

# Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products

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## Draft Guidance for Industry

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U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
May 2015

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### I. INTRODUCTION

This guidance document provides 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 (FDA) are also recommending that you make corresponding revisions to your donor education materials, donor history questionnaires and accompanying materials, along with revisions to your donor requalification and product management procedures. This guidance also incorporates certain other recommendations related to donor education materials and testing contained in the memorandum to blood establishments entitled, "Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products," dated April 23, 1992 (1992 blood memo) (Ref. 1). When finalized, it will supersede that 1992 blood memo. The recommendations contained in this guidance apply to the collection of blood and blood components, including Source Plasma.

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 emergence of Acquired Immune Deficiency Syndrome (AIDS) in the early 1980s and the recognition that it could be transmitted by blood and blood products had profound effects on the United States (U.S.) blood system (Refs. 2, 3, 4). Although initially identified in men who have

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sex with men (MSM) and associated with male-to-male sexual contact, AIDS was soon noted to be potentially transmitted by transfusion of blood components, and by infusion of clotting factor concentrates in individuals with hemophilia (Refs. 5, 6). Subsequently, AIDS was also found to be associated with heterosexual transmission through commercial sex work and with intravenous drug use (Refs. 7, 8). In 1983, AIDS was reported to be associated with the virus now known as human immunodeficiency virus (HIV). The historical understanding of HIV transmission at this point in 1983 informed the first blood donor deferral policy, which at the time was seeking to reduce the transmission of HIV through blood product transfusion.

### **A. History of Efforts to Reduce HIV Transmission by Blood Products**

Beginning in 1983, the FDA issued recommendations for providing donors with educational material on risk factors for AIDS and for deferring donors with such risk factors in an effort to prevent transmission of AIDS (later understood to be caused by HIV) by blood and blood products (Refs. 2, 9, 10, 11). Providing donor education material and asking at-risk donors not to donate was demonstrated to have a significant impact on preventing HIV transmission prior to the availability of testing (Ref. 12). However, thousands of recipients of blood and blood components for transfusion and recipients of plasma-derived clotting factors became infected with HIV before the causative virus was identified and the first screening tests for HIV were approved in 1985 (Refs. 2, 4, 10).

Since September 1985, FDA has recommended that blood establishments indefinitely defer male donors who have had sex with another male, even one time, since 1977, due to the strong clustering of AIDS illness in the MSM community and the subsequent discovery of high rates of HIV infection in that population (Ref. 13). On April 23, 1992, FDA issued the 1992 blood memo, which contains the current recommendations regarding the deferral for MSM as well as the deferral recommendations for other persons with behaviors associated with high rates of HIV exposure, namely commercial sex workers, intravenous drug users, and certain individuals with other risk factors.

The use of donor education material, specific deferral questions, and advances in HIV donor testing (e.g., HIV antibody assays, p24 antigen assays, and nucleic acid tests (NAT)) have reduced the risk of HIV transmission from blood transfusion from about 1 in 2500 units prior to HIV testing to a current estimated residual risk of about 1 in 1.47 million transfusions (Refs. 14, 15). The development of pathogen inactivation procedures for products manufactured from pooled plasma in the 1980s improved the safety of these products by inactivating lipid-enveloped viruses. 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 two decades (Ref. 16).

Relating in large part to the development of more sensitive HIV testing methodologies, there have been calls in the social and scientific literature to revisit the blood donor deferral policies that were established about three decades ago, in particular, with regard

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to the deferral of MSM. During the period from 1997 to 2010, FDA held a number of public meetings, including workshops and Blood Product Advisory Committee (BPAC) meetings to further review evidence and to discuss its blood donor deferral policies to help prevent the transmission of HIV (Refs. 17, 18, 19, 20). In June 2010, the Department of Health and Human Services (HHS) brought the issue of deferral of men who have had sex with another man, even one time, since 1977, for public discussion at a meeting of the Advisory Committee on Blood Safety and Availability (the Committee). The Committee heard presentations of currently available scientific data as well as comments from the public. The Committee recommended to the HHS Secretary “that the current MSM deferral policy, while suboptimal, should be retained pending the completion of targeted research studies that might support a safe alternative policy” (Ref. 21).

Based on these recommendations, in September 2010, an Interagency Blood, Organ & Tissue Safety Working Group on MSM (BOTS Working Group), consisting of representatives from the Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration (HRSA), National Institutes of Health (NIH), HHS Office of Civil Rights, Office of the Assistant Secretary for Health (OASH), and FDA, was charged by the Assistant Secretary for Health with exploring the feasibility of a data and science-driven policy change. Subsequently, the BOTS Working Group designed and implemented one operational assessment and three research studies to gain more information to help inform a potential policy change. In addition, it considered the possibility of conducting a pilot study to assess the effect of a policy change. However, following review of comments received in response to a *Federal Register* notice titled, “Request for Information (RFI) on Design of a Pilot Operational Study To Assess Alternative Blood Donor Deferral Criteria for Men Who Have Had Sex With Other Men (MSM)” (77 FR 14801, March 13, 2012) (Ref. 22), requesting comment on potential pilot study designs, as well as further considerations regarding the significant statistical, financial and logistical challenges in implementing such a study, the BOTS Working Group decided that such a pilot study examining the potential effects of a policy change would not be feasible. Instead, the BOTS Working Group determined that resources at HHS could be used in more efficient ways to carefully review the studies that had been initiated (results of which are summarized in section II.C. below), to complete its review of the blood donation deferral criteria, and to establish a blood safety monitoring system.

