

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2014-D-2175]

#### Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus; 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 “Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus; Guidance for Industry.” The guidance document notifies blood establishments that FDA has determined Ebola virus to be a transfusion-transmitted infection (TTI) and provides blood establishments that collect blood and blood components for transfusion or further manufacture, including Source Plasma, with FDA recommendations for assessing blood donor eligibility, donor deferral, and blood product management in the event that an outbreak of Ebola virus disease (EVD) with widespread transmission is declared in at least one country. The guidance document applies to Ebola virus (species *Zaire ebolavirus*). The recommendations apply to routine collection of blood and blood components for transfusion or further manufacture, including Source Plasma. The guidance announced in this notice finalizes the draft guidance of the same title dated December 2015.

**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:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://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 <https://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-2014-D-2175 for “Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus; Guidance for Industry.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://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 <https://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 <https://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:** Jessica T. Walker, 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 “Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus; Guidance for Industry.” The guidance document notifies blood establishments that FDA has determined Ebola virus to be a TTI under 21 CFR

630.3(I) because of the severity of the disease and the risk of transmission by blood and blood products. The guidance also provides blood establishments that collect blood and blood components for transfusion or further manufacture, including Source Plasma, with FDA recommendations for assessing blood donor eligibility, donor deferral, and blood product management in the event that an outbreak of EVD with widespread transmission occurs in at least one country.

Ebola virus is a member of the family *Filoviridae* that can cause severe hemorrhagic fever in humans and non-human primates with historically high morbidity and mortality rates of up to 90 percent. However, in the 2014 outbreak in West Africa, the mortality rate was markedly lower. In humans, EVD is typically characterized at onset by fever, severe headache, muscle pain, and weakness, followed by diarrhea, vomiting, abdominal pain, and sometimes diffuse hemorrhage (bleeding or bruising). In previous outbreaks of EVD, symptoms generally appeared within 21 days and most often within 4 to 10 days following infection; however, based on mathematical models, symptom onset later than 21 days is estimated as possible in 0.1 to 12 percent of cases. Although viremia in survivors typically resolves within 21 days of disease onset, infectious virus and viral ribonucleic acid (RNA) has been detected in other body components or fluids (e.g., aqueous humor, semen, and vaginal fluids) for longer periods. For instance, infectious virus and viral RNA have been detected in semen up to 82 and 272 days post-EVD onset, respectively, and a case of sexual transmission of Ebola virus was reported in which the patient was exposed to Ebola virus through sexual contact with a survivor 179 days after likely disease onset.

Transmission of Ebola virus from human to human occurs by direct contact with body fluids (such as blood, urine, stool, saliva, semen, vaginal fluids, or vomit) of symptomatic infected individuals. Therefore, blood and blood products from symptomatic individuals, if they were to donate, would have the potential of transmitting Ebola virus to recipients.

Under 21 CFR 630.10(a) and (f)(1), a donor must be in good health and have a normal temperature at the time of donation. Standard procedures that are in place to assure that the donor feels healthy at the time of donation serve as an effective safeguard against collecting blood or blood components from a donor who seeks to donate after the onset of clinical symptoms of EVD. FDA

is providing guidance to reduce the risks of collecting blood and blood components from potentially Ebola virus-infected persons during the asymptomatic incubation period before the onset of clinical symptoms, as well as from individuals with a history of Ebola virus infection or disease.

The guidance recommends blood establishments update their donor educational materials to instruct donors with a history of Ebola virus infection or disease to not donate blood or blood components. In the event that one or more countries is classified by Centers for Disease Control and Prevention (CDC) as having widespread transmission of Ebola virus, blood establishments must update their donor history questionnaire (DHQ), including the full-length and abbreviated DHQ and accompanying materials, to assess donors for a history of Ebola virus infection or disease and travel to, or residence in, an area endemic for Ebola virus. The guidance recommends indefinite deferral of a donor with a history of Ebola virus infection or disease and for a donor who has been a resident of or has travelled to a country with widespread transmission of EVD. FDA recommends that establishments defer a donor for 8 weeks from the time of the donor's departure from that country. The guidance document provides additional recommendations for blood establishments in the event that one or more countries are classified by CDC as having widespread transmission of Ebola virus. For a donor who has had close contact with a person confirmed to have EVD or a person under investigation for Ebola virus infection or disease in whom diagnosis is pending, FDA recommends that establishments defer a donor for 8 weeks after the last contact. In addition, FDA recommends that establishments defer a donor for 8 weeks after the last sexual contact with a person known to have recovered from EVD, regardless of the time since the person's recovery. FDA also recommends that establishments defer for a period of 8 weeks after exposure a donor who has been notified by a Federal, State, or local public health authority that he or she may have been exposed to a person with EVD.

The guidance includes FDA recommendations on retrieval and quarantine of blood and blood components from a donor later determined to have Ebola virus infection or disease or risk factors for Ebola virus infection or disease, notification of consignees, and reporting a biological product deviation to FDA. The guidance also addresses

convalescent plasma intended for transfusion.

In the **Federal Register** of December 3, 2015 (80 FR 75681), FDA announced the availability of the draft guidance of the same title dated December 2015. FDA received comments on the draft guidance and those comments were considered as the guidance was finalized. A summary of changes made in the final guidance includes: (1) Notifying blood establishments that FDA has determined Ebola virus to be a TTI under § 630.30(I); (2) providing a recommendation that the donor educational materials instruct donors with a history of EVD to self-defer; (3) adding a recommended timeframe for when blood establishments should discontinue donor questioning after CDC declares there is no longer widespread transmission of Ebola virus; and (4) clarifying certain recommendations on product retrieval, quarantine, and notification of consignees of blood and blood components from donors at risk of Ebola virus infection or disease. In addition, editorial changes were made to improve clarity. The guidance announced in this notice finalizes the draft guidance of the same title dated December 2015.

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 assessment of blood donor eligibility, donor deferral, and blood product management in response to Ebola virus. 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

This 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 part 312 have been approved under OMB control number 0910–0014; the collections of information in 21 CFR 600.14 and 606.171 have been approved under OMB control number 0910–0458; the collections of information in 21 CFR 601.12 and Form FDA 356h have been approved under OMB control number 0910–0338; the collections of information in 21 CFR 606.160 have been approved under OMB control numbers 0910–0116 and 0910–0795; and the collections of information in 21

CFR 630.10 and 630.40 have been approved under OMB control number 0910-0795.

### 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 <https://www.regulations.gov>.

Dated: January 3, 2017.

**Leslie Kux,**

*Associate Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2016-D-4646]

#### Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers: Questions and Answers; Draft 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 draft guidance for industry entitled “Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers: Questions and Answers.” This draft addresses questions about and clarifies FDA’s expectations for annual reporting to FDA by prescription drug wholesale distributors (wholesale distributors) and third-party logistics providers (3PLs) as required under the Federal Food, Drug, and Cosmetic Act (the FD&C Act) as amended by the Drug Supply Chain Security Act (DSCSA).

**DATES:** Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by March 13, 2017.

**ADDRESSES:** You may submit comments as follows:

#### Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal:* <https://www.regulations.gov>. Follow the

instructions for submitting comments. Comments submitted electronically, including attachments, to <https://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 <https://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-2016-D-4646 for “Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers: Questions and Answers; Draft Guidance for Industry; Availability.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://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 <https://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 <https://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 draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or 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 that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:** Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-3130, [WDD3PLRequirements@fda.hhs.gov](mailto:WDD3PLRequirements@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

Section 204 of the DSCSA (Title II of Pub. L. 113-54) amended section 503(e)