

Guidance for Industry

Donor Screening for Antibodies to HTLV-II

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GUIDANCE FOR INDUSTRY¹: DONOR SCREENING FOR ANTIBODIES TO HTLV-II

I. INTRODUCTION

This guidance document provides the recommendations of the Food and Drug Administration (FDA) on the implementation of donor screening for antibodies to human T-lymphotropic virus type II (HTLV-II).

II. BACKGROUND

In November, 1988, FDA issued a guidance document which recommended testing donations of whole blood and cellular components intended for transfusion for antibodies to human T-lymphotropic virus type I (HTLV-I). That recommendation, which was concurrent with licensing of the first test kit to detect antibodies to HTLV-I, was made because HTLV-I was identified as the etiologic agent of a number of disorders, including adult T-cell leukemia and HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP). Especially significant were reports of individuals who developed HAM/TSP within 12 months following transfusion with blood from HTLV-I-infected donors. Three test kits to detect antibodies to HTLV-I from three manufacturers are currently licensed for this purpose.

HTLV-II is a virus closely related to HTLV-I, sharing approximately 60% sequence homology. Antibodies to HTLV-II often are cross-reactive for HTLV-I, and currently licensed screening assays are unable to distinguish between the two viruses. In fact, it appears that approximately half of the HTLV infections detected among blood donors are due to HTLV-II.(1)

In March, 1993, the Blood Products Advisory Committee (BPAC) was asked to consider a claim for the detection of antibodies to HTLV-II for a test that contained an HTLV-I viral lysate and a recombinant form of the HTLV-I p21e protein. This request was made based on the cross-reactivity of antibodies to HTLV-II for HTLV-I antigens. Data were presented which indicated that, at that time, licensed HTLV-I test kits detected from 46-91% of a panel of 110

¹ This guidance document represents the FDA's current thinking on donor screening for antibodies to HTLV-II. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternate approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. Written requests for single copies of this document may be submitted to the Office of Communication, Training and Manufacturers Assistance, HFM-40, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist that office in processing your requests. The document may also be obtained by mail by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800, or by fax by calling the FAX Information System at 888-CBER-FAX or 301-827-3844. Persons with access to the INTERNET may obtain the document using the World Wide Web (WWW) by connecting to CBER at <http://www.fda.gov/cber/guidelines.htm>

HTLV-II samples assembled by FDA, most of which had been selected using HTLV-I tests. Because of the absence of an HTLV-II antigen-based comparator test, the Committee felt that HTLV-II antigen(s) must be present in the kit to allow a labeling claim for the detection of HTLV-II antibodies. The Committee did not vote at that time to recommend that blood donors be routinely screened for antibodies to HTLV-II because evidence for the involvement of HTLV-II in disease, while accumulating, was not strong enough to warrant a recommendation. In addition, a recommendation for donor screening would have been premature in the absence of a candidate licensed screening test for antibody to HTLV-II.

In December, 1996, the Blood Products Advisory Committee again considered the question of whether to recommend routine screening of blood donors for antibodies to HTLV-II. At that time, a test kit containing HTLV-II antigens was under review by FDA that met the criteria set forth by the Committee in March, 1993, for a labeling claim of sensitivity for HTLV-II. Based on the availability of a suitable test and on additional data establishing the association of HTLV-II with disease,(2) the Committee recommended that donor blood be routinely screened for antibodies to HTLV-II (in addition to screening for antibodies to HTLV-I) when a licensed test becomes available for this purpose. The Committee also considered strategies to implement this testing and revisited the issue of detection of antibodies to HTLV-II based on cross-reactivity with HTLV-I antigens. Data were presented which showed that, due to recent technical improvements, some currently licensed test kits for detection of antibodies to HTLV-I exhibit a high degree of sensitivity for detection of antibodies to HTLV-II.

After considering the available information and the opinions of the BPAC members, FDA is now recommending that blood establishments implement donor screening for antibodies to HTLV-II using licensed tests that are approved for this indication. Such testing should begin within 6 months of the date of licensure of the first test specifically labeled for this purpose.