### **B. Current Risk of HIV Infection Associated with Specific Behaviors**

Recent data indicate that commercial sex work (CSW) and injection drug use (IDU) are behaviors that continue to place individuals both at a relatively high risk of HIV infection and at a relatively high risk of window period transmission of HIV (Ref. 23) and few data are available on the HIV risk in individuals who have discontinued CSW and IDU (Ref. 24). Deferral policies for CSW and IDU are also based on risks for transfusion transmitted infectious diseases, in addition to HIV, that are associated with these behaviors (Ref. 25).

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Together, these findings continue to support an indefinite deferral of individuals currently or previously involved in CSW and IDU behaviors. Therefore, absent additional data, we have not proposed a change to current deferral policies for CSW or IDU.

Although MSM represent a small percentage of the U.S. male population (approximately 7% of men report that they have ever participated in MSM activity and approximately 4% of men report that they engaged in MSM activity in the last 5 years<sup>1</sup>) (Ref. 26), they comprise a large proportion of adults in the United States with existing and newly diagnosed HIV infections. Among persons living with HIV in 2011, CDC estimates that 57% were MSM (including MSM who were also IDU) (Ref. 27). MSM remain at increased risk of HIV infection. In 2010, male-to-male sexual contact accounted for 63% of newly diagnosed HIV infections among adults, and 78% of newly diagnosed HIV infections in men, indicating that male-to-male sexual contact remains associated with high risk of HIV exposure (Ref. 28).

### **C. Recent Data Relevant to the Deferral for MSM**

The following results became available by mid-2014, from the operational assessment and all three of the research studies recommended by the BOTS Working Group.

#### 1. Operational Assessment

The operational assessment examined quarantine release errors. Such errors occur when a blood establishment accidentally releases a unit of blood that should not have been released due to issues with donor qualification or testing. It became clear at an FDA workshop held in September 2011 that HIV risk from quarantine release errors has been minimized effectively by increased use of computerized inventory management, with a remaining small risk of human errors. Following the workshop, a White Paper was produced by AABB on this topic which describes a number of measures that could be taken to characterize and prevent such errors (Ref. 29). Quarantine release errors currently appear to contribute minimally to the risk of HIV transmission through the blood supply (Ref. 30).

#### 2. Donor History Questionnaire Study

The Donor History Questionnaire (DHQ) Study involved cognitive interviews with potential donors. After receiving donor education materials, the potential donors completed the donor history questionnaire, and were then interviewed regarding their responses (Ref. 31). The key result of this study, which was

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<sup>1</sup> Purcell et al., have reported that the estimation of the MSM population as a percent of all males over 13 years differ by recall period: Past 1 year = 2.9%; past 5 years = 3.9%; and ever = 6.9%.

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highly consistent for both individuals who only have sex with partners of the opposite sex and MSM, was that individuals respond to questions posed by the questionnaire as if they were answering the more general and subjective question in the self-assessed context of “is my blood safe,” rather than providing an answer to the literal questions as asked. In addition, the study found that potential donors might have benefited from shorter donor education materials and the ability to answer “I don’t know” to questions that currently accept only “yes” or “no” responses.

#### 3. Retrovirus Epidemiology Donor Study-II (REDS II) Transfusion-Transmitted Retrovirus and Hepatitis Virus Rates and Risk Factors Study

The REDS-II Transfusion-Transmitted Retrovirus and Hepatitis Virus Rates and Risk Factors Study 2011-2013 was a pilot blood donor surveillance study that evaluated four viral markers (HBV, HCV, human T cell lymphotropic virus (HTLV), and HIV) in just over 50% of the nation’s blood supply (Ref. 32). It also determined behavioral risk factors that were associated with donations of blood that tested positive for one of these viruses compared with control donations. In addition to demonstrating the feasibility of conducting such a surveillance program, there were several key findings. These included the finding that for each of these viral infections, the primary behavioral risk factors were consistent with the known epidemiology for each infection in the United States and validated the current blood donor deferral criteria. Sex with an HIV-positive partner and a history of male-to-male sexual contact remained the two leading independent risk factors for HIV infection in blood donors as originally observed in CDC-funded studies from the early 1990’s. Sex with an HIV-positive partner was associated with a 132-fold increase in risk (multivariate adjusted odds ratio) for being HIV-positive, and a history of male-to-male sexual contact was associated with a 62-fold increase in risk. By comparison, the increase in risk for a history of multiple sexual partners of the opposite sex in the last year was 2.3-fold.

