Plasma Protein Therapeutics Association

Date: March 7, 2017
Reference No.: FDAA18003 **VIA EMAIL**

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

SUBJECT: Standards Development and the Use of Standards in Regulatory Submissions Reviewed in the Center for Biologics Evaluation and Research (Docket Number FDA-2017-D-6535-001)

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) thanks FDA for the opportunity to participate in the guidance development process and is pleased to provide these comments on the draft guidance for industry and FDA staff, "Standards Development and the Use of Standards in Regulatory Submissions Reviewed in the Center for Biologics Evaluation and Research," dated December 2017 (hereinafter, "Draft Guidance").[1]

About PPTA

PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies, collectively referred to as plasma protein therapies. Plasma protein therapies are used mostly in the treatment of several rare diseases. These diseases are often genetic, chronic, life-threatening conditions that require patients to receive regular infusions or injections of plasma protein therapies for the duration of their lives. These therapies include clotting therapies for individuals with bleeding disorders, immunoglobulins (IG) to treat a complex of diseases in persons with severe autoimmune deficiencies, therapies for individuals who have alpha-1 anti-trypsin deficiency, which typically manifests as adult-onset emphysema and substantially limits life expectancy, and albumin, which is used to treat individuals with severe liver diseases and, in emergency-room settings, shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

About the PPTA Voluntary Standards Program

PPTA's voluntary standards program provides global leadership for the plasma protein industry's goal of continuous improvement with a focus on safety and quality from the donor to the patient.

The International Quality Plasma Program (IQPP) consists of eleven standards related to Source plasma collection. Ninety-nine percent of centers in the United States are IQPP-certified or (in the case of new centers) are in the process of becoming IQPP-certified. The program is also available worldwide to any qualifying Source plasma collection center. IQPP certification

[1] Standards Development and the Use of Standards in Regulatory Submissions Reviewed in the Center for Biologics Evaluation and Research, https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM589416.pdf accessed Feb. 19, 2018

provides independent, third-party evaluation and recognition of a center's adherence to global industry standards for Source plasma.

The Quality Standards for Excellence, Assurance and Leadership (QSEAL) program consists of five standards related to manufacture of products made from human plasma, regardless of its source (including Source plasma and Recovered plasma). The program is available worldwide to any facility that manufactures plasma protein therapies using human plasma. QSEAL certification provides independent, third-party evaluation and recognition of a center's adherence to global industry standards for plasma fractionation.

Introduction

PPTA understands that the Draft Guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under the Public Health Service Act (PHS Act) and is one in a series of guidances that the Agency has developed to implement the Biologics Price Competition and Innovation Act of 2009 (BPCI Act).[2] FDA, particularly the Center for Biologics Evaluation and Research (CBER), clearly recognizes the uniqueness of plasma protein therapies and their vital role for patients with several rare diseases; PPTA's comments are limited to the effects of the BPCI Act on plasma protein therapies.

Comments

1. **Recognition of the PPTA Voluntary Standards Program.**

   Section I, Introduction, paragraph 1. We appreciate that CBER recognizes the value of standards in product development and the use of such standards in CBER's managed review process. We also appreciate that CBER upholds the principles described in the 2016 revision to OMB Circular A119 "Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities," in particular for its supporting a preference for using voluntary consensus standards over government-unique standards in Federal regulation.

   We bring to CBER's attention the following PPTA voluntary standards:

   - IQPP Community-based Donor Standard
   - IQPP Cross Donation Management Standard
   - IQPP Standard for Recording Donor Adverse Events
   - IQPP Donor Education Standard
   - IQPP Donor Fluid Administration Standard
   - IQPP Use of the National Donor Deferral Registry® Standard (NDDR®)
   - IQPP Qualified Donor Standard
   - IQPP Viral Marker Standard
   - IQPP Personnel Education and Training Programs in Plasmapheresis Establishments Standard
   - IQPP Professional Plasma Collection Facility Standard
   - IQPP Quality Assurance Standard
   - QSEAL Controls on Incoming Plasma Standard
   - QSEAL Inventory Hold Standard
   - QSEAL NAT Testing Standard
   - QSEAL Intermediates Purchased from an External Supplier Standard

[2] *See* FR Notice, 82 Fed. Reg. 5579 (Jan. 18, 2017)

- QSEAL Recovered Plasma Specification

The text for these documents are publically available at http://www.pptaglobal.org/safety-quality/standards/iqpp and http://www.pptaglobal.org/safety-quality/standards/qseal.