The specific recommendations contained in Section III of this guidance document are intended to supplement previous guidance documents on HTLV-I antibody testing and product disposition which issued on November 29, 1988 (3) and July 19, 1996 (4).

The testing algorithm used to screen donations for antibodies to HTLV-II, the manner in which repeatedly reactive donations are handled, and recommendations for donor deferral, notification and counseling, are consistent with those outlined in the November 29, 1988 guidance(3) to registered blood establishments on HTLV-I antibody testing. Recommendations for quarantine of prior collections and disposition and release of units are consistent with those outlined in the July 19, 1996 guidance(4) to registered blood establishments on product retrieval.

III. SPECIFIC RECOMMENDATIONS

A. IMPLEMENTATION OF SCREENING FOR ANTIBODIES TO HTLV-II

All donations of Whole Blood and blood components intended for use in transfusion and Source Leukocytes intended for manufacturing use should be screened for antibodies to HTLV-II by an FDA licensed test labeled specifically for use in donor screening. This recommendation should be implemented within 6 months of the commercial availability of the first such test. Following the date of implementation, only units from donors found to be negative on screening test(s) for antibodies to both HTLV-I and HTLV-II should be released for use in transfusion.

Licensed establishments implementing these recommendations should submit by official correspondence within 6 months of receipt of this guidance document a statement to their product license file indicating the date that revised standard operating procedures, consistent with the recommendations, have been established and implemented.

FDA is not recommending that inventoried units of Whole Blood and blood components collected prior to the date of implementation be rescreened for antibodies to HTLV-I and HTLV-II.

B. HANDLING OF DONATIONS WITH REPEATEDLY REACTIVE EIA TEST RESULTS

Whole Blood and blood components that test repeatedly reactive by FDA licensed screening tests for the detection of antibodies to HTLV-I and HTLV-II, should not be used for transfusion and should be quarantined and destroyed unless labeled with two cautionary statements as follows:

“Reactive by a test for HTLV-I or HTLV-II antibodies. The risk of transmission of HTLV-I or HTLV-II is present.”

and

“For further manufacture into in vitro diagnostic reagents for which there are no alternative sources” or “For laboratory research use only”.

C. QUARANTINE AND DISPOSITION OF UNITS FROM PRIOR COLLECTIONS FROM DONORS WHO SUBSEQUENTLY TEST REPEATEDLY REACTIVE FOR ANTI-HTLV-I OR ANTI-HTLV-II

1. Quarantine of Prior Collections, Notification of Consignees, and Additional Testing

Prior collections of Whole Blood and blood components should be excluded from use for transfusion,

1) from a donor who subsequently tests repeatedly reactive for anti-HTLV-I or anti-HTLV-II by a licensed screening test, and who does not have a nonreactive test result by a second, licensed screening test of a different type² for anti-HTLV-I and anti-HTLV-II on the current repeatedly reactive donor sample (i.e., the sample tests reactive in a second, licensed screening test, or such a test on the sample is not performed),

or

2) from a donor who tests anti-HTLV-I or anti-HTLV-II repeatedly reactive, and is then indefinitely deferred because a repeatedly reactive anti-HTLV-I or anti-HTLV-I/II test result had been obtained on a previous occasion.(3)

Whenever such a donor has a repeatedly reactive screening test for anti-HTLV-I or -II, blood establishments should, within 1 week, identify and quarantine in-date, prior collections of Whole Blood and blood components in inventory extending back 5 years. If there is a record available of the donor's last negative test result for anti-HTLV-I and -II, using an FDA licensed screening test, then quarantine of prior collections need only extend back to 12 months before such a test.

Blood establishments should, within 1 week, request consignees to immediately quarantine all previously distributed in-date products from such collections extending back either 5 years or 12 months before the donor's last negative test result using an FDA licensed screening test for anti-HTLV-I and -II. FDA is not recommending quarantine of frozen products from prior collections from donors who subsequently test repeatedly reactive for anti-HTLV-I or -II.

