PPTA
Plasma Protein Therapeutics Association

November 1, 2010
Reference: FDAA10013 **VIA WEB**

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

SUBJECT: Request for Comments on Food and Drug Administration Fiscal Year 2011-2015 Strategic Priorities Document [Docket No. FDA-2010-N-0506]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide comments on the Food and Drug Administration (FDA) Fiscal Year 2011-2015 Strategic Priorities Document [hereinafter, "Strategic Priorities"]. PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies. PPTA members provide 60 percent of the world's needs for Source Plasma and plasma protein therapies. Such therapies include clotting therapies for individuals with bleeding disorders, immunoglobulins to treat complex diseases in individuals 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 ensuring the safety and availability of such medically needed, life-sustaining therapies.

Introduction

PPTA supports FDA in its efforts to achieve its public health mission and is encouraged that FDA has made significant progress in its strategic planning. PPTA understands that the Strategic Priorities were released to outline FDA's strategic intentions and plans for the next five years, *i.e.,* fiscal year 2011 through 2015. PPTA believes that the following comments will refine and strengthen further the strategic management structure already in place at FDA and will enable key stakeholders to support the public health mission of FDA and, ultimately, the larger mission of the Department of Health and Human Services.

Comments on Strategic Priorities

Innovation/Collaboration

PPTA supports and is encouraged by much of the language in the Strategic Priorities. For instance, under one of its Guiding Principles, Innovation/Collaboration, FDA highlights its Critical Path Initiative as the foundation for its recently established Advancing Regulatory Science Initiative, "a formal collaboration with the National Institutes of Health [NIH] to

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advance regulatory science and build the capacity needed to ensure the safety and effectiveness of innovative new products and technologies."[1] PPTA supports this important initiative and is encouraged by FDA's dedication to regulatory science. PPTA is committed to ensuring the safety and availability of plasma protein therapies and looks forward to working with both FDA and NIH through this Initiative.

Transparency Initiative

Transparency

Another Guiding Principle is Transparency.[1] PPTA appreciates FDA's ongoing efforts through its Transparency Initiative, including its establishment of a Transparency Task Force. PPTA has participated in FDA Public Meetings on Transparency and in the Transparency Task Force Listening Session and has submitted comments to FDA regarding transparency.

PPTA would like to reiterate its previous suggestions: establishing and publishing work-plans, improving Good Guidance Practices 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; more recently, PPTA commented on FDA's Draft Proposals Regarding Disclosure Policies and, at the PPTA-FDA Liaison Meeting, reiterated its suggestions regarding publications of final regulations.

While PPTA appreciates the opportunity to provide suggestions to FDA regarding transparency, PPTA is disappointed by one of FDA's recent decisions. 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 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.

In this case, the proposed rule "Safety Reporting Requirements for Human Drug and Biological Products" [hereinafter, "Proposed Rule"] was published in March, 2003, and its comment period closed in October, 2003; the 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 the Proposed Rule in part, was published in September, 2010, and will be effective in March, 2011, eight years after the Proposed Rule was published.

[1] FDA Strategic Priorities 2011-2015; p. 3

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. 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.

Open Government

PPTA supports and is encouraged by FDA's Strategic Goal and Long-Term Objective 3.4 "Manage for Organizational Excellence and Accountability." In particular, PPTA urges FDA to focus on Open Government,[2] which also implicates FDA's Transparency Initiative. FDA Basics has proven a valuable, Web-based resource, and PPTA expects that, through the full implementation of FDA-TRACK, FDA will continue to foster open government.

Special Populations

PPTA also supports and is encouraged by FDA's Cross-Cutting Strategic Priority 2.4 "Expand Efforts to Meet the Needs of Special Populations." PPTA believes that meeting the needs of special populations is an important issue and that all stakeholders should be engaged to identify solutions. PPTA appreciates FDA's ongoing efforts to review available laws, regulations, and policies with a focus on development of biological products used to treat patients with rare plasma protein disorders. Such efforts are part of an FDA paradigm shift, over the last several years, from reviewing drugs merely for orphan indications, to reviewing drugs also as part of the overarching goal of providing therapies to patients with rare disorders.

PPTA agrees with FDA's recognition that "[a]ssuring that products are safe and effective for people with rare diseases is particularly challenging, because the patient populations are too small to support standard clinical trials."[3] FDA also recognizes that, for small patient populations, "there may be fewer – or riskier – available therapies."[3] PPTA urges FDA to maintain its "commit[ment] to reducing this risk through targeted scientific programs and culturally sensitive outreach efforts."[3]

In particular, PPTA concurs with FDA's Signature Initiative "Scientific Innovation for Rare Disease Therapies," based on FDA's recognition that "product testing presents significant

[2] FDA Strategic Priorities 2011-2015; p. 32

[3] FDA Strategic Priorities 2011-2015; p. 9

scientific challenges calling for innovative approaches."[4] As PPTA has stated in previous comments to FDA, double-blind, placebo-controlled clinical trials are burdensome, expensive, and not feasible for small patient populations; issues include study size, participant recruitment and compliance, endpoints, and surrogate/biomarker use. The special needs of small patient populations must be recognized; consequently, novel designs, such as patient registries, one-arm studies, historical controls, adaptive clinical trials, phase IV studies, and pharmacovigilance, in the U.S. and abroad, must be considered.