#### 4. Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) Blood Donation Rules Opinion Study (BloodDROPS)

BloodDROPS examined the opinions of MSM regarding the blood donor deferral policy (Ref. 33) through web-based surveys of the MSM community and non-compliant MSM who donated blood. A key finding of particular note was that MSM, who comprise approximately 7% (Ref. 26) of the U.S. male population represent an estimated 2.6% of male blood donors. Although the data were determined by different methodologies, they suggest an increase in the proportion of blood donors reporting MSM behavior from 0.7% in 1993 and 1.7% in 1998. The qualitative responses by both donating and non-donating groups of MSM revealed that these individuals view the current policy as discriminatory and

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stigmatizing, and that some individuals knowingly donate despite the deferral. When asked about shortening the deferral period, since last male-to-male sexual contact, the most common response was that one year was “acceptable as a compromise,” especially if shorter periods might be considered after confirming the safety of the new policy. The web-based community survey revealed that approximately 90% of MSM think the MSM blood donation deferral should change, and 59% of MSM reported they would comply with a change to a one-year deferral. Of the 83 blood donors who reported male-to-male sexual contact, 50.6% reported that they would adhere to a one-year deferral and 18.4% reported “don’t know.” Among the subset of the 30 MSM blood donors who had reported male-to-male sexual contact in the past year, 19 (62%) reported that they would adhere to a future one-year deferral and 3 (10%) indicated that they “don’t know” if they would adhere to a one-year deferral (Ref. 32).

The prevalence of HIV infection in male blood donors who reported that they were MSM was determined to be 0.25%, which is much lower than the estimated 11-12% HIV prevalence in the population of individuals reporting regular MSM behavior (Ref. 33). This indicates that considerable self-selection likely took place in individuals who presented to donate.

### 5. Supportive Data on Australian MSM Policy Change

Some epidemiologic data are available from countries that have changed their deferral policy for MSM (Refs. 34, 35). The most robust data measuring the impact of these policy changes are available from Australia (Ref. 36). Australia also has a voluntary blood donor system and has a similar percentage of men reporting male-to-male sexual contact at some time during their lives (5% compared with 7% in the United States (Ref. 26). During the five years before and five years after a change from a lifetime deferral to a one-year deferral in Australia, there was no change in risk to the blood supply, defined by the number of HIV positive donations per year and the proportion of HIV-positive donors with male-to-male sex as a risk factor. In addition, the compliance rate with the one-year MSM deferral among male donors in Australia following the policy change was >99.7% (Ref. 37). Of note, unlike in the U.S., donors in Australia must sign a declaration in the presence of blood center staff that they understand that there are penalties, including fines and imprisonment, for providing false or misleading information.

### D. Considerations of the BOTS Working Group

Over the course of its deliberations, the BOTS Working Group reviewed and discussed several different options for the MSM policy:

- no change,
- change to a five-year deferral,

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- change to a one-year deferral,
- change to a deferral less than one year,
- pre-testing of potential donors, and
- deferral based upon individual risk assessment.

Although not making a change would maintain the current level of safety of the blood supply, as noted above, there is evidence that the deferral policy is becoming less effective over time. In addition, the policy is perceived by some as discriminatory. The data that a five-year deferral would be safer than a one-year deferral are not compelling. However, some have argued that a five-year deferral would, in theory, add a safeguard by allowing time for intervention against an emerging infectious disease that might spread rapidly among MSM and be transmitted through blood transfusion. Sufficient data are not available to assess the effectiveness of selecting MSM with low HIV risk based on deferral times of less than one year since last exposure. The individual risk-based options were not determined to be viable options for a policy change at this time for a number of reasons: pretesting would be logistically challenging, and would likely also be viewed as discriminatory by some individuals, and individual risk assessment by trained medical professionals would be very difficult to validate and implement in our current blood donor system due to resource constraints. Additionally, the available epidemiologic data in the published literature do not support the concept that MSM who report mutual monogamy with a partner or who report routine use of safe sex practices are at low risk for HIV. Specifically, the rate of partner infidelity in ostensibly monogamous heterosexual couples and same-sex male couples is estimated to be about 25%, and condom use is associated with a 1 to 2% failure rate per episode of anal intercourse (Refs. 38, 39, 40, 41). In addition, the prevalence of HIV infection is significantly higher in MSM with multiple male partners compared with individuals who have only multiple opposite sex partners (Ref. 28).

Change to a one-year deferral is also supported by other evidence, including the experience in countries that have already changed their policies to a one-year deferral (Argentina, Australia, Brazil, Hungary, Japan, Sweden and United Kingdom). In addition, this change would potentially better harmonize the deferral for MSM with the one-year deferral in place for both men and women who engage in certain other sexual behaviors associated with an increased risk of HIV exposure (e.g., sex with an HIV-positive partner, sex with a commercial sex worker). Thus, following careful review, the BOTS Working Group was supportive of a policy change to a one-year deferral for MSM.

