Implementation of Acceptable Full-Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Source Plasma

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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)(4)(i). Submit one set of either electronic or written comments on this guidance at anytime. 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 docket number FDA-2016-D-1533.

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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Contains Nonbinding Recommendations

Implementation of Acceptable Full-Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Source Plasma

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 recognizes the standardized full-length and abbreviated donor history questionnaires and accompanying materials, version 2.0 dated July 2016, prepared by the Plasma Protein Therapeutics Association (PPTA) as an acceptable mechanism for collecting donor history information from Source Plasma donors that is consistent with FDA's requirements and recommendations for collecting Source Plasma donor history information. The PPTA Source Plasma donor history questionnaire documents are being updated to align with the requirements promulgated in the final rule published in the *Federal Register* of May 22, 2015, entitled "Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use" (80 FR 29842), which became effective May 23, 2016, and incorporate the recommendations provided 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 (Ref. 1). In the future, we may recognize other PPTA Source Plasma donor history questionnaires and accompanying materials (PPTA SPDHQ documents) as acceptable.

This guidance supersedes the document entitled "Implementation of an Acceptable Full-Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Source Plasma" dated February 2013, which accepted version 1.2 of the full-length and abbreviated PPTA SPDHQ documents (Ref. 2).

The PPTA SPDHQ documents provide blood establishments that collect Source Plasma (referred to as "manufacturers" or "you") with a specific process for administering questions to Source Plasma donors (referred to as "donors") to determine their eligibility to donate. We are using the term "eligibility" in this guidance to refer to the donor eligibility requirements described in Title 21 of the Code of Federal Regulations 630.10, 630.15 and 640.65 (21 CFR 630.10, 630.15 and

640.65). Acceptable PPTA SPDHQ documents are those documents that FDA has determined provide manufacturers with one means of obtaining donor history information from a donor to determine if the donor is eligible, consistent with the requirements in 21 CFR 630.10 and 630.15.

This guidance also advises Source Plasma manufacturers who choose to implement the acceptable PPTA SPDHQ documents on how to report the manufacturing change consisting of the implementation of the acceptable PPTA SPDHQ documents under 21 CFR 601.12 (§ 601.12).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, these 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

Section 630.10(c) requires the eligibility of all donors to be determined on the day of donation and before collection, with certain exceptions (21 CFR 630.10(c)(1)-(2)). Such determination is intended to ensure a donor's overall good health and that the donor is free from transfusion-transmitted infection (21 CFR 630.10(a)(1)-(2)). A donor's eligibility to donate blood and blood components is determined in part by a physical assessment and the donor's answers to questions concerning medical history and risk factors associated with exposure to, or clinical evidence of a relevant transfusion-transmitted infection and other conditions that may adversely affect the health of the donor or the safety, purity, or potency of the blood or blood components or any product manufactured from the blood or blood components (21 CFR 630.10(e)-(f)). The donor screening interview is especially important in identifying risks for diseases and conditions for which there are no adequate laboratory tests or for which tests are unable to identify early stage or window period infection. Sections 630.15(b) and 640.65 include additional donor eligibility requirements for blood establishments that collect Source Plasma and plasma by plasmapheresis.

The first formal uniform questionnaire developed for the purpose of blood donor screening was implemented nearly sixty years ago (Ref. 3). Though the donor interview process is helpful in excluding ineligible donors, errors in this process do occur because some information may not be understood or captured during the screening process (Ref. 4). As noted during public workshops sponsored by FDA to discuss this issue, the blood donor screening process should consider such factors as question complexity, donor recall ability, donor health and safety, donor satisfaction and willingness to return, any further processing which a product may undergo prior to use, and risk to the end user/recipient of blood and blood components (Refs. 5 and 6). Strategies such as using self-administered computer-assisted and abbreviated questionnaires have been implemented as approaches to improve donor understanding and satisfaction over what some view as a lengthy and time-consuming process, particularly for frequent donors (Refs. 5 through 7).

