4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-5073]

Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a document entitled "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry." The guidance document provides establishments that make donor eligibility determinations for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps), with recommendations concerning the use of FDA-licensed nucleic acid tests (NAT) in donor testing for hepatitis B virus (HBV) deoxyribonucleic acid (DNA). The guidance finalizes the draft guidance of the same title dated January 2016 and supplements previous FDA recommendations to HCT/P establishments concerning donor testing for hepatitis B surface antigen (HBsAg) and total antibody to hepatitis B core antigen (anti-HBc), in the document entitled "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)" dated August 2007 (2007 Donor Eligibility Guidance).

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-5073 for "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based 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: Angela Moy, 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 "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry." The guidance provides establishments that make donor eligibility determinations for donors of HCT/Ps, with

recommendations concerning the use of FDA-licensed NAT in donor testing for HBV DNA. FDA considers the use of FDA-licensed HBV NAT in testing HCT/P donors to be necessary to adequately and appropriately reduce the risk of transmission of HBV. The FDA-licensed HBV NAT can detect evidence of the viral infection at an earlier stage than the HBsAg and total anti-HBc tests. Therefore, FDA recommends the use of FDA-licensed HBV NAT for testing donors of HCT/Ps for evidence of infection with HBV.

HBV is a major global public health concern and has been transmitted by blood transfusions and tissue transplantation. Available literature has indicated possible transmissions of HBV by hematopoietic stem cells and blood with HBV NAT positive/hepatitis B surface antibody (anti-HBs) positive/HBsAg negative blood, irrespective of anti-HBc test results. In blood donors, adding the HBV NAT testing for HBV reduces the residual risk of transmission of HBV infection beyond that which can be achieved by screening donors using only HBsAg and total anti-HBc tests. In addition, it can detect breakthrough infections in previously vaccinated individuals who are exposed to the virus, and HBV mutants appear to be more likely detected by HBV NAT than by HBsAg assays.

In the United States, there are currently FDA-licensed HBV NAT assays intended to screen blood samples from donors of whole blood and blood components, other living donors (individual organ donors when specimens are obtained while the donor's heart is still beating), and blood specimens from cadaveric (non-heart-beating) donors. Some of these are multiplex assays that can simultaneously detect HIV, HCV, and HBV in a single blood specimen, thus improving the feasibility of routine NAT testing for HBV. By analogy to the experience in the blood donor setting, it is reasonable to expect that the residual risk of transmission of HBV infection would be reduced by adding HBV NAT to the testing strategy for HCT/P donors. HBV

NAT's potential utility in further reducing risk of HBV transmission by transplantation is mainly restricted to the early HBsAg-negative phase of infection. In summary, the available scientific data and the availability of FDA-licensed assays support a recommendation that all HCT/P donors should be tested using an FDA-licensed HBV NAT.

In the Federal Register of January 8, 2016 (81 FR 937), FDA announced the availability of the draft guidance of the same title dated January 2016. FDA received a few comments on the draft guidance and those comments were considered as the guidance was finalized. The guidance announced in this notice finalizes the draft guidance of the same title dated January 2016 and supplements previous FDA recommendations to HCT/P establishments concerning donor testing for HBsAg and total antibody to anti-HBc, in the 2007 Donor Eligibility Guidance.

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 the "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based 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. 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: August 11, 2016.

Jeremy Sharp,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

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