### **E. Outcome of HHS and FDA Advisory Committee Meetings**

Following deliberation of the BOTS Working Group, two advisory committee meetings were held. The HHS Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) met on November 13, 2014, to review the MSM deferral policy (Ref. 33). The scientific information described in sections II.C. and D. was presented to the

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ACBTSA members along with the BOTS Working Group recommendation. Additionally, the meeting included an open public hearing session. The Committee voted 16 to 2 to recommend a policy change to a one-year MSM deferral. It also recommended that this change be accompanied by establishment of a robust system to monitor the safety of the blood supply and a communication plan on the policy change targeted to all stakeholders.

Subsequently, on December 2, 2014, the FDA BPAC met to consider measurement of HIV incidence in blood donors as an additional method to assess transfusion risk, and the potential value of laboratory tests to detect recently acquired HIV infections in seropositive donors as part of a Transfusion Transmissible Infections Monitoring System (TTIMS) (Ref. 42). An open public hearing was also held. At that meeting, FDA noted that it intended to establish a general program to monitor the safety of the blood supply in collaboration with the National Heart, Lung and Blood Institute (NHLBI), which could monitor for a number of different transfusion-transmitted viral infections. FDA also noted that it intended to engage in public discussions of issues such as enhancements to education about the donation of safe blood and further evaluation of the effectiveness of the blood donor history questionnaire. In their comments, some BPAC committee members indicated support for a change in MSM deferral policy to one year, and most members noted that they considered concomitant establishment of a blood donor monitoring program a prerequisite for any policy change. On the topic of testing for recency of HIV infection, several BPAC committee members commented that tests looking at how recently HIV infection had been (recency tests<sup>2</sup>) could potentially be very useful additions to the established measures of incidence for monitoring the safety of the blood supply.

### **F. Status of Other Deferral Categories**

In addition to the behavioral deferrals noted for MSM, CSW and IDU, the 1992 blood memo addressed several other deferrals that had been recommended in order to reduce the risk of HIV transmission through the blood supply (Ref. 1). For most of these deferrals, directly applicable data are not available at this time to support a change in the existing deferral policies. In the case of the deferral for persons with hemophilia or related clotting disorders who have received clotting factor concentrates, the rationale for deferral has changed from prevention of HIV transmission to that of ensuring that donors are not harmed by the use of large bore needles used during the donation process. While

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<sup>2</sup> HIV recency tests typically involve detailed assessment of the strength and characteristics of antibody profiles that develop and change over time in response to HIV infection. Thus, it appears to be technically feasible that a serologically-based HIV recency test, once validated in a blood donor setting, could reflect a high likelihood that an HIV infection occurred within a certain interval of time (e.g., in the past six months). While such tests are not yet FDA-approved for this purpose, this additional measure of new HIV infection may increase the statistical power to assess whether HIV incidence in the blood donor pool changed significantly after a change in the deferral recommendations.

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21 CFR 640.3(c)(3) currently requires deferral for receipt of any derivative of human blood which the FDA has advised is a possible source of viral hepatitis, given the enhanced safety measures now used in the manufacture of clotting factor concentrates (Ref. 16), FDA does not consider the receipt of FDA-licensed clotting factor concentrates to be a risk factor for hepatitis. Further, FDA has not recommended a deferral for the receipt of other FDA-licensed plasma-derivatives because of HIV or hepatitis risk<sup>3</sup>, and we intend to consider revisions to the current regulations.

### III. RECOMMENDATIONS

The following sections summarize the revised recommendations related to blood donor deferral and requalification related to reducing the risk of HIV transmission by blood and blood products. Given the passage of time, and in order to simplify practical application of these criteria for donors and blood collection establishments, reference to “since 1977” present currently for some criteria has been dropped as the period of time during which individuals are assessed to be at risk of transmitting HIV.

#### A. Donor Education Material and Donor History Questionnaire

1. We recommend that donors be provided donor education material before each donation explaining the risk of HIV transmission by blood and blood products, certain behaviors associated with the risk of HIV infection, and the signs and symptoms associated with HIV infection, so that donors can self-defer. The donor education material should be presented to donors in a manner they will understand, which may include oral, written, or multimedia formats. The donor education material should instruct the donor not to donate when a risk factor for HIV infection or signs or symptoms of HIV infection are present. The donor education material should indicate that individuals who have engaged in any activity or who have any risk factor that would result in a deferral (see section III.B. of this guidance) should not donate blood or blood components.
2. We recommend that blood collection establishments update their donor education material, 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:

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<sup>3</sup> Consistent with the donor history questionnaires and accompanying materials prepared by AABB and Plasma Protein Therapeutics Association (PPTA) and found acceptable by FDA, a voluntary donor deferral exists for the receipt of Hepatitis B Immune Globulin because the donor had been recently exposed to hepatitis B virus.

