Revised Recommendations for Determining Eligibility of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products Who Have Received Human-Derived Clotting Factor Concentrates

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Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(2) without initially seeking prior comment because the Agency has determined that prior public participation is not appropriate.

FDA invites comments on this guidance. Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (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*. FDA will review any comments we receive and revise the guidance when appropriate.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

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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Table of Contents

Contains Nonbinding Recommendations

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Guidance for Industry

This guidance represents 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

This guidance provides you, establishments that make donor eligibility (DE) determinations for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps), with information on infectious-disease risks related to receipt of FDA licensed human-derived clotting factor concentrates (HDCFCs). This guidance explains that FDA no longer considers FDA licensed HDCFCs as a risk factor for Human immunodeficiency virus (HIV), Hepatitis B virus (HBV), or Hepatitis C virus (HCV). As such, receipt of FDA licensed HDCFCs, or sex with a person who has received FDA licensed HDCFCs, should not be considered a risk factor when determining eligibility of a donor of HCT/Ps. This guidance supplements the recommendations regarding HDCFCs that are contained in the guidance entitled "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps); Guidance for Industry" dated August 2007 (August 2007 Guidance).

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 manufacture of HDCFCs requires pooling of plasma from a large number of donors. From the 1970s through the early 1980s, there were numerous reported cases of HIV, HBV, and/or HCV transmissions by pooled plasma products such as HDCFCs (Refs. 1, 2). Methods for viral inactivation using solvent-detergent treatments were developed in 1985 and shown to be very effective against enveloped viruses, including HIV, HBV, and HCV (Refs. 3, 4, 5, 6). These viral inactivation methods, which are currently being used by manufacturers, have led to

substantial improvements in the safety of HDCFCs. In addition, the licensure of new infectious-disease testing technologies, such as nucleic acid tests (NATs), has improved HDCFC safety (Refs. 7, 8).

In the August 2007 Guidance, FDA explained that HCT/P donors who have received HDCFCs, or who have had sex with a recipient of HDCFCs, should be considered ineligible to donate cells or tissues, in accordance with 21 CFR 1271.75(d), due to a risk of HIV, HBV, and HCV (Ref. 9). However, since publication of the August 2007 Guidance, it has become evident that the significant advances in viral inactivation technologies, pathogen reduction technologies, enhanced donor screening requirements, and improved testing technologies were effective in increasing HDCFC safety, as no transmissions of HIV, HBV, or HCV by an FDA licensed HDCFC have been documented in the past 25 years[1] (Refs. 1, 2, 3, 10).

In the document entitled "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry" dated December 2015, FDA explains that, given the enhanced safety measures now used in the manufacture of clotting factor concentrates, FDA does not consider the receipt of FDA licensed clotting factor concentrates or sex with a person who has received clotting factor concentrates to be a risk factor for HIV or hepatitis (Ref. 11). Accordingly, FDA no longer recommends deferral for donors of blood and blood products who have had sex with an individual with hemophilia or related clotting factor deficiencies requiring treatment with clotting factor concentrates. Further, FDA has not recommended a deferral for the receipt of other FDA licensed plasma-derivatives because of HIV or hepatitis risks (Ref. 11).

III. RECOMMENDATIONS

For the purpose of determining eligibility of a donor as required under 21 CFR 1271.45, FDA no longer considers the receipt of clotting factor concentrates, or sex with a person who has received clotting factor concentrates, to be a risk factor for HIV, HBV, or HCV. As such, HCT/P donors should not be considered ineligible due to the following conditions, and screening for these conditions is no longer necessary:

1. Persons with hemophilia or other related clotting disorders who have received HDCFCs at any time;
2. Persons who received clotting factors once to treat an acute bleeding event at any time; or
3. Persons who have had sex at any time with either of the persons described above.

These recommendations supersede the recommendations listed in section IV.E.3. of the August 2007 Guidance.

[1] FDA licensed clotting factor concentrates are manufactured using viral inactivation technologies.

IV. IMPLEMENTATION

This guidance is being issued for immediate implementation. However, in accordance with 21 CFR 1271.47, establishments must revise their relevant procedures prior to implementing changes. Therefore, the recommendations apply to all HCT/Ps that an establishment recovers after it has revised its relevant procedures to reflect the contents of this guidance document.

V. REFERENCES

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