

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-1211]

Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a document entitled “Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry.” The guidance document provides blood establishments that collect blood or blood components, including Source Plasma, with revised donor deferral recommendations for individuals at increased risk for transmitting human immunodeficiency virus (HIV) infection. The guidance document recommends corresponding revisions to donor educational materials, donor history questionnaires and accompanying materials, along with revisions to donor requalification, product management, and testing procedures. The guidance announced in this notice finalizes the draft guidance of the same title dated May 2015 and supersedes the memorandum to blood establishments entitled “Revised Recommendations for the Prevention of Human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). While this guidance represents FDA’s current thinking on the subject, our recommendations may evolve over time as new scientific evidence becomes available.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are

solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2015-D-1211 for “Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION”. The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available

for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the guidance to the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist the office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Valerie A. Butler, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a document entitled, “Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry.” 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

U.S. blood system. Although initially identified in men who have sex with men (MSM) and associated with male-to-male sexual contact, AIDS was soon noted to be potentially transmitted by transfusion of blood products, and by infusion of clotting factor concentrates in individuals with hemophilia. Beginning in 1983, FDA issued recommendations for providing donors with educational material on risk factors for AIDS and for deferring donors at increased risk for AIDS in an effort to prevent transmission of the agent responsible for AIDS (later understood to be caused by HIV) by blood and blood products. MSM (originally identified as gay or bisexual men) were deferred due to the strong clustering of AIDS illness among MSM and the subsequent discovery of high rates of HIV infection in that population. FDA's recommendation for deferral of MSM was modified over time to improve its clarity and to promote compliance, including a shift of focus from a deferral based on group identification to a deferral based on specific behavior (male sex with another male).

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. On April 23, 1992, FDA issued the 1992 blood memo, which consolidated its recommendations regarding the deferral of donors at risk of HIV, including the deferral for MSM, as well as deferral recommendations for other persons with behaviors associated with high rates of HIV exposure, namely commercial sex workers, those who inject non-prescription drugs, and certain other individuals with HIV risk factors.

The use of donor educational material, specific deferral questions, and advances in HIV donor testing have reduced the risk of HIV transmission from blood transfusion from about 1 in 2500 transfusions prior to HIV testing to a current estimated residual risk of about 1 in 1.47 million transfusions. Since the implementation in 1985 of donor testing for antibodies to HIV, FDA and the U.S. Department of Health and Human Services (HHS) have held a number of public meetings, including public scientific workshops and meetings of the Blood Products Advisory Committee and the HHS Advisory Committee on Blood Safety and Availability (ACBSA) to further review evidence and discuss FDA's blood donor deferral policies to reduce the risk of transmission of HIV by blood and blood products. Consistent with recommendations of the ACBSA in June 2010, studies that might support a

policy change were carried out by the Public Health Service in 2011 to 2014. A recommendation for a policy change to the blood donor deferral period for MSM from indefinite deferral to 1 year since the last sexual contact was announced by the Commissioner of Food and Drugs in December 2014. This guidance implements that recommended policy change.

In addition, the guidance provides donor deferral recommendations for other individuals at increased risk for transmitting HIV infection, including commercial sex workers, non-prescription injection drug users, women who have sex with MSM, and certain other individuals with other risk factors. The guidance provides revised recommendations for donor educational materials, donor history questionnaires and accompanying materials, as well as for donor requalification and product management procedures.

In the **Federal Register** of May 15, 2015 (80 FR 27973), FDA announced the availability of the draft guidance of the same title dated May 2015. FDA received over 700 comments on the draft guidance and those comments were carefully considered as the guidance was finalized. Comments were received from a variety of organizations, including patient advocacy groups representing users of blood products; lesbian, gay, bisexual and transgender advocacy groups; medical and professional societies; academic institutions; human rights organizations; local governments; members of Congress; and, the blood industry. Comments were also received from hundreds of individual commenters.

Approximately one-half of the comments opposed FDA's time-based deferral policy for MSM and considered the proposed policy to be discriminatory and lacking a scientific rationale. Many of these comments recommended that FDA adopt an individual risk assessment based approach, regardless of an individual's sexual orientation or gender identity. Other comments supported a time-based deferral policy shorter than 1 year, or no deferral period at all, because of advances in blood donor testing technologies that permit earlier detection of new HIV infections. Comments requested that FDA commit to reexamining its deferral policies as new technologies, such as pathogen reduction technology are implemented and data regarding compliance with the revised policies become available.

Most of the remaining comments advocated for the continuation of the indefinite deferral policy for MSM and expressed concern regarding the safety

of the blood should the revised policy for MSM donors be adopted. Opponents of the proposed change commented on the HIV incidence and prevalence rates among MSM; the potential failure of HIV tests to capture window-period infections; the risk of emerging pathogens for which testing does not exist; and, the potential for decreased compliance rates with the new deferral policy. Other comments argued that FDA should not compromise public health and the safety of the blood supply to satisfy special interest groups.

A smaller number of comments, including those from certain patient advocacy organizations, supported the proposed 1-year deferral policy for MSM predicated on the establishment of a transfusion-transmitted infectious disease monitoring system to enhance safety monitoring and allow rapid responses to emerging threats to the blood supply. Further, similar comments advocated for an evaluation of the effectiveness of the donor educational materials and donor history questionnaires prior to the implementation of new donor deferral policies.