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- i. A history ever of a positive<sup>4</sup> test for HIV,
- ii. A history ever of exchanging sex<sup>5</sup> for money or drugs,
- iii. A history ever of non-prescription injection drug use<sup>6</sup>,
- iv. A history in the past 12 months of sex with a person with a positive test for HIV, a history of exchanging sex for money or drugs, or a history of non-prescription injection drug use,
- v. A history in the past 12 months of receiving a transfusion of Whole Blood or blood components such as packed red blood cells, platelets, or plasma,
- vi. A history in the past 12 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,
- vii. A history in the past 12 months of a tattoo, ear or body piercing,
- viii. A history in the past 12 months of syphilis or gonorrhea, or treatment for syphilis or gonorrhea,
- ix. For male donors: a history in the past 12 months of sex with another man,
- x. For female donors: a history in the past 12 months of sex with a man who has had sex with another man.

Note: In the context of the donor history questionnaire, male or female gender is taken to be self-identified and self-reported. In instances where a donor has asserted a change in gender identification, medical directors may exercise discretion with regard to donor eligibility.

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<sup>4</sup> In this context, “positive” includes positive test results on an HIV diagnostic assay and repeatedly reactive or reactive results on antibody or NAT blood donor screening assays, respectively.

<sup>5</sup> 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.

<sup>6</sup> 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.

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### **B. Donor Deferral**

We recommend that you defer as follows:

1. Defer indefinitely an individual who has ever had a positive test for HIV.
2. Defer indefinitely an individual who has ever exchanged sex for money or drugs.
3. Defer indefinitely an individual who has ever engaged in non-prescription injection drug use.
4. Defer for 12 months from the most recent contact any individual who has a history of sex with a person who: has ever had a positive test for HIV, ever exchanged sex for money or drugs, or ever engaged in non-prescription injection drug use.
5. Defer for 12 months from the most recent transfusion any individual who has a history of receiving a transfusion of Whole Blood or blood components.
6. Defer for 12 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.
7. Defer for 12 months from the most recent tattoo, ear or body piercing, an individual who has a history of tattoo, ear or body piercing. However, individuals who have undergone tattooing within 12 months of donation are eligible to donate if the tattoo was applied by a state regulated entity with sterile needles and non-reused ink. Individuals who have undergone ear or body piercing within 12 months of donation are eligible to donate if the piercing was done using single-use equipment.
8. Defer for 12 months after completion of treatment, an individual with a history of syphilis or gonorrhea, or an individual with a history of diagnosis or treatment for syphilis or gonorrhea in the past 12 months.
9. Defer for 12 months from the most recent contact, a man who has had sex with another man during the past 12 months.
10. Defer for 12 months from the most recent contact, a female who has had sex during the past 12 months with a man who has had sex with another man.

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.

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Note: Additional recommendations for donor deferral to reduce the risk of HIV transmission by blood and blood products have been established in other FDA guidance documents, including:

- “Guidance for Industry: Recommendations for Screening, Testing, and Management of Blood Donors and Blood and Blood Components Based on Screening Tests for Syphilis,” dated September 2014;
- “Guidance for Industry - Recommendations for Management of Donors at Increased Risk for Human Immunodeficiency Virus Type 1 (HIV-1) Group O Infection,” dated August 2009; and,
- “Memorandum to All Registered Blood Establishments - Recommendations for the Deferral of Current and Recent Inmates of Correctional Institutions as Donors of Whole Blood, Blood Components, Source Leukocytes, and Source Plasma,” dated June 8, 1995.

Note: Collections from donors at risk of HIV infection must be approved by CBER consistent with the “Guideline for Collection of Blood or Blood Products from Donors with Positive Tests for Infectious Disease Markers (“High Risk” Donors),” dated September 1989.

### **C. Donor Requalification**

1. Donors deferred because of a history of sex during the past 12 months with any of the following individuals: a person who has a positive test for HIV; a person with a history of exchanging sex for money or drugs; or a person with a history of non-prescription injection drug use, may be eligible to donate provided that 12 months since the last contact have passed and they meet all other donor eligibility criteria.
2. Donors deferred because of a history of receiving a transfusion of Whole Blood or blood components such as packed red blood cells, platelets, or plasma during the past 12 months may be eligible to donate if 12 months have passed since their last transfusion and they meet all other donor eligibility criteria.
3. Donors deferred because of 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 during the past 12 months may be eligible to donate if 12 months have passed since their last exposure and they meet all other donor eligibility criteria.
4. Donors deferred because of a history of tattoo, ear or body piercing in the past 12 months may be eligible to donate if 12 months have passed since their last tattoo, ear or body piercing and they meet all other donor eligibility criteria.

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5. Donors deferred because of a history of syphilis or gonorrhea, or treatment for syphilis or gonorrhea in the past 12 months may be eligible to donate if 12 months have passed since diagnosis and completion of treatment and they meet all other donor eligibility criteria.
6. Male donors previously deferred because of a history of sex with another man, even one time, since 1977, may be eligible to donate provided that they have not had sex with another man during the past 12 months and they meet all other donor eligibility criteria
7. Male donors deferred because of a history of sex with another man in the past 12 months may be eligible to donate provided they have not had sex with another man during the past 12 months and they meet all other donor eligibility criteria.
8. Female donors deferred because of a history of sex in the past 12 months with a man who has had sex with another man may be eligible to donate provided that during the past 12 months they have not had sex with a man who has had sex with another man and they meet all other donor eligibility criteria.

