Recommendations for Evaluating Donor Eligibility Using Individual Risk-Based Questions to Reduce the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products

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Draft Guidance for Industry

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Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that FDA considers your comment on this draft guidance before we begin work on the final version of the guidance, submit either electronic or written comments on the draft guidance within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov/. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Contains Nonbinding Recommendations

Draft – Not for Implementation

Recommendations for Evaluating Donor Eligibility Using Individual Risk-Based Questions to Reduce the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products

Draft Guidance for Industry

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

We, FDA, are issuing this draft guidance to receive comments on revised recommendations for evaluating donor eligibility using individual risk-based questions. This draft guidance, when finalized will provide you, blood establishments that collect blood or blood components, including Source Plasma, with FDA's revised donor deferral recommendations for individuals with increased risk for transmitting human immunodeficiency virus (HIV) infection. We are also recommending that you make corresponding revisions to your donor educational materials, donor history questionnaires and accompanying materials, along with revisions to your donor requalification and product management procedures. This guidance, when finalized, will supersede the guidance entitled, "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products" dated April 2020, updated August 2020 (April 2020 guidance). The recommendations contained in this draft guidance, when finalized, will apply to the collection of blood and blood components, including Source Plasma.

The revised recommendations in this draft guidance reflect the Agency's current thinking on donor deferral recommendations for individuals with increased risk for transmitting HIV infection. Based on our review of the available science as discussed below, we recommend eliminating the time-based deferrals for men who have sex with men (MSM) and women who have sex with MSM. Instead, we recommend assessing donor eligibility using gender-inclusive, individual risk-based questions relevant to HIV risk. In addition, we recommend deferral of any individual taking medications to treat or prevent HIV infection (e.g., pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), and antiretroviral therapy (ART)). FDA-approved antiretroviral drugs are safe and effective and can reduce the HIV viral load of individuals to undetectable levels as determined by testing. However, these antiretroviral drugs do not fully

eliminate the virus from the body, and donated blood from individuals infected with HIV taking ART can potentially still transmit HIV to a transfusion recipient. Although undetectable equals untransmissible for sexual transmission, this does not apply to transfusion transmission. Further, the available data demonstrate that the use of PrEP and PEP may delay detection of HIV by currently licensed screening tests for blood donations, potentially resulting in false negative results. We have not changed the other recommendations and donor deferral time periods to reduce the risk of transfusion transmission of HIV from the April 2020 guidance. Based on the Agency's careful evaluation of the available data, including data regarding the performance characteristics of nucleic acid testing, FDA expects implementation of these revised recommendations will not be associated with any adverse effect on the safety or availability of the blood supply.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency'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 Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The emergence of acquired immune deficiency syndrome (AIDS) in the early 1980s had profound effects on the United States (U.S.) blood system (Refs. 1-3). Although initially identified in MSM and associated with male-to-male sexual contact, AIDS was soon identified as a blood-borne disease, transmitted by blood transfusion and receipt of clotting factor concentrates (Refs. 4-5). Subsequently, AIDS was also disproportionately identified among people who exchanged sex for money or drugs and people who used intravenous drugs (Refs. 6-7).

The identification of risk factors for AIDS in 1983 informed the first blood donor education and deferral policy, which at that time was the only way to reduce the chance of transmission of AIDS through blood transfusion (Refs. 4-7). Beginning in 1983, FDA issued recommendations for providing donor educational material about risk factors for AIDS (Refs. 8-10). In addition, blood centers began asking risk questions and deferring from blood donation individuals who were at higher risk of having AIDS, even before the availability of tests to screen the blood supply. These measures had a significant effect on reducing the risk of transmitting AIDS through blood transfusion (Ref. 11). Still, thousands of transfusion recipients of blood and blood components and recipients of plasma-derived clotting factor concentrates were infected with HIV before the causative virus was identified (Refs. 1, 3, 9) and testing became possible.

In 1984, the virus now known as HIV was determined to be associated with AIDS, which led to the development of blood donor screening tests. FDA approved the first screening tests for antibodies against HIV in 1985 (Ref. 1). Advances in HIV donor screening tests (e.g., HIV antibody assays, p24 antigen assays, and nucleic acid tests (NAT)), along with the use of donor educational material and specific deferral recommendations, progressively reduced the risk of

HIV transmission from blood transfusion over time, from about 1 in 2,500 units prior to HIV testing in the 1980's to an estimated residual risk of about 1 in 1.47 million transfusions in 2022 (Refs. 12-13). Moreover, no transmissions of HIV, hepatitis B virus (HBV), or hepatitis C virus (HCV) have been documented through U.S.-licensed plasma-derived products in the past three decades (Ref. 14).

