Plasma Protein Therapeutics Association

March 8, 2011
Reference: FDAA11005 **VIA WEB**

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

SUBJECT: FDA Transparency Initiative: Improving Transparency to Regulated Industry [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: Improving Transparency to Regulated Industry [hereinafter, "Report"].[1] 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. 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 the 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. Members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

Introduction

PPTA strongly supports the Food and Drug Administration (FDA) 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, overall, FDA communicates effectively and has made efforts to become more open and transparent. PPTA appreciates the efforts of FDA to attend meetings and share information with industry. It is vital that this type of dialogue continue, allowing industry and regulators to communicate fully concerns and to understand better decisions. It is important that consumers as well as industry have confidence in FDA, which plays such a vital role in consumer protection and safety.

[1] *See* Federal Register / Vol. 76, No. 5 / Friday, January 7, 2011 / Notices, pp. 1181-2

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Transparency Initiative

PPTA appreciates FDA's ongoing efforts through its Transparency Initiative, including the Agency's establishment of a Transparency Task Force. PPTA has participated in FDA Public Meetings on Transparency and in the Transparency Task Force Listening Session, has submitted comments to FDA regarding transparency, and has discussed transparency at the FDA-PPTA Liaison Meeting. PPTA would like to reiterate its previous suggestions: establishing and publishing work-plans, improving Good Guidance Practices[2] (GGP) processes, improving processes for publications of final regulations, publishing agendas and background materials for public meetings and advisory committees at least 30 days in advance, real-time submission, and improving Freedom of Information Act processes.

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 web-based resource, FDA Basics, will assist the public in better understanding the Agency's functions and the information already available. PPTA also is encouraged that FDA is reviewing comments, including those submitted by the Association, received on its Draft Proposals for Public Comment Regarding Policies of the U.S. Food and Drug Administration; the Association looks forward to the Agency's recommendation of specific proposals to the FDA Commissioner for consideration.[3] PPTA also looks forward to FDA's issuance by March, 2011, of a final version of the Strategic Priorities FY 2011-2015;[4] the Association has submitted comments to the docket on the draft version.

Report

PPTA understands that the Report was released to provide regulated companies with additional transparency about the standards to which their products are held, the process for soliciting guidance from FDA, and the progress of regulatory efforts at the Agency. PPTA believes that the following comments will enhance policies already in place and allow for greater openness and predictability. The comments will improve the necessary, cooperative working relationship of industry and regulators, while increasing public confidence in FDA decisions, by encouraging the public use of accurate information.

Comments

A. Communicating Information about Agency Procedures

ACTION 6:

[2] *See* 21 C.F.R. § 10.115
[3] *See* Report, p. 7
[4] *See* Report, p. 2

FDA will post on the FDA Web site slide presentations that are delivered by FDA employees to external audiences at events sponsored by, or co-sponsored by, the agency.[5]

DRAFT PROPOSAL 1:
FDA should maintain on the FDA Web site a list of presentations given by FDA employees to external audiences.[6]

PPTA supports the notion that providing members of regulated industry access to information about FDA policies and procedures presented at meetings to external audiences will lead to a more efficient regulatory process. As noted, FDA's attendance at meetings and sharing of information with industry are vital to allowing industry and regulators to communicate fully concerns and to understand better decisions. Unfortunately, industry is not always able to attend such meetings; even when industry is able to do so, FDA slide presentations are not always provided. While PPTA thus is encouraged by Action 6, the Association also appreciates that FDA recognizes that the Action is only a "first step."[7] PPTA also is encouraged by Draft Proposal 1 but, like Action 6, views the Proposal as a first step. The Association respectfully requests that FDA set a goal to post on the Agency Web site all slide presentations that are delivered by Agency employees to external audiences. One suggestion for helping to achieve such a goal is beginning earlier the process of making presentations 508 compliant.

B. Product Application Review Process

ACTION 7:
FDA will compile all FDA Center guidance and standard operating procedures [SOPs] on FDA employees meeting with sponsors about product applications on the web-based resource, *FDA Basics for Industry*.[8]

ACTION 10:
FDA will explain via the *FDA Basics for Industry* web-based resource how a sponsor is informed about whether the review of its product application is on track to meet the target date for FDA action on the application. FDA is also willing to hold further discussions with industry about application tracking systems, and explore the feasibility of implementing such a system at FDA.[9]

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[5] Report, p. 18
[6] Report, p. 18
[7] *See* Report, p. 18
[8] Report, p. 27
[9] Report, p. 29

PPTA believes that, similar to FDA Basics for the public, the Agency's newest web-based resource, FDA Basics for Industry, will assist industry in better understanding the Agency's functions and the information already available. However, while the availability of FDA guidance and SOPs on the web is vital to transparency, PPTA respectfully requests that the Agency focus not only on reorganization of already-available resources but also on practical actions that will increase transparency. For instance, FDA's willingness to hold further discussions with industry about application tracking systems is one example of the Agency exploring ways to increase transparency. PPTA is encouraged that FDA has participated in initial discussions with Health Canada about that agency's application tracking system. PPTA hopes that FDA will continue its proactive approach to increasing transparency and looks forward to further discussions with the Agency, including on the benefits to industry of an application tracking system.