### **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, 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. 2-10 of this guidance, for reasons other than a positive HIV test result.

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 all blood and blood components. We recommend that the consignee retrieve and quarantine the in-date blood and blood components collected from that donor. We do not recommend retrieval and quarantine of plasma pooled for further

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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**

1. 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 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 or for manufacture into noninjectable products or in vitro diagnostic reagents when no other suitable sources are available.
  - a. You must use the following statement 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”

In addition, you should include one of the following cautionary label statements, as applicable:

“Caution: For Laboratory Research Only”

or

“Caution: For Further Manufacturing into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources”

or

“Caution: For Use in Manufacturing Noninjectable Products Only”

And, for recovered plasma<sup>7</sup>:

“Not for Use in Products Subject to License Under Section 351 of the Public Health Service Act”

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<sup>7</sup> See FDA Compliance Policy Guide Sec 230.100 for the definition of recovered plasma.  
<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073861.htm>

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- b. You should use the following statements to prominently re-label the un-pooled blood or blood components originally collected or intended for further manufacture:

“Collected from a Donor Determined to be at Risk for Infection with HIV”

And

“Caution: For Laboratory Research Only”

or

“Caution: For Further Manufacturing into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources”

or

“Caution: For Use in Manufacturing Noninjectable Products Only”

And, for recovered plasma:

“Not for Use in Products Subject to License Under Section 351 of the Public Health Service Act”

2. You must destroy or re-label blood or blood components, including Source Plasma, collected from a donor who currently tests reactive for HIV or collected from a donor deferred for reactive HIV testing (21 CFR 610.40(h)). If you re-label the blood or blood components, including Source Plasma, in accordance with 21 CFR 610.40(h) and 606.121, the blood or blood components may be released for research or for manufacture into noninjectable products or in vitro diagnostic reagents when no other suitable sources are available. You must label the reactive unit with the “BIOHAZARD” legend (21 CFR 610.40(h)(2)(ii)(B)), and:

- a. You must use the following statement to prominently re-label the blood or blood components originally collected for transfusion (21 CFR 606.121(f)):

“NOT FOR TRANSFUSION: Collected From a Donor Determined To Be Reactive for HIV”

In addition, you should use one of the following cautionary label statements, as applicable:

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“Caution: For Laboratory Research Only”

or

“Caution: For Further Manufacturing into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources”

or

“Caution: For Further Manufacturing Use as a Component of a Medical Device For Which There Are No Alternative Sources”

- b. You must use the following statement to prominently re-label the un-pooled blood or blood components, including Source Plasma, originally collected or intended for further manufacture (21 CFR 610.40(h)(2)(ii)(C)):

“Collected from a Donor Determined to be Reactive for Infection with HIV”

In addition, you should use one of the following cautionary label statements, as applicable:

“Caution: For Laboratory Research Only”

or

“Caution: For Further Manufacturing into In Vitro Diagnostic Reagents For Which There Are No Alternative Sources”

or

“Caution: For Further Manufacturing Use as a Component of a Medical Device For Which There Are No Alternative Sources”

### **F. Biological Product Deviation Reporting**

If you have distributed blood or blood components for transfusion or for further manufacturing, collected from a donor who should have been deferred according to section III.B. of this guidance, you should report a biological product deviation as soon as possible, but you must report within 45 calendar days from the date you acquire the information reasonably suggesting that a reportable event has occurred (21 CFR 606.171).

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### **G. 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 use in preparing 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 test as necessary to reduce adequately and appropriately the risk of transmission of HIV-1 and HIV-2. FDA has considered the use of approved 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 recommendations on the use of approved HIV-1 nucleic acid donor screening tests to meet the requirements under 21 CFR 610.40(b) are found in, “Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components (including Source Plasma and Source Leukocytes) to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV,” dated October 2004.

You must defer a donor who tests reactive by a donor-screening test for HIV-1 or HIV-2 (21 CFR 610.41), you must perform a supplemental (additional, more specific) test on donations that test reactive on a screening test (21 CFR 610.40(e)), and you must make reasonable attempts to notify a donor who has been deferred based on the results of tests for communicable diseases (21 CFR 630.6). Where appropriate, donors who are deferred because of reactive test results should be provided information about the need for medical follow-up and counseling.

Current FDA recommendations are found in “Guidance for Industry: Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor Deferral and Reentry, dated May 2010.” In addition, for the purpose of donor counseling, if a donation tests repeatedly reactive for antibodies to HIV-1/HIV-2 or for HIV-2 on an approved donor screening test, but HIV-1 positivity is not confirmed on an approved supplemental test, further testing may be performed using licensed or approved tests to diagnose HIV-2 infection and clarify the donor’s infection status.

