Plasma Protein Therapeutics Association

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Reference No.: FDAA07012

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

SUBJECT: Guidance entitled, "Guidance for Industry: Adequate and Appropriate Donor Screening Tests for Hepatitis B; Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Donors of Whole Blood and Blood Components, Including Source Plasma and Source Leukocytes" [Docket No. 2002D–0081]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA) "Guidance for Industry: Adequate and Appropriate Donor Screening Tests for Hepatitis B; Hepatitis B Surface Antigen (HBsAg) Assays Used to Test Donors of Whole Blood And Blood Components, Including Source Plasma and Source Leukocytes"[hereinafter, "Guidance"]. 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.

We appreciate the opportunity to comment on this Guidance. While PPTA supports continuous improvement in the sensitivity and specificity of tests to screen donors and test plasma, we are concerned that this Guidance sets unrealistic expectations for implementation based on the availability of tests that meet the recommended sensitivity threshold. There are few tests marketed today that meet the recommended "lower limit of detection capability of 0.5ng HBsAg/mL or less." Those on the market, approved for donor screening, that we know meet this level, include Abbott's PRISM HBsAg, and Auszyme Monoclonal for Commander; and BioRad's Antibody to Hepatitis B Surface Antigen (mouse monoclonal) Genetic Systems ™ EIA 3.0.

Many in the source plasma testing community use the Abbott Commander HBsAg test for donor screening. The package insert describes 4 procedures for performing the assays which vary in incubation temperature and time. Most laboratories use Procedure C which requires an initial incubation time of 75 minutes at 38C. While the package insert describes Procedure B as meeting the limit (Typically the sensitivity results from clinicals and studies done at Abbott Laboratories have ranged from 0.3 to 0.7 ng/mL for Procedures A and C and from 0.2 to 0.4

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ng/mL for Procedure B. Sensitivity testing demonstrated that AUSZYME Monoclonal was as sensitive or more sensitive than AUSZYME II), Procedure B requires a 12- 20 hour room temperature incubation. Although the long incubation time is somewhat problematic, of more impact is informal feedback from Abbott that this method may not, in fact, meet the FDA recommended level.

This complication means that users of Abbott technology would have to switch to the Abbott PRISM for Hepatitis B testing but maintain an additional platform for HIV testing. Alternatively, to meet the recommended level of sensitivity would require switching to an alternative platform for one or more tests. Neither mixing platforms within a single laboratory nor switching platforms in a laboratory is simple and neither could be accomplished without great difficulty before the January 31, 2008 implementation time frame. The following list includes some, but not all, of the issues that must be resolved by laboratories using the Abbott Auszyme Monoclonal Commander assay in order to implement the Guidance:

- Make necessary commercial arrangements to acquire equipment and reagents
- Renovate existing laboratory environments without disrupting ongoing testing
- Acquire, install and validate equipment and assays
- Establish operating procedures and train staff
- Create or modify and validate IT systems to manage data
- Modify US and European regulatory filings to include use of the new assay(s)

It is highly unlikely that these issues can be resolved by January 31, 2008. We encourage FDA to consider a longer period of time for laboratories to comply with the Guidance.

PPTA appreciates the opportunity to comment on the Guidance. In addition to written comments, we request that the Guidance and implementation schedule be discussed with us at our annual liaison meeting on October 12, 2007. Should you have any questions regarding these comments or would like additional information, please contact PPTA.

Respectfully submitted,

Mary Gustafson
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Plasma Protein Therapeutics Association