The PPTA SPDHQ documents include the following materials and are intended to be used in their entirety, with the exceptions noted in sections III and IV.A.2 of this guidance:

- Full-Length PPTA Donor History Questionnaire.
- Full-Length PPTA Donor History Questionnaire Directions for Use – includes glossary, flow charts and references; describes how questions can be administered; and contains follow-up questions to further evaluate a potential donor's response to "capture questions."[1]
- Abbreviated PPTA Donor History Questionnaire – to be used by frequent Source Plasma donors.
- Abbreviated PPTA Donor History Questionnaire Directions for Use – includes glossary, flow charts and references; describes which donors may complete the questionnaire and how the questions can be administered; and contains follow-up questions to further evaluate a potential donor's response to capture questions.
- Medication List – contains a list of medications that may serve as a basis for donor deferral.
- Risk Posters – educate the donor about risks and conditions that are a basis for donor deferral.
    - Poster I – to be used by Source Plasma establishments that implement all the recommendations in the "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry" dated December 2015.
    - Poster II – to be used by Source Plasma establishments that do not implement all the recommendations in the "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry" dated December 2015.
- Travel Posters – identify countries endemic for diseases that can be transmitted by blood and blood components.

The full-length and abbreviated donor history questionnaires are designed to be implemented together. For example, if you choose to implement the Abbreviated PPTA Donor History Questionnaire, you should also implement the Full-Length PPTA Donor History Questionnaire as described in the Directions for Use. Both the full-length and abbreviated donor history questionnaires are designed to be administered either by Source Plasma establishment personnel or self-administered with follow-up by establishment personnel.

III. RECOGNITION OF PPTA SPDHQ DOCUMENTS

We find the PPTA SPDHQ documents version 2.0 dated July 2016, to be acceptable for use in screening Source Plasma donors. These documents are consistent with FDA requirements and recommendations related to donor eligibility interviews, subject to the following exceptions: the

[1] Capture questions ask general questions about a potential donor's history and are followed up by more specific questions, if needed.

acceptable PPTA SPDHQ documents contain questions related to the following donor medical history issues for which we currently do not have requirements or recommendations: cancer; certain organ, tissue, or bone marrow transplant; bone or skin graft; nervous system disease; diabetes; history of fainting, seizures or convulsions; relapsing disease; surgery, diagnostic or dental procedures; or acupuncture. By recognizing the acceptable PPTA SPDHQ documents as one way to satisfy FDA's regulatory requirements, we are not requiring or recommending that donors be screened or deferred for these issues. If you choose to implement the acceptable PPTA SPDHQ documents and omit these questions, you would still be in compliance with FDA requirements.

In addition, the acceptable PPTA SPDHQ documents include a donor acknowledgement statement. Note that the use of this statement alone does not meet the requirements for donor acknowledgement as described in 21 CFR 630.10(g)(2). You must establish procedures in accordance with 21 CFR 606.100 to ensure that the requirements in 21 CFR 630.10(g)(2) have been satisfied.

While we recognize that the acceptable PPTA SPDHQ documents provide an effective tool for screening donors, we do not require that you implement the acceptable PPTA SPDHQ documents. You may use full-length and abbreviated donor history questionnaires and accompanying materials developed by your establishment and approved by FDA. These materials may include procedures and wording that are different from those in the acceptable PPTA SPDHQ documents. In the future, you may implement, consistent with § 601.12, new procedures and materials that differ from those in acceptable PPTA SPDHQ documents (Ref. 8).

IV. REPORTING TO FDA THE IMPLEMENTATION OF ACCEPTABLE DONOR HISTORY QUESTIONNAIRES AND ACCOMPANYING MATERIALS

As discussed in section II of this guidance, we recommend that the full-length and abbreviated donor history questionnaires be used together. For example, if you choose to implement the Abbreviated PPTA Donor History Questionnaire, we recommend that you also implement the Full-Length PPTA Donor History Questionnaire.

A. Implementation of the Acceptable PPTA SPDHQ Documents

You must report the implementation of the acceptable PPTA SPDHQ documents to FDA under § 601.12 as follows:

1. If the acceptable PPTA SPDHQ documents are implemented without modifications and in their entirety as a complete process for administering questions to Source Plasma donors, the change is considered to be minor, with a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. You must report such changes to FDA in your annual report under § 601.12(d), noting the date the process was implemented.

If donors will be allowed to self-administer the acceptable PPTA SPDHQ documents, see section IV.B of this guidance.

Note: You must submit your standard operating procedures (SOP) for implementing the donor acknowledgment requirements in 21 CFR 630.10(g)(2) as a Changes Being Effected supplement consistent with 21 CFR 601.12(c)(5). See 21 CFR 601.12(a)(3).