## **IV. IMPLEMENTATION**

You may implement the recommendations once you have revised your donor education material, DHQ, including full-length and abbreviated DHQs, and accompanying materials to reflect the new donor deferral recommendations. Licensed blood establishments must report the indicated revisions to FDA in the following manner (21 CFR 601.12):

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1. Revision of your donor education materials, DHQ and accompanying materials must be submitted to FDA as a prior approval supplement (PAS) under 21 CFR 601.12(b). Revision of a previously FDA accepted DHQ and accompanying materials must be reported as a major change if you are revising the FDA accepted DHQ and accompanying materials to implement these new recommendations. Report such a change to FDA as a prior approval supplement (PAS) under 21 CFR 601.12(b).
2. If the current version of the donor educational materials, DHQ and accompanying materials prepared by the AABB Donor History Task Force or PPTA are revised to contain the recommendations in this guidance and are found acceptable by FDA, we would consider the implementation of the donor education materials, DHQ and accompanying materials to be minor changes, if implemented without modification and in their entirety as a complete process for administering questions to donors. Report such a change to FDA in your annual report under 21 CFR 601.12(d), noting the date the process was implemented.

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### V. REFERENCES

1. FDA Memorandum to All Registered Blood Establishments: Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products, April 23, 1992.
2. Epstein JS, Jaffe HW, Alter HJ, Klein HG, Blood system changes since recognition of transfusion-associated AIDS, *Transfusion* 2013, 53:2365-2374.
3. Stramer SL, Dodd RY, Transfusion-transmitted emerging infectious disease: 30 years of challenges and progress, *Transfusion* 2013, 53:2375-2383.
4. Dubin C, Francis D, Closing the circle: a thirty-year retrospective on the AIDS/blood epidemic, *Transfusion* 2013, 53:2359-2364.
5. Centers for Disease Control and Prevention, Epidemiologic Notes and Reports Pneumocystis carinii Pneumonia among Persons with Hemophilia A, *MMWR* 1982, 31:365-367.
6. Centers for Disease Control and Prevention, Epidemiologic Notes and Reports Possible Transfusion-Associated Acquired Immune Deficiency Syndrome (AIDS)—California, *MMWR* 1982, 31:652-654.
7. Ginzburg HM, Intravenous drug users and the acquired immune deficiency syndrome, *Public Health Rep* 1984, 99:206-212.
8. Van de Perre P, Clumeck N, Carael M, Nzabihimana E, Robert-Guroff M, De Mol P, Freyens P, Butzler JP, Gallo RC, Kanyamupira JB, Female prostitutes: a risk group for infection with human T-cell lymphotropic virus type III, *Lancet* 1985, 8454:524-527.
9. FDA Memorandum: Recommendations to Decrease the Risk of Transmitting Acquired Immune Deficiency Syndrome (AIDS) from Blood Donors, March 24, 1983.
10. Leveton LB, Sox Jr HC, Stoto MA, eds, HIV and the blood supply: an analysis of crisis decisionmaking, Institute of Medicine, National Academy Press, Washington DC 1995.
11. Centers for Disease Control and Prevention, Current Trends Prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of Inter-Agency Recommendations, *MMWR* 1983, 32:101-103.
12. Perkins HA, Busch MP, Transfusion-associated infections: 50 years of relentless challenges and remarkable progress, *Transfusion* 2010, 50:2080-2099.
13. Centers for Disease Control and Prevention, Update: Revised Public Health Service Definition of Persons Who Should Refrain from Donating Blood and Plasma – United States. *MMWR* 1985, 34(35); 547-548.

## Contains Nonbinding Recommendations

*Draft – Not for Implementation*

14. Ward JW, Grindon AJ, Feorino PM, Schable C, Parvin M, Allen JR, Laboratory and epidemiologic evaluation of an enzyme immunoassay for antibodies to HTLV-III, JAMA 1986, 256:357-361.
15. Zou S, Stramer SL, Dodd RY, Donor testing and risk: current prevalence, incidence, and residual risk of transfusion-transmissible agents in US allogeneic donations, Transfus Med Rev 2012, 26:119-128.
16. Klamroth R, Gröner A, Simon TL, Pathogen inactivation and removal methods for plasma-derived clotting factor concentrates, Transfusion 2014, 54:1406-1417.
17. FDA Blood Products Advisory Committee Meeting, December 11-12, 1997, <http://www.fda.gov/ohrms/dockets/ac/cber97t.htm>
18. FDA Workshop on Donor Suitability, 1998, <http://www.fda.gov/downloads/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/TranscriptsMinutes/UCM056297.pdf>
19. FDA Blood Products Advisory Committee Meeting, September 14, 2000, <http://www.fda.gov/ohrms/dockets/ac/cber00.htm#Blood%20Products>
20. FDA Workshop on Behavior-Based Donor Deferral in the NAT Era, 2006, <http://www.fda.gov/downloads/biologicsbloodvaccines/newsevents/workshopsmeetingsconferences/transcriptsminutes/ucm054430.pdf>
21. HHS Advisory Committee for Blood Safety and Availability Meeting, 2010, [https://wayback.archive-it.org/3919/20140402193351/http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/06112010\\_recommendations.pdf](https://wayback.archive-it.org/3919/20140402193351/http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/06112010_recommendations.pdf)
22. Federal Register Notice, “Request for Information (RFI) on Design of a Pilot Operational Study To Assess Alternative Blood Donor Deferral Criteria for Men Who Have Had Sex With Other Men (MSM)” (77 FR 14801, March 13, 2012) <https://www.federalregister.gov/articles/2012/03/13/2012-6091/request-for-information-rfi-on-design-of-a-pilot-operational-study-to-assess-alternative-blood-donor>
23. Kucirka LM1, Sarathy H, Govindan P, Wolf JH, Ellison TA, Hart LJ, Montgomery RA, Ros RL, Segev DL, Risk of window period HIV infection in high infectious risk donors: systematic review and meta-analysis, Am J Transplant 2011, 11:1176-1187.
24. United Kingdom Scientific, SaBTO Advisory Committee on the Safety of Blood, Tissues and Organs, Donor Selection Criteria Review, April 2011, [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/216109/dh\\_129909.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216109/dh_129909.pdf)
25. Soriano V, Vispo E, Labarga P, Medrano J, Barreiro P, Viral hepatitis and HIV co-infection, Antiviral Res 2010, 85:303-315.