The specific donor history questions and deferral recommendations for behaviors and other factors that are known to increase the risk of HIV infection have evolved over time. Consequently, FDA has revised its deferral recommendations in a stepwise approach, supported by scientific data, including the epidemiology of HIV infection and the performance of HIV donor screening tests.

Beginning in September 1985, FDA recommended that blood establishments indefinitely defer male donors who have had sex with another male, even one time, since 1977, because of the strong clustering of AIDS and the subsequent discovery of high rates of HIV infection among MSM (Ref. 15). In subsequent years, FDA and the Department of Health and Human Services (HHS) held several public meetings, including scientific workshops and advisory committee meetings, to discuss blood donor deferral polices to prevent HIV transmission (Refs. 16-20). In 2010, an Interagency Blood, Organ & Tissue Safety Working Group (BOTS Working Group) consisting of representatives from the Center for Disease Control and Prevention (CDC), Health Resources and Services Administration (HRSA), National Institutes of Health (NIH), HHS Office for Civil Rights (OCR), Office of the Assistant Secretary for Health (OASH), and FDA, was charged with exploring the feasibility of a data and science-driven policy change. Subsequently, the BOTS Working Group designed and implemented several research studies to help inform a potential policy change for MSM, including an assessment of quarantine release errors (Refs. 21-22); a study to evaluate comprehension of the donor history questions, which involved cognitive interviews with potential donors (Ref. 23); the Retrovirus Epidemiology Donor Study-II (REDS-II) on behavioral risk factors for HIV among blood donors (Ref. 24); and, a study that surveyed the opinions of MSM regarding FDA's blood donor deferral policy (Ref. 25). Data from these studies became available in 2014 and were presented to the BOTS Working Group, the HHS Advisory Committee on Blood and Tissue Safety and Availability (ACBSTA) and the FDA Blood Products Advisory Committee (BPAC). In addition, epidemiologic data from countries that had shortened the deferral period for MSM, including Australia, indicated no safety concerns (Refs. 26-28). The advisory committees agreed that the available scientific evidence supported a change in the deferral policy from an indefinite deferral to a 12-month deferral for MSM. At the same time, they recommended further study of alternatives to time-based deferrals for MSM. FDA subsequently concluded that the available evidence supported a change from the indefinite deferral for MSM, and in December 2015, recommended a 12-month deferral for MSM.

Also in 2014, FDA launched the Transfusion Transmissible Infections Monitoring System (TTIMS) in the U.S., as part of the effort to advance blood donor deferral recommendations based on scientific data. TTIMS monitors the safety of the U.S. blood supply and evaluates the rate of relevant transfusion transmitted infections (RTTIs) detected among blood donors before and after policy changes (Ref. 29). Data from TTIMS in the two years following implementation

of the 12-month donor deferral for MSM comparing the rates of HIV in those donating blood indicated that there was no increase in risk to the U.S. blood supply (Ref. 29). Additionally, other countries, including the United Kingdom and Canada, had further moved to a 3-month deferral period for MSM, and there had been no reports from these countries suggesting safety concerns following the implementation of this change. The totality of the surveillance information and the experience with a 3-month deferral in other countries, combined with the uniform use of nucleic acid testing for HIV, HBV, and HCV, which can detect each of these viruses within a 3-month period following initial infection, supported a recommendation for a 3-month deferral for MSM. Consequently, in April 2020, based on FDA's evaluation of the available data, FDA recommended a 3-month deferral for MSM. The recommendations in the April 2020 guidance were issued for immediate implementation to respond to the COVID-19 public health emergency and reported shortages in the U.S. blood supply.

In addition to shortening the recommended deferral period for MSM, FDA concurrently evaluated the available scientific evidence that could support modification of several other blood donor deferrals related to risk for HIV. Based on the experience in the United Kingdom and Canada, along with the detection characteristics of the nucleic acid testing noted above, in April 2020, FDA also revised the recommended deferrals for individuals who exchange sex for money or drugs or engage in non-prescription injection drug use from indefinite to 3-month deferrals. In addition, for similar reasons, the recommended 12-month deferral for other risk factors, including contact with another person's blood, receipt of a blood transfusion or a recent tattoo or piercing, was revised to 3 months.