2. If the acceptable PPTA SPDHQ documents are implemented in their entirety, but modified by: (a) adding additional, more restrictive selection criteria that are specific to your establishment; (b) omitting questions related to: cancer; organ, tissue, or bone marrow transplant, except for xenotransplantation; bone or skin graft; nervous system disease; diabetes; history of fainting, seizures or convulsions; relapsing disease; surgery, diagnostic or dental procedures; or acupuncture, which FDA has not required or recommended for determining donor eligibility; or (c) omitting the donor acknowledgement statement and using your own materials to satisfy the requirements in 21 CFR 630.10(g)(2), the changes are considered to be minor. You must report such changes to FDA in your annual report under § 601.12(d), noting the date the process was implemented and describing the additional criteria or the questions or statements that were omitted from your questionnaire.

3. If the acceptable PPTA SPDHQ documents are implemented in their entirety but modified by displaying the flow charts in another format that is compatible with your current process, the changes are considered minor, provided there is no change to the content in the PPTA SPDHQ flow charts, other than changes incorporating donor deferral criteria that are stricter than the FDA required/recommended donor deferral criteria. You must report such changes to FDA in your annual report under § 601.12(d), noting the date the process was implemented and describing how you modified the acceptable PPTA SPDHQ documents.

4. If the acceptable PPTA SPDHQ documents are implemented in their entirety, but modified by reformatting any of the acceptable PPTA SPDHQ documents (other than the flow charts) to be consistent with your current process, the changes are considered to be minor, provided you do not change the wording and the order of content in the acceptable PPTA SPDHQ documents. You must report such changes to FDA in your annual report under § 601.12(d), noting the date the process was implemented and describing how you modified the acceptable PPTA SPDHQ documents.

5. Donor screening procedures have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of blood and blood components, as they may relate to the safety or effectiveness of the product. Therefore, the implementation of the acceptable PPTA SPDHQ documents that have been modified other than as specifically described in sections

IV.A.2-4 of this guidance is considered a major change. If you wish to implement the acceptable PPTA SPDHQ documents modified in a manner other than as described in sections IV.A.2-4 of this guidance, you must report such changes as a Prior Approval Supplement (PAS) under § 601.12(b). We recommend that you include the following in the submission:

a. FDA Form 356h "Application to Market a New Drug, Biologic or an Antibiotic Drug for Human Use" which may be obtained at http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm;
b. A cover letter describing the request and the contents of the submission;
c. An SOP describing the donor questions and questionnaire process; and
d. The donor history questionnaires and accompanying document(s). Please highlight the modifications.

For assistance in preparing the supplement, please refer to FDA's guidance entitled "Guidance for Industry: For the Submission of Chemistry, Manufacturing and Controls and Establishment Description Information for Human Blood and Blood Components Intended for Transfusion or for Further Manufacture and for the Completion of the Form FDA 356h 'Application to Market a New Drug, Biologic or an Antibiotic Drug for Human Use,'" dated May 1999 (Ref. 9).

B. Implementation of Self-Administered Acceptable PPTA SPDHQ Documents

In July 2003, we issued a document entitled "Guidance for Industry: Streamlining the Donor Interview Process: Recommendations for Self-Administered Questionnaires" (Streamlining Donor Interview guidance) (Ref. 7), advising licensed blood establishments to submit procedures for self-administering the donor history questionnaire to FDA as a Changes Being Effected in 30 Days supplement (CBE30) under § 601.12(c). We advised in the Streamlining Donor Interview guidance that a CBE30 was an appropriate supplement to ensure that controls were in place to manage this process. However, we have since determined that when acceptable donor history questionnaire documents include instructions for controlling the self-administration process, such as in the PPTA SPDHQ Directions for Use, this change may be reported in an annual report or, in some situations, as a CBE30, as described in sections IV.B.1 and IV.B.2 of this guidance. These recommendations modify those stated in the Streamlining Donor Interview guidance. Licensed manufacturers planning to implement self-administration of a questionnaire other than the acceptable PPTA SPDHQ documents should continue to consult the Streamlining Donor Interview guidance (Ref. 7).