## Contains Nonbinding Recommendations

*Draft – Not for Implementation*

26. Purcell DW, Johnson CH, Lansky A, Prejean J, Stein R, Denning P, Gaul Z, Weinstock H, Su J, Crepaz N, Estimating the population size of men who have sex with men in the United States to obtain HIV and syphilis rates, *Open AIDS J* 2012, M6:98-107.
27. CDC, HIV Surveillance Report, 2012; vol 24. Published November 2014, <http://www.cdc.gov/hiv/library/reports/surveillance>
28. CDC, Estimated HIV incidence in the United States, 2007–2010. HIV Surveillance Supplemental Report 2012; 17(No. 4). Published December 2012.
29. AABB on Quarantine Release Errors, White Paper 2013, <http://www.aabb.org/research/whitepapers/Documents/quarantine-release-errors-white-paper.pdf#search=qre>
30. FDA workshop on Quarantine Release Errors in Blood Establishments, September 2011, <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm263117.htm>
31. HHS Advisory Committee on Blood and Tissue Safety and Availability, Results from the Uniform Donor History Questionnaire, December 2013, [http://www.hhs.gov/ash/bloodsafety/advisorycommittee/acbtsa\\_201312meeting\\_agenda.html](http://www.hhs.gov/ash/bloodsafety/advisorycommittee/acbtsa_201312meeting_agenda.html)
32. Custer B, Kessler D, Vahidnia F, Leparc G, Krysztof DE, Shaz B, Kamel H, Glynn S, Dodd RY, Stramer SL; NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II), Risk factors for retrovirus and hepatitis virus infections in accepted blood donors, *Transfusion* 2014, doi: 10.1111/trf.12951.
33. Custer B, Sheon N, Siedle-Khan B, Pollack L, Spencer B, Bialkowski W, D’Andrea P, Sullivan M, Glynn S, Williams A, NHLBI Recipient Epidemiology and Donor Evaluation-III (REDS-III), Noncompliance with the men who have sex with men (MSM) deferral among U.S. male blood donors, Blood Donation Rules Opinion Study (BloodDROPS), November 13, 2014.
34. Benjamin RJ, et al, Deferral of males who had sex with other males, *Vox Sanguinis* 2011, 101: 339-367.
35. Offergeld R, et al, Sexual risk behavior and donor deferral in Europe, *Vox Sanguinis* 2014, 107:420-427.
36. Seed CR, Kiely P, Law M, Keller AJ, No evidence of a significantly increased risk of transfusion-transmitted human immunodeficiency virus infection in Australia subsequent to implementing a 12-month deferral for men who have had sex with men, *Transfusion* 2010, 50:2722-2730.
37. Lucky TTA, Seed CR, Waller D, Lee JF, McDonald A, Wand H, Wroth S, Shuttleworth G, Keller AJ, Pink J, Wilson DP, Understanding noncompliance with selective donor deferral criteria for high-risk behaviors in Australian blood donors, *Transfusion* 2014, 54:1739-1749.

## Contains Nonbinding Recommendations

*Draft – Not for Implementation*

38. Mark KP, Janssen E, Milhausen RR, Infidelity in heterosexual couples: demographic, interpersonal, and personality-related predictors of extradyadic sex, Arch Sex Behav 2011, 40:971-982.
39. Stone E, Heagerty P, Vittinghoff E, Douglas JM Jr, Koblin BA, Mayer KH, Celum CL, Gross M, Woody GE, Marmor M, Seage GR III, Buchbinder SP, Correlates of condom failure in a sexually active cohort of men who have sex with men, J Acquir Immune Defic Syndr Hum Retrovirol 1999, 20:495-501.
40. Weller S, Davis-Beaty K, Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database of Systematic Reviews 2002. (1):CD003255.
41. Smith DK, Herbst JH, Zhang X, Rose CE, Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the united states, J Acquir Immune Defic Syndr 2015, 68(3):337-344.
42. FDA Blood Products Advisory Committee Meeting, December 2014 transcript <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm386681.htm>