

March 14, 2007
Reference No.: FDAA07004

Division of Dockets Management, HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

VIA WEB & USPS

SUBJECT: Proposed Rule, 21 CFR 312, Expanded Access to Investigational Drugs for Treatment Use [Docket No. 2006N-0062; RIN 0910-AF14]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA's) Proposed Rule to amend 21 CFR 312 to provide for Expanded Access to Investigation Drugs for Treatment Use. PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies. Our members provide 60 percent of the world's needs for Source Plasma and protein therapies. These include clotting therapies for individuals with bleeding disorders, immunoglobulins to treat a complex of diseases in persons with immune 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 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.

We appreciate the opportunity to comment on this Proposed Rule. PPTA appreciates the Agency's intent to clarify existing regulations and set forth specific criteria to be met in authorizing expanded access use and in submitting protocols for expanded access use. PPTA's comments follow:

General Comments:

To improve the readability of the Rule, we suggest that the Rule be divided according to:

- Sponsor-supported and clinical investigator expanded access
- New molecular entities and new indications for an already approved drug

The applicability to approved drugs that are being studied for an additional indication is not clear.

For both individual patient use and intermediate-size patient use, the proposed rule states that FDA may ask the sponsor to submit an IND or protocol for expanded use when a significant number of patients request expanded access. There is concern that expanding and publicizing the use through expanded access may create supply and resource constraints that may impact ongoing clinical trials. This is true especially for early stage and/or orphan drugs. Uncontrolled use of the drug outside of the clinical trial could adversely affect the drug's development, slowing down time to approval and/or result in unfavorable patient outcomes.

PPTA believes that FDA has significantly underestimated the costs associated with sponsor expanded access INDs or protocols. Substantial time and resources may be expended in terms of overall management, of providing the drug product, data collection, monitoring, verification and summary preparation.

Upon implementation of a final rule for expanded access, FDA should address adverse event reporting requirements.

- In instances of an approved drug being studied for a new indication, adverse event reporting should be limited to serious and unexpected adverse events as defined in ICH Guideline (E2A)—Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.
- For new molecular entities, adverse event reporting should be limited to serious adverse events and deaths unless there are specific adverse events related to an identified safety concern that may impact risk/benefit assessment.

Specific comments:

Proposed 21 CFR 312.310(c)(4) states that “. . .FDA may ask the sponsor to submit an IND or protocol for use under §312.315 or §312.320.” However, the preamble states, “. . .FDA will consider whether to request that a potential sponsor submit an intermediate-size patient population IND or protocol for the expanded access use and, possibly, conduct a clinical trial of the expanded access use.” It appears that the preamble goes beyond the language of the regulation. What is meant by “conduct a clinical trial of expanded access use” in the preamble?

Proposed 21 CFR 312.310(d)(2) states that parties “. . .must agree to submit an expanded access submission within 5 working days of FDA's authorization of the use.” We believe the 5-day requirement is unrealistic. Companies with experience in administering emergency use INDs report that it usually takes up to 30 days to collect necessary information.

Proposed 21 CFR 312.315(d)(2) states that “The sponsor is responsible for monitoring the expanded use protocol to ensure that licensed physicians comply with the protocol and the regulations applicable to investigators.” Guidance is needed to define the scope and activities included in “monitoring.”

PPTA appreciates the opportunity to comment on the Proposed Rule. Should you have any questions regarding these comments, please contact PPTA. Thank you for your consideration of these comments.

Respectfully submitted,



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Plasma Protein Therapeutics Association