Date : December 11, 1996

From : Director, Center for Biologics Evaluation and Research

Subject : Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection

To : All Registered Blood and Plasma Establishments

The first report confirming the identification of human immunodeficiency virus, type 1 (HIV-1) group O viruses in patients from Central and West Africa was published in 1994. Two HIV-1 strains, ANT70 and MVP5180, were isolated from Cameroonian patients and were classified as group O (outlier group) on the basis of their genetic distance from other HIV-1 isolates. These variants were identified as HIV-1 because of similarities to other HIV-1 isolates in their genomic organization. DNA sequence analysis showed that the ANT70 and MVP5180 strains had an average of 65 to 70% homology to HIV-1 and 56% homology to HIV-2. Since that time, additional cases have been identified; most involve individuals whose country of origin (birth or residence) was in West Africa.

In 1994, the Centers for Disease Control and Prevention (CDC) conducted a study to examine the sensitivity of HIV antibody screening tests licensed by the Food and Drug Administration (FDA) to detect HIV-1 group O specimens. The study findings indicated that several screening tests currently in use in the U.S. did not detect one or two of the eight group O sera in that evaluation. All tests based on recombinant or synthetic peptide antigens failed to detect at least one specimen; three of the five tests based on whole virus lysate antigen and the immunofluorescence assay based on HIV-1 infected lymphocytes detected all eight specimens.

In June 1994, in response to these findings, the FDA Blood Products Advisory Committee (BPAC) discussed the need for manufacturers of test kits for antibodies to HIV-1 to modify their kits to detect group O in clinical specimens. Since that time, FDA has required manufacturers developing new test kits for detecting antibodies to HIV-1 to modify these tests to enhance sensitivity for group O viruses and to include group O specimens in the clinical evaluation of the tests. In July 1996, FDA sent letters to Investigational New Drug application and Product License Application holders and manufacturers of licensed kits requesting them to modify their kits to enhance sensitivity for group O viruses by incorporating in the test a group O consensus antigen or an antigen or sequence that is representative of group O isolates. An update on HIV-1 group O was provided at the September 1996 meeting of BPAC.

Two cases of HIV-1 group O infection were identified for the first time in the United States this year, resulting in increased concern regarding adequacy of current screening of the blood supply for HIV-1. Additional cases may be identified in ongoing surveillance studies. At present, the risk of an HIV-1 group O strain occurring in a blood donor is thought to be

very low based on the low prevalence in the general population and the ability of current donor screening kits to detect most cases. The current criteria for temporary deferral of donors at risk for malaria also may contribute to exclusion of donors at risk for HIV-1 group O infection. As part of the criteria for deferral of donors for malaria risk, permanent residents of nonendemic countries who travel to an area considered endemic for malaria are not accepted as donors of whole blood and blood components until at least one year after departure from the endemic area. Emigrants, refugees, citizens or residents of countries where malaria is endemic are currently not accepted as donors of whole blood or blood components until at least three years after departure from the area. These geographic exclusion criteria would eliminate some donors at increased risk for HIV-1 group O infection from West Africa. However, they would not exclude donors who left these areas more than three years previously who might still be eligible to donate blood.

Cameroon and adjacent countries in which HIV-1 group O cases have been identified most likely represent an area which is endemic for HIV-1 group O viruses. Thus, individuals who were born in or have resided in Cameroon or an adjacent country may be considered to be at increased risk for HIV-1 group O infection.

Since there are currently no licensed tests that reliably detect infection with HIV-1 group O based on inclusion of an HIV-1 group O antigen, **FDA recommends the following questions be added to the direct questions on high risk behavior to exclude donors who are at increased risk for HIV-1 group O infection. An affirmative answer to any of the following questions should result in indefinite deferral of a potential donor:**

1. **Were you born in or have you lived in any of the following countries since 1977: Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria?**

2. **If you have travelled to any of those countries since 1977, did you receive a blood transfusion or any medical treatment with a product made from blood?**

3. **Have you had sexual contact with anyone who was born in or lived in these countries since 1977?**

These recommendations should be considered interim measures to reduce the risk of HIV-1 group O transmission by blood and blood products pending the licensure of test kits specifically labeled for detection of antibodies to HIV-1 group O viruses.

The recommendations contained in this memorandum may be implemented immediately without prior approval by FDA. Licensed establishments implementing these recommendations should submit by official correspondence a statement to their product license file indicating the date that revised standard operating procedures consistent with the recommendations have been

established and implemented.

The procedures cited in this memorandum are recommendations. If an establishment believes that an alternative approach would provide equivalent protection, the establishment is invited to discuss the approach with FDA for FDA's evaluation. FDA may find those alternative procedures acceptable. FDA recognizes that the scientific technology for controlling the risk of transmission of HIV-1 may continue to advance and that this document may become outdated as those advances occur. Although this guidance document does not create or confer any rights, privileges, or benefits on or for any person and does not operate to bind FDA or the public, it does represent the agency's current thinking with regard to deferral of donors at increased risk for HIV-1 group O infection.

Questions about these recommendations should be directed by Fax to the Division of Transfusion Transmitted Diseases, Office of Blood Research and Review, Fax: (301) 480-7928.

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