Plasma Protein Therapeutics Association

July 29, 2013
Reference No.: FDAA13016

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

SUBJECT: Draft Guidance for Industry on Contract Manufacturing Arrangements for Drugs: Quality Agreements; Availability [Docket No. FDA-2013-D-0558]

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these comments on the *Guidance for Industry – Contract Manufacturing Arrangements for Drugs: Quality Agreements – Draft Guidance* (May 2013) ("*Draft Guidance*").[1] PPTA understands that the *Draft Guidance* describes FDA's current thinking on defining, establishing, and documenting the responsibilities of each party (or all parties) involved in the contract manufacturing, testing, and other support operations of drugs subject to Current Good Manufacturing Practice (CGMP), particularly how parties involved in contract drug manufacturing can utilize written Quality Agreements as tools to delineate their responsibilities and assure drug product quality, safety, efficacy, and effectiveness.[2] While PPTA agrees with FDA that written Quality Agreements are not explicitly required under existing CGMP regulations for human drugs and do not relieve any party to a contract of their responsibilities under CGMP or under the Federal Food, Drug, and Cosmetic Act, the Association appreciates that the *Draft Guidance* describes how Owners and Contracted Facilities can draw on quality management principles to carry out the complicated process of contract drug manufacturing.[3] While PPTA also appreciates that FDA is considering including (references to) examples of Quality Agreements in the *Guidance*, the Association cannot, at this time, provide specific comments on publicly available, useful Quality Agreements for contract arrangements for drug manufacturing, as requested, but may be able to do so in the future.[4]

[1] *See* FR Notice, 78 Fed. Reg. 31943-44 (May 28, 2013)
[2] *See id*.
[3] *See id*. at 31944
[4] *See id.*

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About PPTA

PPTA is the international trade association and standards-setting organization for the world's major collectors of Source Plasma and manufacturers of plasma-derived products and recombinant analogues, collectively referred to as plasma protein therapies, which are used in the treatment of a number of 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. Plasma protein therapies include clotting-factor therapies for individuals with hemophilia A and B and other bleeding disorders; immunoglobulins to treat a complex of diseases in individuals with immune deficiencies; therapies for individuals who have alpha-1 anti-trypsin deficiency, which typically manifests as adult onset emphysema and limits substantially life expectancy; and albumin, which is used in emergency-room settings to treat individuals with shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

General Comments

In general, the *Draft Guidance* reads well, delineates important elements to be included in Quality Agreements, and aligns well with FDA's *Guidance for Industry – Q10 Pharmaceutical Quality System* (April 2009) ("*ICH Q10*"). PPTA agrees that the elements commented upon below should be covered in Quality Agreements.

Suggested Edits

Line	Current language	Suggested language
179	Responsibilities, including communication *mechanisms* & contacts	Responsibilities, including communication *processes* & contacts

ICH Q10 indicates that "[t]he pharmaceutical company is ultimately responsible to ensure processes are in place to assure the control of outsourced activities and quality of purchased materials" and that "[t]hese processes should incorporate quality risk management and include: … (b) Defining the responsibilities and communication processes for quality-related activities of the involved parties."[5] PPTA takes "communication processes" to mean processes to be followed such as when certain events occur and must be communicated, which party does the communication, and in what timeframe, e.g. exceptions are reported by the Contracted Facility to the Owner

[5] *See ICH Q10* at 7-8

within 10 business days. "Communication processes" does *not* mean communication mechanisms such as weekly or biweekly meetings.

Lines	Current language	Suggested language
197-198	Owners and Contracted Facilities may opt to document the specific terms of their Quality Agreements with respect to CGMP responsibilities in a wide variety of formats, such as charts, matrices, or narratives, or a combination of these.	Owners and Contracted Facilities may opt to document the specific terms of their Quality Agreements with respect to CGMP responsibilities in a wide variety of formats, such as charts, matrices, *information mapping,* or narratives, or a combination of these.

Additional Comments

PPTA agrees with FDA that "the Owner should conduct a risk review that evaluates the extent of controls required for the particular supplier … ,"[6] which reflects similar language in *ICH Q10*: "The pharmaceutical company … should [monitor] and review … the performance of the contract acceptor or the quality of the material from the provider, and the identification and implementation of any essential improvements."[7] One concern is, if manufacturers want to document the completion of this risk review, how would it be captured and then linked to the extent of controls built into the Quality Agreement?

PPTA also agrees with FDA that "[a]ll parties performing manufacturing operations should monitor incoming ingredients and materials to ensure they are from approved sources using the agreed supply chain,"[8] which again reflects similar language in *ICH Q10*: "The pharmaceutical company … should [assess] prior to outsourcing operations or selecting material suppliers, the suitability and competence of the other party to carry out the activity or provide the material using a defined supply chain (e.g., audits, material evaluations, qualification)."[9] Given the *ICH Q10* language, the Quality Agreement should spell out the supply chain activities and who does them.

PPTA reads FDA's statement, "Procedures delineating controls over sampling and testing samples should be established in the Quality Agreement,"[10] to mean that the Quality Agreement will identify who controls and tests the samples and under whose

[6] *See Draft Guidance* at 4
[7] *ICH Q10* at 7-8
[8] *See Draft Guidance* at 4
[9] *ICH Q10* at 7-8

procedures. Otherwise, manufacturers would need to build “procedures” into each and every Quality Agreement delineating this.

Conclusion

PPTA appreciates the opportunity to comment on the *Draft Guidance* and looks forward to continued work with FDA on defining, establishing, and documenting the responsibilities of each party (or all parties) involved in the contract manufacturing, testing, and other support operations of drugs subject to CGMP. PPTA welcomes from FDA any questions regarding these comments or requests for more information.

Thank you for your consideration.

Respectfully Submitted,

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[10] *Draft Guidance* at 8