Although issued to address the COVID-19 public health emergency, the April 2020 guidance signaled FDA's intent to issue further guidance that would remain in effect after the end of the public health emergency. The guidance also restated FDA's commitment to further investigate individual risk assessment as an alternative to time-based deferrals for MSM.

FDA subsequently helped facilitate and funded the ADVANCE (Assessing Donor Variability And New Concepts in Eligibility) study, a pilot study intended to evaluate individual risk assessment strategies as an alternative to time-based deferrals for MSM (Ref. 30). The ADVANCE study examined a number of HIV risk factors, such as anal sex, and rates of HIV infection among MSM study participants. In addition, the ADVANCE study determined the rates of PrEP and PEP use among MSM study participants.

FDA recognizes that other countries with similar HIV epidemiology as the U.S. have revised their donor eligibility criteria for MSM, based on risk assessments performed in these countries. Notably, the United Kingdom in 2021 and Canada in 2022 introduced a new approach for donor questioning based on individual risk factors (Refs. 31-35). The approach is based on surveillance, epidemiology, and risk assessments that demonstrate that new or multiple sexual partners, and for those with new or multiple partners, anal sex, are the most significant risk factors that increase the likelihood of HIV infection (Refs. 31-36). Thus, the United Kingdom and Canada have adopted a gender-inclusive, individual risk-based approach that asks all presenting blood donors (without considering self-reported gender), if they have had a new sexual partner or more than one sexual partner in the last 3 months, and if so, they are asked if

they had anal sex (Refs. 33, 37). Individuals who report having a new sexual partner and anal sex or having more than one sexual partner and anal sex in the last three months are deferred from blood donation. To date, the United Kingdom and Canada have not reported safety concerns following the implementation of this individual risk-based deferral policy.

FDA also has considered the following alternatives to the current FDA recommendation of a 3-month deferral for MSM: 1) further shortening of the time-based recommended deferral for MSM (e.g., 1 or 2 months); 2) prescreening and qualification of MSM for donation of pathogen-reduced platelets or plasma or Source Plasma; and 3) re-testing donors for HIV after a quarantine hold period for the plasma components for transfusion or further manufacture collected from MSM. While these strategies may maintain the safety of the blood supply, we do not recommend them because they are operationally complex and because pathogen reduction devices are currently approved only for platelets and plasma for transfusion.

In considering the available data and the feasibility of other approaches, we believe implementation of the gender-inclusive, individual risk-based approach recommended in this guidance will maintain the current high level of safety of blood and blood components, including Source Plasma in the U.S. Consequently, we propose to recommend individual risk-based questions that ask all donors about new or multiple sexual partners. Under this proposed approach, donors who report having a new sexual partner or more than one sexual partner in the past three months would be asked about a history of anal sex in the past three months. The deferral of individuals who report a new sexual partner or more than one sexual partner in the past three months and anal sex in the past three months would be expected to reduce the likelihood of donations by individuals with new or recent HIV infection who may be in the window period for NAT detection (Ref. 36).

In addition, we recommend asking all donors about the use of medications to treat or prevent HIV infection. FDA-approved antiretroviral drugs are safe and effective and can reduce the HIV viral load of individuals to undetectable levels as determined by conventional testing. However, these antiretroviral drugs do not fully eliminate the virus from the body, and donated blood can potentially still transmit HIV infection to a transfusion recipient. Although undetectable still equals untransmissible for sexual transmission, this does not apply to transfusion transmission (Ref. 38). Further, the available data demonstrate that the use of PrEP or PEP may delay the detection of HIV by currently licensed screening tests for blood donations, potentially resulting in false negative results in infected individuals (Refs. 39-40). The recommendation for a three-month deferral following the most recent dose of an oral medication to prevent HIV infection and a two-year deferral following the most recent injection of a medication to prevent HIV infection is based on the pharmacokinetics of the short-acting or long-acting antiviral drugs, respectively (Ref. 41). Also, individuals have been identified who donated blood even though they were taking ART for a known HIV infection (Ref. 42). Donated blood from individuals taking ART can potentially transmit HIV infection to a transfusion recipient (Ref. 38). Consequently, we recommend asking all donors if they are currently taking any medication to treat an HIV infection and to permanently defer such donors.

