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Revised Recommendations for Testing Whole Blood (8/5/93)

Date: August 5, 1993

From: Acting Director, Office of Blood Research and Review,  
Center for Biologics Evaluation and Research

Subject: Revised Recommendations for Testing Whole Blood,  
Blood Components, Source Plasma and Source Leukocytes  
for Antibody to Hepatitis C Virus Encoded Antigen  
(Anti-HCV)

To: All Registered Blood Establishments

This memorandum transmits Revised Recommendations for Testing for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV) in Blood Establishments, August, 1993. These revised recommendations modify those issued on April 23, 1992, in regard to testing for anti-HCV. A donor who currently tests, or who in the past had tested, repeatedly reactive for anti-HCV with a solid phase enzyme linked immunoassay (ELISA), licensed by the Food and Drug Administration (FDA), may now be considered for re-entry provided that certain criteria, described in this document, are fulfilled.

On April 23, 1992 FDA recommended (1) that units of Whole Blood and blood components intended for transfusion, and Source Plasma and Source Leukocytes intended for further manufacture, be screened by an FDA licensed test for anti-HCV and (2) that no products repeatedly reactive for anti-HCV be used. In memoranda issued by FDA concerning testing for anti-HCV dated November 29, 1990 and April 23, 1992, no donor re-entry protocol for donors who were repeatedly reactive for anti-HCV by ELISA was recommended because of the lack of an available licensed additional (supplemental), more specific test.

In public meetings on March 12, 1992 and March 26, 1993, FDA's Blood Products Advisory Committee (BPAC) recommended the use of a re-entry algorithm for donors who test repeatedly reactive for anti-HCV in ELISA tests, should suitable supplemental tests for anti-HCV become available for donor re-evaluation.

According to the attached recommendations, donors testing (or who, in the past, tested) repeatedly reactive in a licensed screening test for anti-HCV may be re-evaluated after a minimum period of six months. During the time period prior to reevaluation, the donor should not donate blood or blood products.

However, additional testing may be done for the purposes of counseling. Upon retest after 6 months or more, to qualify for re-entry, the donor should test nonreactive in both a licensed multi-antigen\* screening test and a licensed multi-antigen\* supplemental test for antibodies to HCV. [\* Footnote: "Multi-

antigen" refers to kit component antigens that, in addition to c100-3, includes antigens other than those contained in c100-3.]

Donors should be indefinitely deferred from donating Whole Blood and blood components intended for transfusion and for further manufacture, and Source Plasma and Source Leukocytes intended for further manufacture whenever they test repeatedly reactive in a licensed multi-antigen ELISA and reactive (indeterminate or positive) for anti-HCV in a multi-antigen supplemental assay. Blood establishments should also defer donors if they test repeatedly reactive in a licensed multi-antigen ELISA assay on more than one occasion. No re-entry procedure should be used for these donors.

The attached document replaces sections I.A. and I.B. (page 3 to page 4, line 7) of the FDA's prior memorandum in regard to anti-HCV testing dated April 23, 1992. Pages 1, 2 and 3 of the April 23, 1992, memorandum should now be replaced by pages 1, 2, 3, 3a, 3b and 3c of the attached document. Guidance on all matters not directly related to donor suitability and re-entry in regard to anti-HCV testing (such as "lookback", use of autologous units, donor deferral due to contact with individuals having viral hepatitis, the labeling, quarantine, storage and shipment of units of blood and blood components, etc.) remain unchanged from the April 23, 1992, memorandum, and those sections of that memorandum should be retained. Labeling, informed consent forms, standard operating procedures, deferral registries, and record keeping procedures should already have been revised as necessary to reflect the blood establishment's implementation of anti-HCV testing.

Questions concerning testing for antibodies to HCV and donor re-entry may be directed in writing to the Division of Transfusion Transmitted Diseases, Laboratory of Hepatitis, HFM-325, HHS/PHS/Food and Drug Administration, Center for Biologics Evaluation and Research, Suite 200N, 1401 Rockville Pike, Rockville, MD 20852-1448, FAX: (301) 227-0209. Questions concerning labeling may be directed in writing to the Division of Blood Establishment and Product Application, HFM-380 (Suite 200N, 1401 Rockville, MD 20852-1448), FAX: (301) 295-8973.

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Revised Recommendations for Testing  
for  
Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV)  
in  
Blood Establishments

August, 1993

U.S. Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Biologics Evaluation and Research

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REVISED RECOMMENDATIONS FOR TESTING FOR ANTIBODY  
TO HEPATITIS C VIRUS ENCODED ANTIGEN  
(ANTI-HCV) IN BLOOD ESTABLISHMENTS  
August, 1993

- I. PERFORMANCE OF ANTI-HCV TESTING AND DONOR SUITABILITY
  - A. Anti-HCV testing, using a multi-antigen\*, enzyme-linked immunoassay (ELISA) test, should be performed and test results interpreted according to the manufacturer's instructions in the package insert. Instructions for currently licensed kits may be summarized as follows:  
[Footnote: \* "Multi-antigen" refers to kit component antigens that, in addition to c100-3, includes antigens other than those contained in c100-3.]
    - 1. A single ELISA test for anti-HCV should be performed on a donor sample for each unit of whole blood or blood component intended for transfusion and on each unit of plasma or source leukocytes for further manufacture. This ELISA test will hereafter be referred to as the "initial test."

