Plasma Protein Therapeutics Association

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

VIA E-MAIL & USPS

SUBJECT: FDA Public Workshop entitled, "Biological Products for Treatment of Rare Plasma Protein Disorders" [Docket No. 2005N-0347]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these additional comments on the Food and Drug Administration's (FDA) public Workshop entitled, "Biological Products for Treatment of Rare Plasma Protein Disorders" [hereinafter, "Workshop"] held on June 13 and 14, 2005. PPTA submitted comments on April 6, 2006, to which we wish to append. 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.

In PPTA"s comment letter dated April 6, 2006, several items were discussed. One area of discussion centered on clinical trial requirements. ". . . the most important point to emphasize in regards to developing therapies for those living with rare plasma protein disorders is the use and utility of clinical trials and the regulatory requirements governing them. Industry is not interested in short-cuts around facilities management, product safety, or Good Manufacturing Practice (GMP) validation. However, it is imperative that standards be developed that recognize the difficulty in meeting current clinical trial requirements for therapies developed for such a small and unique patient population."

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To provide more detail to this discussion, we add the following:

- While economic factors should not be the driver in decision making, it is important for FDA to recognize the economic realities in bringing a niche therapy to market and sustaining the marketing of a therapy that treats a very small patient population.
- FDA should consider whether valuable information in rare disorders can be obtained and evaluated without the use of a control arm (historical, placebo or active).
- FDA should work with companies to enable the use of one pivotal clinical study with meaningful surrogate endpoints.
- FDA should consider whether dose-ranging studies are necessary.
- Consideration should be given to approving the product based on surrogate endpoints with early agreement between the sponsor and FDA/CBER on post-approval commitments for Phase IV study.
- The need for Phase IV studies should be defined as early as possible in the product's development to enable companies to factor these studies into a viable business plan.
- FDA should embrace cooperation between CBER and CDER in finding alternatives to traditional clinical trials as part of its Critical Path Initiative. When biologics and drugs indicated for the same disease population are being developed, there should be close coordination of clinical trial requirements between CBER and CDER.

As an additional comment relating to non-clinical studies, repeat-dose (acute or chronic) or fetal-development studies should not be required as human-derived proteins are to be administered to other humans. Additionally, foreign proteins (human) being administered to animals are likely to generate results that are not representative to a human response.

PPTA thanks FDA for initiating the Workshop and recognizing the uniqueness of developing therapies for those with rare plasma disorders. We are eager to make a meaningful contribution to this effort and look forward to working closely with FDA on this topic. Should you have any questions regarding these comments or would like more information, please contact PPTA.

Respectfully submitted,

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Plasma Protein Therapeutics Association