PPTA
Plasma Protein Therapeutics Association

July 20, 2010
Reference: FDAA10010 **VIA WEB**

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

SUBJECT: Food and Drug Administration Transparency Task Force; FDA Transparency Initiative: Draft Proposals for Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration [Docket No. FDA-2009-N-0247]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide comments on the FDA Transparency Initiative: Draft Proposals for Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration [hereinafter, "Draft Proposals"], by the Food and Drug Administration's (FDA) Transparency Task Force. 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 complex 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.

Introduction

PPTA strongly supports the agency in its efforts to improve transparency for all stakeholders, as it is beneficial to both industry and the general public to understand how and why decisions are made. PPTA would like to reiterate previous comments that it believes that overall the agency communicates effectively and has made efforts to become more open and transparent. There is an abundance of information available on the FDA website regarding product approvals, recalls, guidance documents, and regulations. To this point, PPTA believes that FDA's newest web based resource, "FDA Basics," will assist the public in better understanding the agency's functions and the information already available. Also, PPTA appreciates the efforts of the agency to attend meetings and share information with industry. It is vital that this type of dialogue continue, allowing industry and regulators to fully communicate concerns and better

147 Old Solomons Island Road · Suite 100 · Annapolis, MD 21401 USA
tel: 202.789.3100 · 410.263.8296 · fax: 410.263.2298 · e-mail: ppta@pptaglobal.org · www.pptaglobal.org
PPTA Offices in Washington · Annapolis · Brussels · Tokyo

understand decisions. It is important that consumers as well as industry have confidence in the agency that plays such a vital role in consumer protection and safety.

PPTA understands that these Draft Proposals were released to facilitate transparency that promotes public health and innovation. PPTA believes that the following comments will enhance policies already in place and allow for greater openness and predictability. These comments will improve the necessary, cooperative working relationship of industry and FDA, while increasing public confidence in agency decisions, by encouraging the public use of accurate information.

Comments on Draft Proposals

Although there is much in the Draft Proposals that is beneficial, PPTA does have particular concerns about the proposed changes regarding adverse event (AE) reports in Draft Proposal 1.

> **DRAFT PROPOSAL 1:**
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> **FDA should expand the areas in which it provides the public with online access to public information from adverse event reports about FDA-regulated products submitted to FDA, in a format that is searchable and allows users to generate summary reports of this information, including, if known and as applicable, the trade name and/or established name of the product, dosage, route of administration, description of the adverse event, and the health outcome. Adverse event report information should continue to be disclosed with a clear disclaimer about the limits of the information.**[1]

In section V.A.2. of the Draft Proposals, FDA cites a public comment that calls for "FDA to make adverse event reporting systems 'straightforward to use' and to make information about adverse events 'as easily retrievable as possible.'"[2] While it may be possible to make a system straightforward to use, interpretation by the lay public may be demonstrably difficult, particularly as it poses challenges in some cases for industry and regulatory pharmacovigilance experts. Data contained in AE reporting systems vary over time and by drug product classes, data type (spontaneous, solicited, clinical, and literature based reports), and source (consumer, health professional). Furthermore, the current FDA AERS database classifies drugs as either "suspect" or "concomitant,"

[1] FDA Transparency Initiative: Draft Proposals for Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration; p. 19

[2] FDA Transparency Initiative: Draft Proposals for Public Comment Regarding Disclosure Policies of the U.S. Food and Drug Administration; p. 17

which could imply that a definitive causality assessment has been made to users. Data are variable in quality and are subject to numerous limitations that should be expected to differentially impact planned or intuitive analyses from simple counts and comparisons of numbers and frequencies to more complex statistical analyses for the generation of positive and negative safety signal information. For pharmacovigilance experts, such analyses are conducted for the purposes of generating questions or hypotheses that require additional adjudication and analysis and in some cases additional safety studies to further evaluate potential safety concerns raised by reported AE data. Given this, FDA should consider:

1. Developing a robust de-duplication and code validation process for the AE database given the anticipated uses of data.

2. Identifying and explaining data type- and source-specific limitations, for example, voluntary or active surveillance reports; differences in ascertainment; influences on spontaneous reporting including time on market, media reports, and mass-immunization; and coding variability and influences of hierarchy.

3. Developing stakeholder-specific disclaimers on the use and limitations of data.

Absent controls and safeguards such as those suggested above, PPTA believes that the unmanaged public use of this system will result in the generation of erroneous or flawed interpretations as to the safety of products and the risks/benefits of therapeutic options. Even more problematic is the potential for misuse of the system to support biased views of products. Such deliberate data manipulation could have the perverse effect of "punishing" companies that have robust and diligent AE reporting systems while "rewarding" companies that make minimal efforts to collect and investigate AEs. It is relevant to note that at least one global regulatory agency (Health Canada) has already implemented a searchable AE database (Canada Vigilance Adverse Reaction Online Database). If not already done, FDA may wish to engage in a dialog with other regulatory agencies regarding their practical experience with similar initiatives. This could provide additional, relevant insights to FDA with respect to their current proposal. If FDA truly wishes to encourage the public use of accurate information on AEs, aside from the suggestions provided above, it may wish to consider making available a limited number of validated database queries, which could be utilized to generate reports with validated outputs and well understood and disclosed limitations.

Conclusion

As stated above, PPTA commends FDA's efforts to improve transparency at the agency. PPTA believes that the creation of this Task Force and the release of these Draft Proposals were important steps in achieving a more open and predictable FDA. PPTA appreciates the opportunity to comment and looks forward to working with FDA

on this important issue. Should you have questions regarding these comments or would like to discuss these issues further, please contact me at the Association.

Thank you for your consideration.

Sincerely,

Mary Gustafson
Vice President, Global Regulatory Policy
Plasma Protein Therapeutics Association