Finally, comments received from the blood industry were generally supportive of the revised MSM donor deferral policy. However, some comments noted that manufacturers of plasma for further manufacturing use (*i.e.*, to make injectable products), including Source Plasma, collected in the United States and intended for further manufacturing use in other countries, may need to retain an indefinite deferral policy for MSM to comply with the indefinite deferral policies established in other countries. Industry commenters also requested revisions to certain other donor deferral criteria for HIV risk and disagreed with FDA's proposal to include the signs and symptoms associated with HIV infection in the donor educational materials. Comments requested clarification regarding the eligibility of donors with false-positive HIV tests and on recommendations for product retrieval and notification of consignees of distributed blood components collected from a donor who should have been deferred for HIV risk factors. Some comments were also supportive of the additional guidance provided by FDA regarding transgender donors.

Finally numerous commenters requested FDA to clarify the recommendation for deferral of women who have had sex with MSM.

FDA carefully considered all of the comments received in response to the draft guidance and the available scientific data, including the results of

recent studies conducted by the Public Health Service and revised the guidance accordingly. FDA considered several options to address the comments in response to the revised MSM donor deferral policy. Because evidence indicates that the indefinite deferral policy for MSM may have become less effective over time, FDA has determined that a change in policy is warranted at this time. Data on the limitations of nucleic acid tests to identify antibody negative window period HIV infections suggests that donor testing alone, absent any deferral for MSM, would result in an unacceptable increased risk of transfusion-transmitted HIV. Similarly, pretesting at risk donors with a rapid HIV test prior to donation would be logistically challenging and would not necessarily identify newly HIV-infected individuals. While individual donor assessment for risk has been implemented in a few countries, the implementation of this strategy in the United States would present significant practical challenges and currently there is no validated and accepted individual risk assessment tool or questionnaire. Therefore, FDA concluded a time-based deferral for history of male-male sex is the most appropriate policy to maintain the safety of the U.S. blood supply. Scientific data regarding the effectiveness of a 1-year deferral in Australia, a country with similar HIV epidemiology to the United States, supports FDA's policy change to the blood donor deferral period for MSM from indefinite deferral to 1 year since the last sexual contact. Scientifically robust data are not available for time-based deferrals of less than 1 year. FDA also concluded that scientific data are not currently available that would support revisions to the indefinite deferral policy for commercial sex workers or intravenous drug users.

In response to comments, FDA made the following changes when finalizing the guidance: (1) Amended the recommendations regarding the inclusion of signs and symptoms associated with HIV in the donor educational materials; (2) revised the recommendation for the deferral of female donors who have had sex with MSM; (3) stated that FDA no longer recommends deferral for individuals who have had sex with an individual with hemophilia or related clotting deficiencies requiring treatment with clotting factor concentrates; and (4) revised the recommendations regarding product retrieval and consignee notification of distributed blood products collected from a donor who should have been deferred for HIV risk

factors. In addition, FDA made the following changes to clarify certain recommendations in the guidance, which are consistent with current policy: (1) Clarified that donors who have been determined to have a false-positive HIV test may be reentered according to a requalification method found acceptable to FDA; (2) noted that recipients of allogeneic blood transfusions (*i.e.*, not autologous transfusions), should be temporarily deferred; (3) provided reference to an FDA guidance on the collection of blood components from donors at risk of HIV infection; and (4) clarified the deferral by the responsible physician of a blood establishment of any donor if the donation could affect the health of the donor or the safety of the blood component. Additionally, the background section has been expanded to summarize FDA's evaluation of the available policy options under the available evidence relevant to the MSM deferral policy. Minor editorial changes have also been made to the guidance.

FDA remains committed to exploring options and engaging in public discussions regarding enhancements to donor and public education regarding safe blood donors and evaluating the effectiveness of the donor history questionnaire. Further, with the implementation of a transfusion transmitted infectious disease monitoring system, FDA will be able to monitor donor risk factors and the safety of the blood supply, as well as investigate and refine blood safety measures in the future. FDA's recommendations may evolve over time as new scientific data become available on strategies to maintain or improve blood safety.

The guidance announced in this notice finalizes the draft guidance dated May 2015 and supersedes the 1992 blood memo.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on recommendations for reducing the risk of HIV transmission by blood and blood products. 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.

II. Paperwork Reduction Act of 1995

The guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and

Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR 601.12 have been approved under OMB control number 0910–0338; the collections of information in 21 CFR 606.171 have been approved under OMB control number 0910–0458; and the collections of information in 21 CFR 610.46, 630.6, 640.3 and 640.63 have been approved under OMB control number 0910–0116.

III. Electronic Access

Persons with access to the Internet may obtain the guidance at either <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: December 17, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Resources and Services Administration

Agency Information Collection Activities: Proposed Collection; Public Comment Request

AGENCY: Health Resources and Services Administration, HHS.

ACTION: Notice.

SUMMARY: In compliance with the requirement for opportunity for public comment on proposed data collection projects (Section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995), the Health Resources and Services Administration (HRSA) announces plans to submit an Information Collection Request (ICR), described below, to the Office of Management and Budget (OMB). Prior to submitting the ICR to OMB, HRSA seeks comments from the public regarding the burden estimate, below, or any other aspect of the ICR.

DATES: Comments on this ICR should be received no later than February 22, 2016.

ADDRESSES: Submit your comments to paperwork@hrsa.gov or mail the HRSA Information Collection Clearance Officer, Room 10C–16, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: To request more information on the proposed project or to obtain a copy of