HBsAg, regardless of age at the time of the positive test, are precluded from donating blood, plasma, or serum under 21 CFR 610.41.

If a clinical history or diagnosis of viral hepatitis occurring at age 11 years or later is established, the donor should be permanently deferred and blood and blood components collected from the donor should not be used in the manufacture of products intended for transfusion. If viral hepatitis infection after the age of 11 years is suspected to have occurred, the donor should be temporarily deferred and blood and blood components collected from the donor should not be used in the manufacture of products intended for transfusion until the circumstances are investigated and a medical opinion rendered on the significance of the history, and the conclusion drawn that there is no history or diagnosis of viral hepatitis after age 11.

B. Laboratory Testing

In the absence of a clinical history of hepatitis, FDA does not consider the results of laboratory testing alone equivalent to a "history of hepatitis" as specified in 21 CFR 640.3(c)(1) and 640.63(c)(11). However, the results of laboratory testing are important to consider in determining the suitability of donated units. The laboratory test results for viral hepatitis markers that should be applied to a donation when assessing acceptability are (1) results

1. At the time of donation of Whole Blood or blood components, laboratory test results which indicate that the collected unit should not be used for transfusion include the following:

   (i) a repeatedly reactive screening test result for hepatitis B surface antigen (HBsAg) (see reference 1); or

(ii) a repeatedly reactive screening test for antibody to hepatitis B core antigen (anti-HBc) (see reference 2); or

(iii) a repeatedly reactive screening test result for antibody to the hepatitis C virus (anti-HCV) (see reference 3).

2. Donors should be indefinitely deferred on the basis of the following laboratory test results:

(i) a repeatedly reactive screening test result for HBsAg that has been confirmed as positive by neutralization test (see reference 4); or

(ii) a repeatedly reactive screening test result for HBsAg, unless the donor has satisfied the FDA recommended re-entry algorithm (See reference 5); or

(iii) a repeatedly reactive screening test result for anti-HBc on more than one occasion (see reference 2); or

(iv) a repeatedly reactive screening test result for anti-HCV on any single occasion, unless the donor has satisfied the FDA recommended re-entry algorithm (see reference 3).

Plasma for Further Manufacture

The suitability of donors of plasma for further manufacture should be assessed in accordance with the same procedures as those for Whole Blood and Components intended for transfusion,

A. Source Plasma: The FDA does not currently recommend that Source Plasma donations be tested for anti-HBc, and that anti-HBc reactive units be withheld from pools used for the manufacture of plasma derivatives, because of the following considerations: If anti-HBc reactive units were excluded from such pools, titers of anti-HBs, the antibody capable of neutralizing undetectable quantities of hepatitis B virus in those pools, would be expected to diminish, as both of these antibodies usually occur together in plasma . Accordingly, as the presence of neutralizing anti-HBs likely contributes to the safety of certain plasma products (in particular, the immunoglobulins), withholding units reactive for anti-HBc might compromise product safety.

B. Recovered Plasma: The FDA currently considers Recovered Plasma units that are untested, nonreactive, or repeatedly reactive for anti-HBc

acceptable for the manufacture of plasma derivatives under short supply agreements with U.S. licensed plasma fractionators (see reference 2

References

1. 21 CFR 610.40(d).

2. FDA Recommendations Concerning Testing for Antibody to Hepatitis B Core Antigen (Anti-HBc); September 10, 1991

3. Revised Recommendations for Testing Whole Blood, Blood Components, Source Plasma and Source Leukocytes for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV); April 23, 1992, and August 5, 1993.

4. 21 CFR 610.41.

5. Recommendations for the Management of Donors and Units that are Initially Reactive for hepatitis B Surface Antigen (HBsAg); December 2, 1987.

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