Finally, based on the available information, we are maintaining the other recommendations for deferral of individuals for HIV risk from the April 2020 guidance. Surveillance information from the U.S. since implementation of the revised recommendations in April 2020, along with the uniform use of nucleic acid testing which can detect HIV within a 3-month period following infection, support a three-month deferral for individuals who exchange sex for money or drugs or engage in non-prescription injection drug, as well as individuals with other HIV risk factors, including contact with another person's blood, receipt of a blood transfusion or a recent tattoo or piercing.

III. RECOMMENDATIONS

The following sections summarize FDA's recommendations for blood donor deferral and requalification related to reducing the risk of HIV transmission by blood and blood products.

A. Donor Educational Material and Donor History Questionnaire

1. Blood establishments must provide educational material to donors before each donation explaining the risk of HIV transmission by blood and blood products and risk factors associated with HIV infection so that donors can self-defer (21 CFR 630.10(b)). We recommend the donor educational materials explain that individuals with risk factors for HIV need to be aware of the signs and symptoms associated with acute HIV infection, namely fever, enlarged lymph nodes, sore throat and rash.[1] The educational material must be presented to donors in a manner they will understand, which may include oral, written, or multimedia formats, and must instruct the donor not to donate when a risk factor for HIV infection is present (21 CFR 630.10(b)). We recommend the donor educational material indicate that individuals who have engaged in any activity or who have any risk factor that would result in a deferral (section III.B of this guidance) should not donate blood or blood components.

2. We recommend that blood collection establishments update their donor educational material, donor history questionnaire (DHQ), including full-length and abbreviated DHQs, and accompanying materials (e.g., flow charts) and processes to incorporate the recommendations provided in this guidance.

3. We recommend that the updated DHQ include the following elements to assess donors for risk:

[1] See CDC website at https://www.cdc.gov/hiv/basics/whatishiv.html.

a. A history ever of a positive[2] test for HIV.
b. A history ever of taking any medication to treat HIV infection.
c. A history in the past 3 months of taking any medication by mouth (oral) to prevent HIV infection.
d. A history in the past 2 years of receiving any medication by injection to prevent HIV infection.
e. A history in the past 3 months of sex[3] with a new partner. Individuals who report sex with a new partner in the past 3 months should be assessed for a history in the past 3 months of anal sex.
f. A history in the past 3 months of sex with more than one partner. Individuals who report sex with more than one partner in the past 3 months should be assessed for a history in the past 3 months of anal sex.
g. A history in the past 3 months of exchanging sex for money or drugs.
h. A history in the past 3 months of non-prescription injection drug use[4].
i. A history in the past 3 months of sex with any of the following individuals: a person with a history ever of a positive test for HIV, a person with a history in the past 3 months of exchanging sex for money or drugs, or a person with a history in the past 3 months of non-prescription injection drug use.
j. A history in the past 3 months of receiving a transfusion of Whole Blood or blood components such as packed red blood cells, platelets, or plasma.
k. A history in the past 3 months of contact with blood of another individual through percutaneous inoculation such as a needle stick or through contact with a donor's open wound or mucous membranes.
l. A history in the past 3 months of a tattoo, ear, or body piercing.
m. A history in the past 3 months of syphilis or gonorrhea, or treatment for syphilis or gonorrhea.

B. Donor Deferral

We recommend that you defer as follows:

[2] In this context, "positive" includes reactive test results on an HIV diagnostic assay and repeatedly reactive or reactive results on antibody or NAT blood donor screening assays, respectively.
[3] Unless specified as "anal sex", throughout this guidance the term "sex" refers to having anal, oral, or vaginal sex, regardless of whether or not a condom or other protection is used.
[4] Non-prescription injection drug use includes not only the injection of non-prescription drugs, but also includes the improper injection of legally-prescribed drugs, such as injecting a prescription drug intended for oral administration or injecting a prescription drug that was prescribed for another individual.

1. Defer permanently an individual who has ever had a confirmed positive test result for HIV infection.[5]

2. Defer permanently an individual who has ever taken any medication to treat HIV infection (i.e., ART).

3. Defer for 3 months from the most recent dose, an individual who has taken any medication by mouth (oral) to prevent HIV infection (i.e., short-acting antiviral PrEP or PEP).

4. Defer for two years from the most recent injection, an individual who has received any medication by injection to prevent HIV infection (i.e., long-acting antiviral PrEP).