FDA is not recommending that products which have been already pooled or further processed be quarantined.

If additional tests on the repeatedly reactive units are completed within 1 week, and final

²For example, by using another manufacturer's kit, or a kit from the same manufacturer that uses a different assay method.

test results provide a basis for release of units as described in 3. below, then quarantine of the previously collected units is not necessary.

Blood establishments should have written procedures to identify prior collections, to quarantine units, to notify consignees, and to perform additional testing if release of units from quarantine will be considered, whenever a repeat donor has a repeatedly reactive test for anti-HTLV-I or -II. In addition, the establishment's records should enable tracking of prior collections, documentation of the quarantine of products and consignee notification, and disposition of products identified as potentially infectious based on subsequent testing.

For units previously distributed and in quarantine, consignees should be notified within 30 days of the results of additional testing, if performed, so that consignees may either release products (as described in 3. below), or properly dispose of products (in regard to labeling or destruction as described in 2. below).

In regard to products already transfused, FDA is not at the present time recommending notification of consignees of the results of additional testing for the purpose of transfusion recipient/patient tracing and notification.

2. Disposition of Units Placed in Quarantine

For donors who test repeatedly reactive for anti-HTLV-I or -II, additional testing on the donor's current, repeatedly reactive sample may permit release of prior collections from quarantine (see 3. below). To preclude the inadvertent release of unsuitable units, if such testing fails to be performed within 30 days or fails to meet procedures established for release of units from quarantine (see 3. below), then the quarantined units should be destroyed or appropriately labeled as "Biohazard" and "Not for transfusion."

3. Release of Units from Quarantine

Prior collections of Whole Blood and blood components from donors who subsequently test anti-HTLV-I or -II repeatedly reactive should be considered for release for transfusion if the donor's current, repeatedly reactive sample is further tested by a second, licensed screening test of a different type for anti-HTLV-I and anti-HTLV-II, and the result is nonreactive. However, release should not occur if the donor is indefinitely deferred because a repeatedly reactive anti-HTLV-I or anti-HTLV-I/II screening test result had been obtained on a previous occasion.(3)

D. DONOR DEFERRAL

Donors with repeatedly reactive donations should be permanently deferred whenever additional, more specific tests confirm that the donor has antibodies to HTLV-I or HTLV-II. At the present time, there are no FDA licensed additional, more specific tests for antibodies to HTLV-I or HTLV-II.

Donors should be indefinitely deferred whenever their donations have repeatedly reactive screening tests for HTLV-I or HTLV-II antibodies on more than one separate donation or when a second, licensed screening test of a different type for anti-HTLV-I and anti-HTLV-II is repeatedly reactive on the same donation. (Additional, more specific tests may be negative or indeterminate).

E. DONOR NOTIFICATION AND COUNSELING

Utilization of investigational additional, more specific tests may be useful in notification and counseling of donors with repeatedly reactive screening tests for antibodies to HTLV-I or -II.

Guidelines for notification and counseling HTLV-seropositive individuals have been provided in detail by the Public Health Service.(1)

F. BLOOD PRODUCT LABELING

The HTLV-I/HTLV-II antibody test results do not have to appear on the product container label. The Circular of Information should indicate that all products have been tested for antibodies to HTLV-I and HTLV-II and found to be negative.

IV. REFERENCES

1. Centers for Disease Control and Prevention and the U.S.P.H.S. Working Group, "Guidelines for counseling persons infected with human T-lymphotropic virus type I (HTLV-I) and type II (HTLV-II). *Ann. Int. Med.* 118:448-454 (1993).
2. Murphy EL. The clinical epidemiology of human T-lymphotropic virus type II (HTLV-II). *J. Acquir. Immune. Defic. Syndr.* 1996;13:S215-219.
3. HTLV-I Antibody Testing, November 29, 1988.
4. Recommendations for the Quarantine and Disposition of Units From Prior Collections From Donors with Repeatedly Reactive Screening Tests for Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Human T-Lymphotropic Virus Type I (HTLV-I), July 19, 1996.