

Guidance for Industry

Recommendations for Management of Donors at Increased Risk for Human Immunodeficiency Virus Type 1 (HIV-1) Group O Infection

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit written comments on this guidance at any time to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.regulations.gov>. You should identify all comments with the title of this guidance.

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For questions on the content of this guidance, contact OCOD at the phone numbers listed above.

**U.S. Department of Health and Human Services
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Center for Biologics Evaluation and Research
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Table of Contents

I. INTRODUCTION..... 1

II. BACKGROUND 1

III. RECOMMENDATIONS..... 3

A. Revised Questions to Identify Donors at Increased Risk of HIV-1 Group O Infection 3

B. Discontinuation of the Questions that Address HIV-1 Group O Risk..... 3

C. Reentry of Donors Deferred on the Basis of a Response to HIV-1 Group O Risk Question(s) 4

IV. REFERENCES..... 7

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I. INTRODUCTION

We, the Food and Drug Administration (FDA), are providing you, blood and plasma establishments, with a revised list of countries that should be included in questions for identifying donors at increased risk for HIV-1 group O infection. We are also providing you with recommendations for discontinuing the use of some questions used to identify these donors and for management of donors previously deferred.

This guidance supersedes the memorandum entitled "Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection," dated December 11, 1996 (Ref. 1). That memorandum contained interim measures to reduce the risk of HIV-1 group O transmission by blood and blood products pending licensure of test kits specifically labeled for detection of antibodies to HIV-1 group O viruses. Now that an FDA-licensed test for detection of antibodies to HIV-1 group O viruses is available, those interim recommendations are no longer current.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The first report confirming the identification of HIV-1 group O in patients from Central and West Africa was published in 1994 (Ref. 2). That same year, the Centers for Disease Control and Prevention (CDC) reported findings of a study indicating that several FDA-licensed HIV antibody screening tests were unable to detect one or two of eight group O sera (Ref. 3). Tests based on recombinant antigens and synthetic peptide antigens failed to detect at least one specimen, whereas three of the five tests based on whole virus lysate antigens detected all specimens.

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In June 1994, in response to the inability of some FDA-licensed HIV antibody assays to detect HIV-1 group O sera, FDA Blood Products Advisory Committee (BPAC) recommended that manufacturers modify their test kits to include detection of HIV-1 group O in clinical specimens. Since then, we have requested manufacturers of HIV-1 assays to include group O specific antigens or sequences in their test kits to detect antibodies to HIV-1 group O or HIV-1 group O nucleic acid. We also requested that manufacturers test HIV-1 group O specimens in their clinical trials to obtain a specific claim of sensitivity for group O for their test. These requests were initially conveyed to manufacturers as letters to their Investigational New Drug Applications (INDs) and Product License Applications (PLAs), currently referred to as Biologics License Applications (BLAs).

In 1996, FDA issued the memorandum “Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection,” to reduce the risk of HIV-1 group O transmission through blood and blood products. In that memorandum we recommended the inclusion of questions related to HIV-1 group O risk in the donor history questionnaire pending the licensure of test kits specifically labeled for detection of antibodies to HIV-1 group O viruses. These direct questions inquire as to whether the donor was born or resides in specific West and Central African countries where HIV-1 group O is prevalent, or had a history of travel to these countries, a history of blood transfusion or medical treatment since 1977 in these countries, or sexual contact since 1977 with anyone who was born or lived in these countries. We also recommended in the 1996 memorandum that donors who gave an affirmative response to one or more of the questions in the donor history questionnaire related to HIV-1 group O risk be indefinitely deferred pending licensure of test kits specifically labeled for detection of HIV-1 group O.

Since the identification of the first two HIV-1 group O cases in the United States (U.S.) around 1996 (Refs. 4, 5) there have been no additional group O cases that have been conclusively identified in the U.S. HIV-1 group O infection in the U.S. continues to be extremely rare.

In August 2003, FDA approved the biologics license application for the first donor screening test specifically labeled as sensitive for detection of antibodies to HIV-1 group O, the Genetic Systems™ HIV-1/HIV-2 *Plus O* EIA. Blood and plasma establishments, manufacturers and testing laboratories that are implementing a licensed test that is sensitive for HIV-1 group O antibody detection may use this test to screen blood and plasma donations for antibodies to HIV-1 and HIV-2, including HIV-1 group O. Other assays for HIV-1 group O detection are under development and if approved by FDA, may be used when available for screening blood and plasma donations.