5. Defer for 3 months from the most recent sexual contact, an individual who has had a new sexual partner in the past 3 months **and** who has had anal sex in the past 3 months.

6. Defer for 3 months from the most recent sexual contact, an individual who has had more than one sexual partner in the past 3 months **and** who has had anal sex in the past 3 months.

7. Defer for 3 months from the most recent event, an individual who has exchanged sex for money or drugs.

8. Defer for 3 months from the most recent event, an individual who has engaged in non-prescription injection drug use.

9. Defer for 3 months from the most recent sexual contact, an individual who has had sex with a person who has ever had a positive test for HIV.

10. Defer for 3 months from the most recent sexual contact, an individual who has had sex with an individual who has exchanged sex for money or drugs in the past 3 months. If the individual has any uncertainty about when their sexual partner exchanged sex for money or drugs, defer the individual for 3 months from their most recent sexual contact.

11. Defer for 3 months from the most recent sexual contact, an individual who has had sex with an individual who has engaged in non-prescription

[5] A donor deferred indefinitely because of a repeatedly reactive or reactive result on an antibody or a NAT blood donor screening assay, respectively, may be considered for re-entry by a requalification method or process found acceptable for such purposes by FDA (21 CFR 610.41(b)). Under 21 CFR 630.35(b), deferred donors with a previously false-positive result on an HIV diagnostic test may be considered for re-entry by a requalification method or process found acceptable for such purposes by FDA (21 CFR 630.35(b)). We recommend that you contact FDA for recommendations on a case-by-case basis for an acceptable requalification method or process.

injection drug use in the past 3 months. If the individual has any uncertainty about when their sexual partner engaged in non-prescription injection drug use, defer the individual for 3 months from their most recent sexual contact.

12. Defer for 3 months from the most recent allogeneic transfusion, any individual who has a history of receiving an allogeneic transfusion of Whole Blood or blood components.

13. Defer for 3 months from the most recent exposure, any individual who has a history of contact with blood of another individual through percutaneous inoculation such as a needle stick or through contact with a donor's open wound or mucous membranes.

14. Defer for 3 months from the most recent tattoo, ear or body piercing, an individual who has a history of tattoo, ear or body piercing. However, FDA is not recommending deferral of individuals who have undergone tattooing within 3 months of donation, if the tattoo was applied by a state regulated entity with sterile needles and non-reused ink. FDA also is not recommending deferral of individuals who have undergone ear or body piercing within 3 months of donation if the piercing was done using single-use equipment.

15. Defer for 3 months after completion of treatment, an individual who has had syphilis or gonorrhea, or received treatment for syphilis or gonorrhea, in the last 3 months.

We recommend that you defer indefinitely an individual with hemophilia or related clotting factor deficiencies requiring treatment with clotting factor concentrates for reasons of donor safety, rather than based upon the risk of HIV infection.

Note: Under 21 CFR 630.5 and 630.10(a), FDA requires the responsible physician of a blood collection establishment to determine the eligibility of a donor, and to defer any donor if the donation could adversely affect the health of the donor or the safety of the blood or blood component.

C. Donor Requalification

Under 21 CFR 630.35, you may determine a deferred donor to be eligible if, at the time of the current collection, the criteria that were the basis for the previous deferral are no longer applicable.

1. A donor deferred for any of the factors in section III.B.3-15 of this guidance may be eligible to donate after the deferral period (i.e., 3-month

or 2-year period as applicable), provided the donor meets all other donor eligibility criteria.

2. A donor previously deferred indefinitely for exchanging sex for money or drugs, for engaging in non-prescription injection drug use, or, for a male donor, having sex with another man, may be eligible to donate, provided the donor meets all donor eligibility criteria.

3. A male donor previously deferred for 3 months for having sex with another man, or a female donor previously deferred for 3 months for having sex with a man who had sex with another man, may be eligible to donate, provided the donor meets all donor eligibility criteria.

Note: A donor deferred permanently for the factors in section III.B.1-2 of this guidance (i.e., a history of a confirmed positive test for HIV infection or a history of taking medication to treat HIV infection) is not eligible for requalification.

D. Product Retrieval and Quarantine; Notification of Consignees of Blood and Blood Components

If you collected blood or blood components from a donor who tests reactive for HIV on that donation, or when you are made aware of other reliable test results or information indicating evidence of HIV infection (i.e., collected blood and blood components from a donor who has a confirmed positive test for HIV infection or taken medication to treat an HIV infection (section III.B.1-2 of this guidance)), you must follow the HIV "lookback" requirements in 21 CFR 610.46.