2. If the initial test result is nonreactive, the donor sample is considered to be negative for anti-HCV.
3. If the initial test result is reactive, the donor sample is considered to be initially reactive.

A sample from the same collection should be retested in duplicate, within a single run, using the same procedure and same manufacturer's ELISA test as that used for the initial test.

- a. If both duplicate ELISA repeat test results are nonreactive, the sample is considered to be negative for anti-HCV.
  - b. If either one or both of the ELISA duplicate repeat test results are reactive, the sample is considered to be repeatedly reactive for anti-HCV in the screening test, and the products should not be used for transfusion or routinely for further manufacture. Possible exceptions to permit use of anti-HCV reactive products in special circumstances are described in Section I.C. and Section III.B. regarding anti-HCV testing. No further screening tests for anti-HCV should be performed on samples from this unit in an effort to qualify it as suitable for release.
  - c. Additional testing may be done for the purpose of counseling the donor (see B.4., below) and in the context of the re-entry algorithm described below. FDA recommends that blood establishments use only licensed supplemental tests for either donor notification or consideration of possible re-entry.
- B. Donors who are repeatedly reactive for anti-HCV, using multi-antigen ELISA screening tests, should be indefinitely deferred. Units collected from deferred donors should be discarded and not released. However, at the discretion of the blood establishment, a donor testing repeatedly reactive in a screening test may be further evaluated for possible re-entry as a qualified donor as follows:
1. A minimum time period of six months should elapse between the index donation (i.e., the

one that tested repeatedly reactive in a screening ELISA test) and the follow-up sample to evaluate any donor for possible re-entry. The follow-up sample should be tested for anti-HCV in a licensed multi-antigen screening ELISA test as described in I.A.

- a. If the ELISA test result is repeatedly reactive, the donor is indefinitely deferred.
  - b. If the ELISA test is non reactive, the sample should be tested in a licensed supplemental test as described below in I.B.2.
2. Anti-HCV testing using a currently licensed multi-antigen supplemental test should be performed on a follow-up sample obtained after a minimum time period of six months from the index donation. The test results should be interpreted according to the manufacturer's instructions in the package insert.
- a. If the supplemental test result is indeterminate or positive, the test result is considered to be supplemental test reactive, and the donor is indefinitely deferred.
  - b. If the supplemental test result is nonreactive, the donor may be re-entered as a qualified donor.
  - c. If the follow-up sample is obtained from a donation of a unit, then the ELISA (described in B.1.) and the supplemental test (described in B.2) should be performed on (a) sample(s) from the same collection as the unit. If both tests are negative, then the current unit may be used.
3. Donors who were indefinitely deferred because of a unit testing repeatedly reactive for anti-HCV in a licensed screening ELISA test, and for which a multi-antigen supplemental test was not performed or for which negative results were obtained in a multi-antigen supplemental test, may be re-evaluated as described in B.1., and B.2., above.

4. Any person testing, or who has tested, either repeatedly reactive in a licensed multi-antigen ELISA assay on more than one occasion, or reactive (indeterminate or positive) in a multi-antigen supplemental assay (including unlicensed assays), is indefinitely deferred from donating. Such persons should not be re-entered+. [Footnote: + To avoid unnecessary re-bleeding of the donor, it may be convenient for blood establishments to perform a licensed supplemental test for anti-HCV on a frozen sample from the index donation.] Donors who were indefinitely deferred based on a repeatedly reactive ELISA screening test for anti-HCV using a single antigen (c100-3) based assay may be considered for re-entry even if such reactivity occurred on more than one determination. The index donation in I.B.1. should be taken as the most recent reactive donation.
5. If any additional optional testing is, or has been, performed using licensed multi-antigen ELISA assays or multi-antigen supplemental assays (including unlicensed assays), either on the index donation or subsequently on the donor, all test results obtained should be non reactive and/or negative, if donor re-entry is to be attempted.
6. General guidance in regard to the testing, counseling, and evaluation of donors tested for hepatitis viruses is described in the Public Health Service Interagency Guidelines for Screening Donors of Blood, Plasma, Organs, Tissues, and Semen for Evidence of Hepatitis B and Hepatitis C, MMWR 1991; 40 (RR-4): 1-17.
7. These recommendations are subject to future revision as improvements and advances in technology become available.

Figure 2

FDA RECOMMENDATIONS FOR DONOR REENTRY AND FOR  
DISPOSITION OF QUARANTINED UNITS FROM PRIOR (NEGATIVE) COLLECTIONS  
FOLLOWING A REPEATEDLY REACTIVE SCREENING TEST  
FOR HIV-1 ANTIGEN(S)

Donor is eligible for reentry based on a  
NEGATIVE or INDETERMINATE test for HIV-1 antigen(s) including Neutralization Testing

Obtain follow-up specimen  $\geq 8$  weeks after repeatedly reactive test

Perform screening tests for HIV-1 Antigen(s) and  
for antibodies to HIV-1 and HIV-2<sup>1</sup>

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Repeatedly Reactive on  
any screening test

□  
□  
□  
□

Defer donor permanently.  
Destroy or suitably label current unit  
and units from prior (negative)  
collections.

Negative  
for all markers

□  
□  
□  
□

Reenter donor.  
Current unit may be used  
if donor is otherwise  
suitable. Quarantined units  
from prior (negative)  
collections may be released.

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<sup>1</sup>If retesting of the donor is not performed within six months, any quarantined  
units from prior collections should be destroyed or suitably relabeled.