Licensed manufacturers must report implementation of self-administered acceptable PPTA SPDHQ documents under § 601.12 as follows:

1. If you choose to implement self-administration of the acceptable PPTA SPDHQ documents using the written form or audio/visual presentation methods described in the acceptable PPTA SPDHQ documents, this is considered a minor change. Report such a change to FDA in your annual report under § 601.12(d), noting the date the process was implemented.

2. If you choose to implement the acceptable PPTA SPDHQ documents using a computer-assisted interactive interview procedure, report this change to FDA as a CBE30 under § 601.12(c). This change presents a moderate potential to adversely affect the identity, strength, quality, purity, or potency of blood and blood components as they may relate to the safety and effectiveness of the product because of concerns that the presentation of the questions and information may not be easily readable in all conditions and by all potential users. Additionally, implementation for the first time of a computer-assisted interactive interview procedure may raise new issues that should be evaluated, such as the management of electronic records. Therefore, we cannot conclude at this time that the implementation of a computer-assisted interactive interview procedure will be a minor change.

For recommendations on the implementation and reporting the use of self-administered questionnaires other than as described above, and for preparing the CBE30 supplement for the computer-assisted interactive interview procedure, see the Streamlining Donor Interview guidance (Ref. 7).

V. RECOGNITION AND IMPLEMENTATION OF FUTURE ACCEPTABLE PPTA SPDHQ DOCUMENTS

In the future, we may issue regulations or guidance documents concerning donor eligibility. For example, we may recommend revised eligibility criteria with respect to transfusion-transmitted infections, medical conditions, behaviors, geographic exposures or medications. Implementation of new eligibility criteria would change your donor interview SOPs, and involve amending accepted PPTA SPDHQ documents (typically by adding a question at the end of the questionnaire in the area designated for additional questions or by implementing new or revised PPTA SPDHQ documents)[2]. We note the Directions for Use describes how to add and administer revised PPTA SPDHQ documents.

We anticipate that in the event we recommend a new donor deferral criterion, we will, in the same guidance, provide recommendations concerning implementing and reporting to FDA the manufacturing changes associated with this change in procedure. If the revised PPTA SPDHQ

[2] If you do not use the acceptable PPTA SPDHQ documents, this would involve amending your own donor history questionnaire.

documents are available and found acceptable, we also intend to recognize those PPTA SPDHQ documents as acceptable in the guidance document addressing the new criterion.

We recommend that you have a procedure in place for implementing updated donor history questionnaire documents in all your facilities.

VI. FOR MORE INFORMATION

If you have questions regarding this guidance and FDA policies for implementing the acceptable PPTA SPDHQ documents, contact OCOD at the phone numbers or email address provided in this guidance.

If you have questions regarding the PPTA SPDHQ documents, contact PPTA by phone at 202-789-3100, by fax at (410) 263-2298 or online at http://www.pptaglobal.org/about-us/contact-us/submit-your-question.

The acceptable PPTA SPDHQ documents can be accessed on the PPTA website at http://www.pptaglobal.org/safety-quality/donor-history-questionnaire.

VII. REFERENCES

1. Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry, December 2015. Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM446580.pdf.
2. *Federal Register* Notice: Guidance for Industry: Implementation of an Acceptable Full-Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Source Plasma; Availability, 78 FR 13071 (February 26, 2013).
3. American Association of Blood Banks, *Technical Methods and Procedures of the American Association of Blood Banks*, pp. 3-5, Minneapolis: Burgess Publishing Co., 1953.
4. Biological Product Deviation Reports Annual Summaries, CBER. Available at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/default.htm.
5. FDA/AABB Workshop on "Streamlining the Blood Donor History Questionnaire" Transcripts, October 16, 2000.
6. FDA/AABB Workshop on "Recruiting Blood Donors – Successful Practices" Transcripts, July 6, 2000.
7. Guidance for Industry: Streamlining the Donor Interview Process: Recommendations for Self-Administered Questionnaires, July 2003. Available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm075086.htm.
8. Guidance for Industry: Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture, November 2014. Available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm354559.htm.
9. Guidance for Industry: For the Submission of Chemistry, Manufacturing and Controls and Establishment Description Information for Human Blood and Blood Components Intended for Transfusion or for Further Manufacture and for the Completion of the Form FDA 356h "Application to Market a New Drug, Biologic or an Antibiotic Drug for Human Use," May 1999. Available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm077087.htm.