PPTA has participated in a Center for Biologics Evaluation and Research (CBER) Public Workshop on Biological Products for Treatment of Rare Plasma Protein Disorders and in FDA's Public Hearing on Considerations Regarding FDA Review and Regulation of Articles of Treatment of Rare Disease and has submitted comments to FDA regarding patients with rare plasma protein disorders. Most recently, in its PPTA-FDA Liaison Meeting presentation on Engagement on Development of Products for Rare Diseases, CBER described recently approved products for rare diseases and recent and upcoming activities related to rare diseases.

PPTA looks forward to continuing its work with FDA on issues related to special populations, especially through FDA's new Rare Disease Review Group and Neglected Disease Review Group. PPTA also looks forward to reviewing the Institute of Medicine study of national policy for rare disease research and related medical product regulation and to participating in FDA's series of scientific workshops to address important and difficult rare disease research issues. Further, PPTA appreciates FDA's development of a "rare disease database" to establish natural histories of rare diseases to assist in planning trials to test such diseases.

Enforcement

PPTA understands the importance of Cross-Cutting Strategic Priority 2.3 "Strengthen Compliance and Enforcement Activities to Support Public Health."[5] In pursuit of the goal of public health, however, FDA must be careful not to overreach. FDA is implementing a number of new enforcement programs that include the establishment of deadlines for industry responses and the prioritization of follow-up inspections. From FDA's description of the programs in the Strategic Priorities, PPTA recognizes the value of their implementation as long-term goals. In the short-term, however, PPTA urges FDA to focus on the training and integration of its 850 new (500 net) investigators. First laying the foundation of a properly trained investigative team is vital to the success any new enforcement programs FDA seeks to implement.

[4] FDA Strategic Priorities 2011-2015; p. 11

[5] FDA Strategic Priorities 2011-2015; pp. 8-9

PPTA also urges FDA to exercise caution when sharing laboratory and enforcement data with regulatory and enforcement partners (*e.g.,* local, state, and territorial regulatory authorities and foreign government officials). FDA must be cognizant, not only of privacy concerns, but also of the legality of FDA's encouragement of such partners to take immediate actions in response to violations where the partners can act more quickly than can FDA. As stated, FDA must be careful not to overreach.

Biologics

PPTA appreciates that, under Strategic Goal and Long-Term Objective 3.2 "Promote Public Health by Advancing the Safety and Effectiveness of Medical Products," FDA has identified 3.2.2 "Advance Biologics Safety and Effectiveness." [6] PPTA finds FDA's long-term objectives and corresponding strategies for biologics largely appropriate; however, some of the strategies cited to achieve long-term objective 2.2.3 "Ensure the safety of biological products" cause concern. Two of the strategies are: "Improve the use of healthcare data to enhance monitoring the safety and quality of licensed biological products" and "Enhance statistical data analysis and mathematical models for improved epidemiological and risk assessments of regulated products."

Though initially attractive, FDA's above two strategies likely are not realistic as PPTA members have experienced limitations during attempted enhancements of data mining systems. FDA must avoid false expectations of the value of data mining systems in the achievement of long-term objective 2.2.3. As PPTA is committed to ensuring the safety of plasma protein therapies, it encourages FDA to focus instead on the other two strategies cited to achieve long-term objective 2.2.3: "Facilitate increased biologics manufacturing capability and improved product quality" and "Promote safe product use through effective risk management and risk communication."

Funding

PPTA encourages FDA to consider potential sources of funding needed to reach the generally laudable goals in the Strategic Priorities. PPTA believes that the Strategic Priorities would benefit from the inclusion of a section describing such sources of funding for FDA's initiatives. PPTA would appreciate FDA's comments on whether such initiatives will create new and/or enhanced fees, particularly user fees; if so, who would pay such fees, and who would benefit from them?

PPTA is concerned about the extent to which such funding may be generated from user fees, to the detriment of companies that develop biological products used to treat patients with rare plasma protein disorders. As PPTA has stated in its comments to FDA on the Prescription Drug User Fee Act, PPTA recognizes FDA's considerable cost increases and will continue to urge Congress to provide FDA with adequate appropriated funding to ensure that both user and non-user fee programs remain viable. In the meantime, PPTA

[6] FDA Strategic Priorities 2011-2015; pp. 21-22

encourages FDA to provide guidance on potential sources of funding related to the Strategic Priorities.

Conclusion

As stated above, PPTA commends FDA's efforts to achieve its public health mission through its strategic planning. PPTA believes that the release of the Strategic Priorities was an important step toward refining and strengthening further FDA's strategic management structure. PPTA appreciates the opportunity to comment and looks forward to working with FDA in the many of the areas outlined in the Strategic Priorities, especially those highlighted above.

Should you have questions regarding these comments, or if you would like to discuss further any of 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