



Plasma Protein Therapeutics Association

December 14, 2005  
Reference No.: FDAA05019

1824 5 DEC 19 A9:40

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

Via E-Mail

**SUBJECT:** Prescription Drug User Fee Act - Public Meeting and Whitepaper, "Prescription Drug User Fee Act: Adding Resources and Improving Performance in FDA Review of New Drug Applications." November 2005 Docket No. 2005N-0410

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA) Prescription Drug User Fee Act (PDUFA) Public Meeting held on Monday, November 14, 2005, and FDA's Whitepaper entitled, "Prescription Drug User Fee Act: Adding Resources and Improving Performance in FDA Review of New Drug Applications" (Whitepaper). 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.

To evaluate PDUFA and begin the reauthorization process, FDA asked for comments on the following questions: 1) what is the assessment of the overall performance of the PDUFA program thus far? and 2) what aspects of PDUFA should be retained, or what should be changed to further strengthen and improve the program? PPTA has analyzed these questions. We appreciate the opportunity to address them and the chance to participate in the reauthorization process.

In general, our member companies assess the overall performance of the PDUFA program as beneficial both to the industry and our patients. The goals established under PDFUA have played a vital role in accelerating the review and approval of new therapies. Furthermore, PDUFA has fostered a process that promotes better communication between industry and FDA during both the development stage and the

2005 N-0410

CR

approval process. Without the development of this user-fee program, many life-saving therapies would not have come to fruition. Because of the success of the user fee program, PPTA supports reauthorization of PDUFA in 2007. At the same time, PPTA is interested in containing costs of the program while ensuring that FDA's important programs, whether user fee funded or not, remain viable.

PPTA member companies have raised concerns about the overall management of resources for FDA. Mainly, PPTA member companies are alarmed at the reduction of appropriated funds to FDA programs. PPTA member companies, including those not subject to user fees, are regulated by the Center for Biologics and Evaluation and Research (CBER). The products produced by our member companies are reviewed by the Office of Blood Research and Review (Office of Blood). CBER operates uniquely under both PDUFA and the Medical Device User Fee Program (MDUFMA). In addition, CBER maintains a significant number of non-user fee programs. Therefore, it is of great importance to our member companies that user-fees, in both programs, be used appropriately (including tracking and accountability), while non-user fee programs continue to receive adequate funds. CBER cannot perform all essential regulatory functions without sufficient funding. User-fees should only be a supplement. They should not be the main resource used in administering CBER programs. For that reason, PPTA encourages Congress to provide FDA, with adequate appropriated funding, and that the funds be allocated to support important non-user fee programs and activities. This will insure that CBER and the Office of Blood function effectively and efficiently.

PPTA views that the PDUFA program could be strengthened by developing a more predictable review process. PPTA recognizes the efforts FDA has made in trying to facilitate a more predictable process for manufacturers. For instance, the timetables in the "Guidance for Review Staff and Industry: Good Review Management Principles for PDUFA Products" provided invaluable information regarding the review process. In addition, the mid-cycle review and subsequent communication have also improved predictability. Nonetheless, the predictability of the program can be further improved by increasing the transparency of the review process. To facilitate the increased transparency, PPTA proposes a goal for PDUFA 4 to establish a real-time submission tracking feature. Ideally, this electronic system would provide tracking information in real-time that could be accessed by the manufacturer. This type of system would make significant improvements over current predictability. This predictability would allow manufacturers to arrange for the launch of a product that may have substantial improvements over the existing product. In addition, the predictability would allow a manufacturer to control inventories, schedule production runs, and plan for release of a newly approved product without delay. Transparency and predictability will bring life-saving therapies to consumers without any undue delay.

Like many other companies, PPTA recognizes that safety needs to be an imperative part of the FDA review process. PPTA appreciates that the FDA spends half of its effort

and resources on drug safety activities and that PDUFA 3 provided for use of user fee funds for some post-market safety activities. PPTA does not believe that PDUFA has lowered FDA's safety review standards or that speed has become more significant than product safety. Recently, many discussions have focused on the post-market safety of a new or changed product. PPTA acknowledges that many are advocating a need for an enhanced post-market surveillance program. At this time, PPTA is not promoting as a goal an enhanced post-market surveillance program. However, if any post-market surveillance program or program to standardize post-market studies undertaken as post market commitments (Phase 4 studies) is being considered under PDUFA, PPTA advocates that it be developed on an interactive basis between FDA, industry, and other interested parties.

To determine additional information on aspects of PDUFA that should be retained or that should be changed to further strengthen and improve the program, PPTA surveyed our member companies. PPTA used two questionnaires to evaluate specific programs established under PDUFA and to determine whether the goals of PDUFA are adequate. The first questionnaire focused on the Continuous Market Application (CMA) pilot programs. CMA pilot 1 provides for the review of a limited number of pre-submitted portions of New Drug Applications (NDA) and Biological Licensing Agreements (BLAs). CMA pilot 2 tested whether increased accessibility to agency reviewers during the development and review process could expedite the process. For various reasons, none of our members participated in these programs. Therefore, our member companies were unable to comment on their effectiveness. As current access to FDA is considered adequate, some members stated that CMA pilot 2 was redundant. Taking this into consideration, CMA should be retained only if the results of the pilot determined that: 1) the cost was reasonable and 2) the program did in fact promote quicker approval in conjunction with consistent advice.

The second questionnaire asked about the effectiveness of the Special Protocol Assessment and whether the performances on Changes Being Effectuated in 30 days (CBE-30's) were adequate. Again for various reasons, no member company had used Special Protocol Assessment to date. Some companies cited they may use it in the future, while others believed the benefit was inadequate to offset the effort and do not see the need to continue this program. As for CBE-30's, our member companies believe CBER is performing effectively. However, PPTA views it time to reconsider the classification of changes to an approved application that are codified in Title 21, Code of Federal Regulations, Part 601.12, and associated guidance documents. Due to the tremendous amount of knowledge and experience gained since the regulation was updated and guidances developed over the past decade, it appears appropriate to re-evaluate and update the classification criteria.

The second questionnaire also inquired as to whether current performance goals were adequate and whether new goals should be considered. Overall, our member companies consider existing goals sufficient and all should be retained. Yet, in order to

improve PDUFA, some suggestions were proposed: 1) timeliness of approval dates – the timeframe should correspond to target approval dates not FDA response timelines; 2) review of labeling needs to be completed sooner in the process limiting the effect changes have on launch dates; and 3) reduce cycle times for resubmissions. In addition, it was suggested that there be a lot release goal of review and release within 10 days of submission.

In conclusion, PPTA member companies consider PDUFA to be a success and should be reauthorized. The current goals are adequate with a few enhancements to improve the program. These enhancements include the development of a more transparent review process. This can be accomplished by establishing a real-time tracking system. Additionally, if the user-fee program is expanded to develop an enhanced post-market surveillance program, PPTA advocates that this occur on an interactive basis. PPTA is concerned that user fee funding not be viewed as the primary funding for the FDA. Industry's contribution to regulatory activities should supplement adequate Congressional appropriations.

PPTA appreciates the opportunity to comment on the PDUFA program. Should you have any questions regarding these comments or would like additional information, please contact PPTA. Thank you for your consideration, and we look forward to working on reauthorization of this beneficial program.

Respectfully submitted,



Mary Gustafson  
Senior Director, Global Regulatory Policy  
Plasma Protein Therapeutics Association