The list of countries included in the interim recommendations in the 1996 memorandum included Cameroon and countries adjacent to Cameroon (Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, and Nigeria). However, subsequent reports indicated the presence of HIV-1 group O in countries in Africa that are not adjacent to Cameroon, including Senegal, Togo, Zambia, Benin, and Kenya (Refs. 6-8). In addition, the country formerly named Zaire, recently renamed Democratic Republic of Congo, has not identified any cases of HIV-1 group O infections thus far, but the name of the country might be confused with the country of

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Congo where HIV-1 group O has been identified. As a result, we recommend revisions to the list of countries of origin or residence where HIV-1 group O is endemic that is used to identify potential donors who are at increased risk of group O infection (see Figure 1 and Table 1).

With the availability of a licensed donor screening test that is sensitive for antibodies to HIV-1 group O, donors who were previously deferred may be eligible for reentry after a waiting period of one year and may be reentered if a current donation from the donor is found to be non-reactive using a group O sensitive anti-HIV-1/2 test.

III. RECOMMENDATIONS

A. Revised Questions to Identify Donors at Increased Risk of HIV-1 Group O Infection

We recommend that the following questions be included in the direct questions on high risk behavior in the donor history questionnaire¹ to exclude donors who are at increased risk for HIV-1 group O infection:

1. Were you born in or have you lived in any of the following countries since 1977: Cameroon, Benin, Central African Republic, Chad, Congo, Equatorial Guinea, Kenya, Gabon, Niger, Nigeria, Senegal, Togo, or Zambia? If so, when?
2. If you have traveled to any of those countries since 1977, did you receive a blood transfusion or any medical treatment with a product made from blood? If so, when?
3. Have you had sexual contact with anyone who was born in or lived in these countries since 1977? If so, when?

We recommend that you defer indefinitely a potential donor who gives an affirmative answer to any of these questions. Donors deferred on this basis (or previously deferred consistent with FDA's 1996 memorandum on "Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection") may be considered for reentry one year after their last potential exposure to HIV-1 Group O as determined by their responses to the above donor questions, in accordance with the recommendations below in III.C.

B. Discontinuation of the Questions that Address HIV-1 Group O Risk

If you implement a licensed anti-HIV-1/2 test for donor screening that is specifically labeled in the "Intended Use" section of the package insert as sensitive for detection of HIV-1 group O antibodies, you may discontinue use of the questions in section III. A.

¹ Establishments that have implemented the AABB (formerly known as the American Association of Blood Banks) full-length donor history questionnaire (DHQ) and accompanying materials should question donors concerning possible exposure to HIV-1 group O virus using the capture question approach developed for this protocol.

Contains Nonbinding Recommendations

that address HIV-1 group O risk. If you hold a biologics license, you must report this minor change in an annual report (section 601.12(d) of Title 21 Code of Federal Regulations (21 CFR 601.12(d)).

FDA recognizes that by implementing these measures, the safety benefit of the deferral due to potential group O risk is being replaced by the greater safety benefit of the group O sensitive test in a setting of low overall risk to blood safety. We believe these measures are warranted given the rarity of Group O infections in the U.S. as indicated by CDC data (Refs. 4, 5). The risk for individuals to acquire HIV-1 group O by sexual exposures in the U.S. appears to be remote given the rarity of HIV-1 group O in this country.

C. Reentry of Donors Deferred on the Basis of a Response to HIV-1 Group O Risk Question(s)

A donor who was deferred because of a previous or current affirmative response to one or more of the questions in the donor history questionnaire related to HIV-1 group O risk may be eligible for reentry after a waiting period of at least one year following the date of the donor's last potential exposure to HIV-1 group O. The donor may be reentered if:

1. a current donation from the donor is tested and found non-reactive using an anti-HIV-1/2 screening test that is specifically labeled in the "Intended Use" section of the package insert as sensitive for detection of HIV-1 group O antibodies, and
2. the donor meets all other donor eligibility criteria².

² Since individuals who travel to an area considered endemic for malaria by the Malaria Branch, CDC, are deferred from donating Whole Blood and blood components for one year following their departure from the endemic area, and since the areas considered endemic for malaria include the countries in which HIV-1 group O has been identified, the current deferral for donors potentially exposed to malaria includes donors potentially exposed to HIV-1 group O while in Africa.