2. Reference PPTA IQPP and QSEAL standards programs.

i. **Section III**, item C defines a Standards Development Organization (SDO). We note that PPTA qualifies, per OMB Circular A-119, as an SDO through its IQPP and QSEAL Voluntary Standards Programs. We therefore suggest that The Plasma Protein Therapeutics Association (PPTA) be added to the text of Item III, section C, as an example of a SDO.

ii. **Section III, item D.** We also note that PPTA qualifies as a Voluntary Consensus Standards Body through its IQPP and QSEAL Voluntary Standards Programs. The program is governed through rules and procedures that meet the description of a "Voluntary consensus standards body" described in OMB Circular A-119 (page 16).

a) Openness:

- *Public Review.* 60-day comment period open to everyone. Development procedures require that all comments received be reviewed within a specified timeframe. Procedures also require that all public review commenters receive a response indicating how the standards-developing committee disposed of the comments, including a clear explanation for any comment that was not accepted.
- *Outreach* to plasma collectors and manufacturers to join the IQPP and QSEAL Standards Committees. We also note that membership on the IQPP and QSEAL Standards developing committees is not restricted by an organization's national or regional domicile.
- *Prior notification* to all stakeholders when a new or revised standard or other deliverable is approved.
- *Clear and Transparent Procedures and Processes:* The PPTA Voluntary Standards Program Policy and Procedures Manual (attached) contains clear and transparent procedures and processes for standards development.
- *International:* The plasma industry is global in nature. Reflecting this, the PPTA standards are developed through committees involving representatives from many countries. Membership on standards development committees and PPTA boards is not restricted to any particular national origin.

b) Balance: For IQPP, the PPTA Source Board of Directors is the final approval body for all new and revised standards and other deliverables. The Board has specific rules to ensure that its membership is balanced, such that independent and private organizations, as well as the collectors of Source plasma and the users of Source plasma (i.e., the organizations that use Source plasma to manufacture plasma protein therapies), are represented in equal numbers. The PPTA IQPP Standards Committee is comprised of technical experts, and which drafts the IQPP standards. This committee membership is equally composed of a balance of Source plasma collectors and users. For QSEAL, the PPTA Global Board of Directors is the final approval body for all new and revised standards and other deliverables. Furthermore, per the procedures for standards development, a 70% approval threshold of the voting membership on the standards-developing committee is required before any new or revised standard or other deliverable is approved.

- **Due Process:** The procedures for developing standards are outlined in the PPTA Voluntary Standards Program Policy and Procedures Manual (attached). This includes rules for adequate notice of meetings and standards development, sufficient time to review drafts and prepare views and objections, access to views and objections of other participants and a fair and impartial process for resolving conflicting views.

- **Appeals Process:** A transparent appeals process for standards development is outlined in the PPTA Voluntary Standards Program Policy and Procedures Manual (attached).

- **Consensus:** The PPTA Voluntary Standards Program Policy and Procedures Manual contains a definition and clear rules for consensus, including requirements that ensure comments and objections are considered using fair, impartial, open and transparent processes.

iii. Section VI, Item C, Accreditation Standards

In addition to the PPTA Standards Program meeting the definition of a Voluntary Consensus Body, as detailed above, PPTA operates certification programs in relation to its IQPP and QSEAL standards. Certifications are conducted through a third-party, independent review process, and are directly based on the requirements in the voluntary IQPP and QSEAL standards.

Section VI, Item C, states:

> "CBER may, when it deems appropriate, take accreditation standards established by these organizations *[accreditation organizations]* into consideration when assessing compliance with CBER regulatory requirements."

The draft guidance lists all major blood sector accreditation organizations *except for* the PPTA. The PPTA is, in fact, the only Voluntary Consensus Body accreditation organization with standards and certification programs for human plasma collection and fractionation; therefore the PPTA should be included among the list of examples given in this section of the guidance.

Conclusion

PPTA appreciates the opportunity to comment on the Draft Guidance. PPTA welcomes from FDA any questions regarding these comments. Thank you for your consideration.

Respectfully submitted,

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