

April 7, 2011

Reference No.: FDAA11007

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

VIA WEB

SUBJECT: Draft Guidance for Industry on Electronic Source Documentation in Clinical Investigations [Docket No. FDA-2010-D-0643]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is the international trade association and standards-setting organization for the world's major producers of plasma derived products and recombinant analogues, collectively referred to as plasma protein therapies. The therapies are used in the treatment of a number of rare diseases. The 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. The 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 member companies are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

Introduction

PPTA welcomes the opportunity to discuss plasma protein therapies via written submissions. The Association would like to thank the Food and Drug Administration (FDA) for the opportunity to participate in the guidance process and is pleased to provide these written comments on the Draft Guidance for Industry on Electronic Source Documentation in Clinical Investigations [hereinafter, "Draft Guidance"].¹ PPTA appreciates FDA's efforts to provide guidance to sponsors, contract research organizations, data management centers, and clinical investigators on capturing, using, and archiving electronic data in FDA-regulated clinical investigations and to describe FDA's recommended procedures to ensure reliability, quality, integrity, and traceability of electronic source data and source records maintained at sites for FDA inspection.²

General Comments

¹ See Federal Register / Vol. 76, No. 5 / Friday, January 7, 2011 / Notices, pp. 1173-4

² See Federal Register / Vol. 76, No. 5 / Friday, January 7, 2011 / Notices, p. 1173

Roles of Investigator and of Sponsor

The Draft Guidance notes that “the investigator could enter data at Tier 1 as *study site clinical staff*, view subject data and sign off on eCRFs [electronic case report forms] at Tier 2 as *investigators*, and analyze and report data as an *investigator/sponsor* at Tier 3.”³ PPTA agrees with FDA that, in some cases, such as Phase I or specialty clinical trial units, the investigator may be responsible for electronic data capture and eCRF. However, overall, compliance of an eCRF with part 11 regulations,⁴ and with the principals identified in the Draft Guidance, usually lies with the sponsor, rather than the investigator. As such, in many cases in the Draft Guidance, the roles identified for the “investigator” in fact will be performed by the sponsor. Thus, the Draft Guidance should reflect more accurately the roles of the investigator and of the sponsor.

Electronic Health Records (EHRs)

PPTA agrees with FDA that:

With the increasing use of computerized systems in clinical investigations, it is common to find source data documented in electronic format, *e.g.*, clinical data initially documented in [EHRs] maintained by hospitals and institutions, [eCRFs], laboratory reports that are electronically generated, electronic medical images from devices, and electronic diaries provided by study subjects. When paper source documents are available for review, tracing of data in paper-based studies can be performed easily.⁵

In fact, many clinical trials are conducted in hospital or clinical settings where an EHR is utilized. However, while the investigator and delegated staff have access to these systems, they are not responsible for EHR maintenance, validation procedures, or archiving. The current solution to maintenance of electronic source documents from EHR, when the retention policy is not adequate, is to retain paper back-up copies.

EHRs currently are not regulated by FDA but may be compliant with standards such as Health Level Seven (HL7). As such, the Draft Guidance should describe what additional requirements a sponsor should look for if a clinical trial site utilizes an EHR system compliant with the HL7 standard. Further, the EHR may be from commercial off the shelf or COTS products that are not validated systems. Thus, the Draft Guidance also should address whether these products are acceptable for collection of clinical trial source data.

III. ELECTRONIC SOURCE DOCUMENTS AND SOURCE DATA

Figure 1: Assembly and processing of data elements using eCRF as platform⁶

Figure 1 and the related text do not address sponsor monitoring of eCRF data. Prior to archival by the clinical investigator, a sponsor must monitor the data and study

³ Draft Guidance, p. 5, lines 139-41

⁴ See 21 C.F.R. Part 11

⁵ Federal Register / Vol. 76, No. 5 / Friday, January 7, 2011 / Notices, p. 1173

⁶ Draft Guidance, p. 4

procedures for safety and compliance and assure that any queries are resolved. While data elements relating to subject safety reports may go from the clinical investigator to the institutional review board (IRB), eCRFs do not typically go from the clinical investigator to the IRB. The sponsor typically is responsible for data submission (including eCRF) to the regulatory authorities. As such, Figure 1 and the related text should reflect more accurately sponsor monitoring of eCRF data.

B. Tier 2 – Data Review

2. The Investigator's Copy of the eCRF⁷

In this section, a list of recommendations by responsibility (sponsor and investigator responsibility) and by chronology (e.g., during the clinical study, compared to after the clinical study) would be helpful to PPTA member companies. Below are comments on specific language in this section.

The clinical investigator should generate a write-protected copy of the eCRF for the study archives following review and sign-off.⁸

Typically, it is the owner of the eCRF (sponsor) that would provide the investigator with a write-protected copy of the eCRF for study archives.

The sponsor should describe in its standard operating procedures [SOPs] the location of the copies so they are available to FDA inspectors as a reference for data validation.⁹

It is unclear whether the SOP reference is to the location of storage at the sponsor or to all locations (clinical trial sites).

Conclusion

PPTA appreciates the opportunity to comment on the Draft Guidance and looks forward to continued work with FDA on its efforts to provide guidance to sponsors, contract research organizations, data management centers, and clinical investigators on capturing, using, and archiving electronic data in FDA-regulated clinical investigations. PPTA welcomes from FDA any questions regarding these comments and/or requests for additional information.

Respectfully Submitted,



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Plasma Protein Therapeutics Association

⁷ Draft Guidance, pp. 11-12

⁸ Draft Guidance, p. 12, lines 375-6

⁹ Draft Guidance, p. 12, lines 380-1