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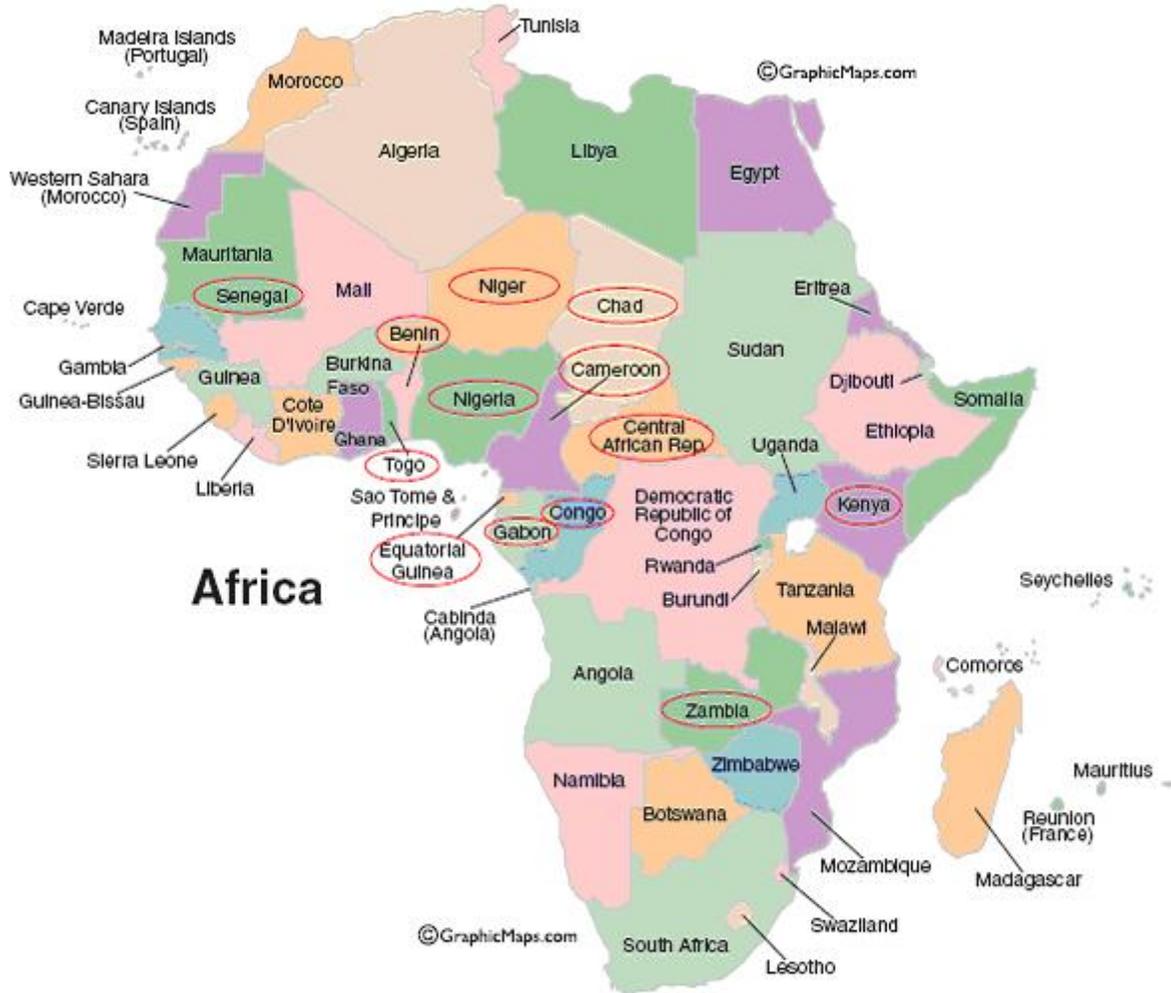


Figure 1. Circled countries are those in which HIV-1 Group O is currently endemic

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Table 1. Current and Previous List of Countries with HIV-1 Group O Risk

Current List of Countries	Previous List of Countries
Cameroon	Cameroon
Central African Republic	Central African Republic
Chad	Chad
Congo	Congo
Equatorial Guinea	Equatorial Guinea
Gabon	Gabon
Niger	Niger
Nigeria	Nigeria
Senegal	
Togo	
Zambia	
Benin	
Kenya	

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IV. REFERENCES

1. FDA Memorandum to All Registered Blood and Plasma Establishments, “Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection” (December 11, 1996).
2. P. Charneau, *et al*, Isolation and Envelope Sequence of a Highly Divergent HIV-1 Isolate: Definition of a New HIV-1 Group, *Virology* 205:247-253 (1994).
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4. Centers for Disease Control and Prevention, Identification of HIV-1 Group O Infection – 1996. *JAMA* 276:521-2 (1996).
5. P.S. Sullivan, *et al*, Human Immunodeficiency Virus (HIV) Subtype Surveillance of African-Born Persons at Risk for Group O and Group N HIV infections in the United States, *J. Infect. Diseases* 181:463-9 (2000).
6. M. Peeters, *et al*, Geographical Distribution of HIV-1 Group O Viruses in Africa, *AIDS* 11:493-8 (1997).
7. M. Heyndrickx, *et al*, HIV-1 Group O and Group M Dual Infection in Benin, *Lancet* 347:902-903 (1996).
8. E. M. Songok, *et al*, Surveillance for HIV-1 Subtypes O and M in Kenya, *Lancet* 347:1700 (1996).