In addition, we recommend that you take the following actions if you determine that blood or blood components have been collected from a donor who should have been deferred according to the recommendations in section III.B.3-15 of this guidance, for reasons other than a positive HIV test result or medication to treat an HIV infection.

1. If you collected blood or blood components from a donor who should have been deferred according to the recommendations in section III.B of this guidance, we recommend that you quarantine and destroy any undistributed in-date blood or blood components collected from that donor.

2. If you distributed blood or blood components collected from a donor who should have been deferred according to the recommendations in section III.B of this guidance, we recommend that you notify consignees of the in-date blood and blood components collected from the donor during the period that he or she should have been deferred. We recommend that the consignee retrieve and quarantine the in-date blood and blood components collected from that donor during the period he or she should have been

deferred. We do not recommend retrieval and quarantine of plasma pooled for further manufacturing into products that are manufactured under processes that include validated viral clearance steps, which have been shown to be robust in the clearance of lipid-enveloped viruses.

E. Product Disposition and Labeling

We recommend that you destroy or re-label blood or blood components that were collected from a donor who should have been deferred based on risk factors for HIV infection, or for a history of a confirmed positive test for HIV infection or for a history of taking any medication to treat HIV infection, in accordance with the recommendations in section III.B of this guidance. If you re-label the blood or blood components as described in this section, they may be released for research.

You must use the following statements, as applicable, to prominently re-label the blood or blood components originally collected for transfusion in accordance with 21 CFR 606.121(f):

> "NOT FOR TRANSFUSION: Collected From a Donor Determined To Be At Risk For Infection With HIV"
>
> or
>
> "NOT FOR TRANSFUSION: Collected From a Donor Determined To Have HIV Infection," and with the "BIOHAZARD" legend
>
> and,
>
> "Caution: For Laboratory Research Only"

F. Testing Requirements and Considerations

Section 610.40(a) (21 CFR 610.40(a)) requires establishments that collect blood or blood components to test each donation intended for transfusion or for use in manufacturing a product, for evidence of infection due to HIV type 1 (HIV-1) and HIV type 2 (HIV-2). In addition, 21 CFR 610.40(b) requires you to use one or more approved screening tests as necessary to reduce adequately and appropriately the risk of transmission of HIV-1 and HIV-2. FDA has considered the use of licensed donor screening tests for antibodies to both HIV-1 and HIV-2 as necessary to reduce adequately and appropriately the risk of transmission of HIV. In addition, FDA recommends the use of licensed HIV-1 nucleic acid donor screening tests to meet the requirements under 21 CFR 610.40(b).

You must defer a donor who tests reactive by a donor screening test for HIV-1 or HIV-2 (21 CFR 610.41) and you must perform further testing using a supplemental test on donations that test reactive on a screening test, when available. If no supplemental test is

available, you must perform one or more licensed, approved or cleared tests as adequate and appropriate to provide additional information regarding the donor's infection status (21 CFR 610.40(e)). You must make reasonable attempts to notify a donor who has been deferred based on the results of tests for evidence of infection with a relevant transfusion-transmitted infection (21 CFR 630.40). Where appropriate, donors who are deferred because of reactive test results should be provided information about the need for medical follow-up and counseling.

IV. IMPLEMENTATION

Licensed blood establishments must report changes to their approved application to FDA in accordance with 21 CFR 601.12.

1. Licensed blood establishments that revise their own DHQs and accompanying materials must report the change to FDA in a Prior Approval Supplement (PAS) Supplement under 21 CFR 601.12(b). Include the following information in your PAS Supplement:

    a. Form FDA 356h "Application to Market a New or Abbreviated New Drug, or Biologic for Human Use."
    b. Cover letter describing the request and contents of the supplement.
    c. The DHQ and accompanying document(s). Please highlight the modifications.

2. Licensed blood establishments that implement a revised version of the DHQ and accompanying materials prepared by the AABB Donor History Task Force or the Plasma Proteins Therapeutic Association (PPTA) and found acceptable by FDA must report the changes to FDA in an annual report under 21 CFR 601.12(d), noting the date the process was implemented (21 CFR 601.12(a)(3)).

Unlicensed establishments are not required to report this change to FDA.

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