Plasma Protein Therapeutics Association

Date: June 14, 2016
Reference No.: FDAA16009 VIA EMAIL

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

SUBJECT: **Comments to Docket No. FDA-2016-D-1113**, "Data Integrity and Compliance With Current Good Manufacturing Practice; Draft Guidance for Industry"

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for the opportunity to participate in the guidance development process and is pleased to provide these comments on the draft guidance for industry "Data Integrity and Compliance With CGMP" dated April 2016 (hereinafter "Draft Guidance").

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 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. These therapies include clotting therapies for individuals with bleeding disorders, immunoglobulins 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.

Review of audit trials (Questions 7 & 8, pp. 6-7, lines 224-45)

PPTA is concerned that FDA's guidance on how often audit trails should be reviewed, and who should review them, creates a new, higher standard level. PPTA agrees with FDA in the answer to question 8 that "review[ing] the audit trails that capture changes to critical data associated with the record … " (p. 6, lines 240-41) has value; however, the example that follows leads one to believe that this will apply to routine record review. Such review of audit trails would be a significant effort and would require new SOPs and documentation steps, while the value added would be minimal. PPTA suggests that a requirement to review audit trails be triggered only if there are "changes" in the system. Accordingly, PPTA suggests that FDA revise the example in the answer to question 8 as in the Table below.

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Similarly, PPTA suggests that FDA add more specific language in the answer to question 7, where "FDA recommends routine scheduled audit trail review based on the complexity of the system and its intended use" (p. 6, lines 232-33). In particular, PPTA suggests that audit trail review apply to changes only, not to routine record review. Again, PPTA is concerned that routine record review of audit trails would be overly burdensome on industry, without adding significant value, and suggests that the answer to question 7 be revised as in the Table below. Lastly, PPTA asks that FDA specify whether this audit trail review will be interpreted also to require trending.

Table. Suggested revisions

Question	Page(s)	Lines	Current language	Suggested revision
7	6	232-33	FDA recommends routine scheduled audit trail review based on the complexity of the system and its intended use.	FDA recommends ~~routine scheduled audit trail~~ review of audit trails that capture changes to critical data associated with the record; this review should be based on the complexity of the system and its intended use.
8	6-7	242-44	For example, all production and quality control records, which include audit trails, must be reviewed and approved by the quality unit (§ 211.192).	For example, the quality unit must review and approve all production and quality control records, ~~which include audit trails, must be reviewed and approved by the quality unit~~ (§ 211.192), including audit trails that capture changes to critical data associated with the record.

Conclusion

PPTA appreciates the opportunity to comment on the Draft Guidance and looks forward to continued work with FDA to clarify the role of data integrity in CGMP. PPTA welcomes from FDA any questions regarding these comments.

Thank you for your consideration.

Respectfully submitted,

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Plasma Protein Therapeutics Association