C. Guidance Development

ACTION 11:
To examine suggestions for improving the guidance process, the Commissioner has formed a cross-agency working group under the leadership of the Office of Policy. This working group is examining the current process and will identify best practices for improving the agency's work on guidance. Topics include streamlining guidance development, reducing the time between issuance of draft and final guidance, and making it easier to find guidance documents on the FDA Web site.[10]

DRAFT PROPOSAL 3:
FDA will inform industry about the progress of certain high priority guidances in development by disclosing a timeline from the start of the agency's work on a draft guidance to publication of the final guidance.[11]

PPTA would like to emphasize the importance to industry that FDA both follow the GGP and finalize draft guidances in a timely manner. Some guidances have remained in draft form for several years; while some have been finalized, others have not.[12] PPTA is discouraged that FDA has chosen to form a working group, effectively delaying action for another year, to address the issue; the Association feels that the Agency has the ability, with the comments already collected, to move forward on the topics mentioned in Action 11. Nonetheless, PPTA would like to instill in the working group a sense of urgency comparable to the importance to industry of timely finalization of guidances.

[10] Report, p. 32
[11] Report, p. 32
[12] *E.g.,* Draft Recommended Methods for Blood Grouping Reagents Evaluation (1992), Draft Recommended Methods for Evaluating Potency, Specificity, and Reactivity of Anti-Human Globulin (1992)

PPTA also commends FDA's decision "to provide timelines associated with the guidance development process in an effort to provide more predictability and clarity" in Draft Proposal 3;[13] of the five Draft Proposals in the Report, Draft Proposal 3 should be given the highest priority. However, PPTA encourages FDA to track the progress of all guidance documents by disclosing their milestone dates. Instead of limiting tracking to "certain high priority guidance documents,"[14] a broader approach will utilize more fully FDA-TRACK technology; further, FDA's definition of "high priority"[15] in the Report may be open to subjective interpretation and thus may create uncertainty. PPTA also suggests that, if a draft guidance is not finalized within a reasonable amount of time after the closing of the comment period, *e.g.,* 12 or fewer months, then the draft guidance must be republished for further comment.

D. Regulations Development

ACTION 14:
FDA, working with the Department of Health and Human Services and the Office of Management and Budget, will improve the accuracy of the timetables included in the agency's regulatory agenda published as part of the *Unified Agenda*.[16]

PPTA encourages FDA, as part of its efforts to improve the accuracy of the timetables in the Agency's regulatory agenda, to increase the amount of detail in the timetables, particularly for Long-Term Actions. While more detailed and otherwise accurate timetables will help to increase transparency, "[t]he Task Force [also] recognizes the importance of finalizing proposed rules as soon as possible."[17] With that sentiment in mind, PPTA also encourages FDA to explore ways to publish rules more quickly and, for rules already in the Agency's regulatory agenda, by the Final Action date; if the Final Action date has passed, then the rule should be published as soon as possible or, in some cases, should be re-proposed, as discussed below. For Long-Term Actions in the Agency's regulatory agenda, PPTA respectfully requests that FDA provide, if not a Final Action date, then more intermediate dates; a mere Final Action date of "To Be Determined" does not provide value to industry or foster transparency.

As PPTA has stated in previous comments to FDA, if a proposed rule is not finalized within a reasonable amount of time after the closing of the comment period, then the applicability of the final rule and comments are questionable. When a proposed rule is open for comment, such comments are based on science and data known at the time. If it takes a number of years for FDA to publish a final rule, then its comments may no

[13] *See* Report, p. 33
[14] *See* Report, p. 33
[15] *See* Report, n. 45, p. 33
[16] Report, p. 36
[17] *See* Report, p. 35

longer be applicable as new data and technology likely are available. PPTA questions whether, at such a point, FDA has provided adequate notice and comment.

For example, a proposed rule, Safety Reporting Requirements for Human Drug and Biological Products [hereinafter, "Proposed Rule"], was published on March 14, 2003, and its comment period closed in October, 2003; as a Long-Term Action in the Spring 2003 Unified Agenda, the rule's Final Action date is "To Be Determined." A final rule, Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans [hereinafter, "Final Rule"], which finalized in part the Proposed Rule, was published in September, 2010, and became effective in March, 2011, eight years after the Proposed Rule was published. The remaining part of the Proposed Rule is not yet finalized.

PPTA questions whether the Final Rule is applicable, as it is based on comments from seven to eight years ago, and suggests that it would have been more transparent for FDA to re-propose the Proposed Rule before finalizing it. As such, PPTA suggests further that FDA develop and publish a process that delineates procedures for finalizing proposed rules. Such a process would state that, if a proposed rule is not finalized within a reasonable amount of time after the closing of the comment period, *e.g.,* 24 or fewer months, then the proposed rule must be re-proposed for further comment. In the meantime, PPTA urges FDA to take such an approach to non-finalized rules, the comment periods of which have ended greater than 24 months ago.

E. Import Process

PPTA has no comments on Part E of the Report.

Conclusion

As stated above, PPTA commends FDA's efforts to improve transparency at the Agency. PPTA believes that the release of the Report was an important step 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 further these issues, please contact me at the Association. Thank you for your consideration.

Sincerely,

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