Plasma Protein Therapeutics Association

September 11, 2012
Reference No.: FDAA12016

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

SUBJECT: Draft Guidance for Industry: Amendment to "Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease [CJD] and Variant Creutzfeldt-Jakob Disease by Blood and Blood Products [vCJD]," Availability
[Docket No. FDA—2012—D—0307]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the draft guidance document entitled "Guidance for Industry: Amendment (revisions to labeling recommendations for potential risk of vCJD) to 'Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of [CJD] and [vCJD] by Blood and Blood Products" ("Draft Guidance").[1] PPTA understands that the Draft Guidance proposes amendments to the labeling recommendations for plasma-derived products, including albumin and products containing plasma-derived albumin, in the May 2010 guidance document entitled "Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of [CJD] and [vCJD] by Blood and Blood Products" ("2010 Guidance") to reflect current knowledge of vCJD transmission through blood.[2] PPTA thanks FDA for the opportunity to participate in the guidance development process through these comments on the proposed amendments to the labeling recommendations, which, when finalized, the Association understands will be incorporated into the 2010 Guidance.[3]

About PPTA

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, which 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 plasma protein therapies for the duration of their lives. The 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

[1] *See* FR Notice, Availability, 77 Fed. Reg. 34,390 (June 11, 2012)
[2] *See id*.
[3] *See id*.

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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. PPTA members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

General comments

Since the occurrence of vCJD regulatory authorities in the US and the European Union have implemented precautionary measures to prevent transmission of vCJD to recipients of labile blood components and plasma protein therapies, to which the members of PPTA adhere. Based on epidemiological evidence, the causative agent of vCJD, pathogenic prion, has not constituted a factual contamination risk to large-scale manufacturing of human plasma-derived proteins. Nonetheless, manufacturers have studied the prion removal capabilities of various manufacturing steps to better understand product safety. Recently, PPTA member companies have performed a data collection of individual company investigations of prion removal capacity of the manufacturing process. Collectively analyzing the results could reveal experimental reproducibility and detect trends and mechanisms driving prion removal.

Prion Removal Capacity of Plasma Protein Manufacturing Processes
A Data Collection from PPTA Member Companies

Recently, PPTA members collected over two hundred prion removal studies on plasma protein manufacturing steps, including precipitation, adsorption, chromatography, and filtration, as well as combined steps. The studies used a range of model spiking agents and bench scale process replicas. Overall prion removal capacities evaluated by independent groups were in good agreement. The removal capacity evaluated using biochemical assays was consistent with prion infectivity removal measured by animal bioassays. Similar reduction values were observed for a given step using various spiking agents, including highly purified prion protein in some circumstances. Comparison between combined and single-step studies revealed complementary or overlapping removal mechanisms. Steps with high removal capacities represent the conditions where the physiochemical differences between prions and therapeutic proteins are most significant. In conclusion, the results demonstrate the intrinsic ability of certain plasma protein manufacturing steps to remove prions in case of an unlikely contamination, providing a safeguard to products. The study has been submitted for publication in a peer reviewed journal and is currently under review.

PPTA recommendations

The risk of transmitting viruses cannot be considered the same as for vCJD, which is in PPTA's understanding what is reflected in the wording proposed by the Draft Guidance. PPTA's proposal from revision of the labeling statement follows:

Plasma-derived products other than Albumin

PPTA agrees in principle with the proposed text, but based on the nature of the manufacturing processes, we would respectfully like to propose to increase the granularity of the recommendations to reflect the prion partitioning measures applied to the different product classes.

Immunoglobulins (IG)
Immunoglobulins (IG) should not be treated differently from albumin. In fact, manufacturing of IG contains more or less equal numbers of partitioning steps as albumin. Transmissible spongiform encephalopathy (TSE) reduction relies mainly on partitioning. Hence, there is no scientific reason to treat IG differently from albumin.

Plasma-derived Albumin
"Albumin is a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jacob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD) also is considered extremely remote. No cases of transmission of viral diseases, CJD or vCJD have ever been identified for licensed albumin."

Products Containing Plasma-derived Albumin
"This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jacob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD) also is considered extremely remote. No cases of transmission of viral diseases, CJD or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products."

Conclusion
PPTA appreciates the opportunity to comment on the Draft Guidance and looks forward to continued work with FDA on efforts to ensure that the labeling recommendations for plasma-derived products in the 2010 Guidance reflect current knowledge of vCJD transmission through blood. PPTA welcomes from FDA any questions regarding these comments or requests for more information.

Thank you for your consideration.

Respectfully Submitted,

Mary Gustafson
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Plasma Protein Therapeutics Association