

October 13, 2003  
Reference No. FDAA03010

020645

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

VIA E-Mail & USPS

**SUBJECT:** Proposed Rule, "Safety Reporting Requirements for Human Drug and Biological Products"  
Docket No. 2000N-1484

Dear Sir or Madam:

PPTA is pleased to provide these comments on the Food and Drug Administration's (FDA's) Proposed Rule entitled, "Safety Reporting Requirements for Human Drug and Biological Products" (hereinafter "Proposed Rule"). The Plasma Protein Therapeutics Association (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.

PPTA would like to present its concerns and comments regarding the Proposed Rule. Our comments are limited to proposed requirements for reporting safety-related information related to plasma donation. Of primary concern is that the reporting requirements as described in the Proposed Rule will increase the burden without yielding tangible benefit. The preamble to the proposed rule states that, "FDA believes that it is critical that we receive all such reports to enhance donor safety and also to ensure the safety, purity, and potency of blood and blood components for administration to patients." However, except for relating two anecdotal incidents (only one involved the collection of blood and it was caused by a clear lapse in cGMP), there seems to be no framework for data assimilation nor a plan for data analysis, and there is no clear link to any public health benefit that will come to be as a result of the increased regulatory burden.

Unlike the administration of new chemical or biological entities for which the majority of the provisions in the proposed rule appear to apply, the collection of blood and plasma has a proven record of safety. Plasma donation was made much safer for the donor

with the advent of automated collection procedures, which have been standard in the industry for nearly twenty years.

Section II.B.3.d. states, “This proposed safety reporting requirement would not impose significant new burdens on blood establishments.” We disagree with this assessment. While establishments are required to maintain records of adverse events associated with the collection of plasma, this proposed rule would require that records/reports adhere to a prescribed reporting format, be reported on required form 3500A, and utilize MedDRA, a commercial medical terminology system that requires licensing to use. These requirements will add significant burden to the plasma collector. Manual systems will require new procedures and recordkeeping methods. For computerized systems, the costs are much greater. It is unfortunate that FDA failed to forecast IT costs for blood facilities (V.D.2.a.) since blood establishment computer systems are highly regulated medical devices. The IT costs to update, expand and validate existing computerized systems to accommodate requirements imposed by the proposed rule are not insignificant. In addition, for both manual and computerized systems, staff will need to be trained on the new systems, quality systems developed and maintained, and for some facilities, new staff may have to be hired and trained to fulfill the Proposed Rule’s goals. Some of our members estimated the time alone of such training and validation program to take up to 12 months to complete.

It is not clear what the true reporting burden might be under the proposed rule because the definitions are ambiguous. “Medical intervention,” for example, is not clearly defined. Plasma centers employ physicians and physician substitutes who may be called upon to provide care in the event of an adverse donor reaction. Possible construction of the term “medical intervention” could range from elevating a donor’s legs (depending on who it is that elevates, or orders the elevation of, the donor’s legs) to emergency surgery. Similarly, the term “serious SAR” or “SAR” presents a lack of clarity that opens the door to wide variation in regulatory interpretation. Our members have reported that more than 90% of reactions at plasma collection centers are vasovagal and hypotension reactions that are alleviated by leg elevation and volume replacement. Under the proposed definition, such reactions could be classified as serious SARs. Submitting reports for these reactions would not only be burdensome, but could also complicate data assimilation for reactions that truly *are* serious. Should FDA move forward with a reporting requirement, we recommend that the language be clarified to include only a death, inpatient hospitalization, or disability of a source plasma donor attributable to plasma donation.

In section III.D.12., the agency states that conforming reporting periods for serious SARs and biological product deviation reports will limit the reporting burden when the two are associated events. In reality, there would be little relationship between biological product deviation reporting and the necessity of a report under the Proposed Rule, as the vast majority of these adverse reactions in plasma donors take place in the

absence of any such deviation. Taken as an industry-wide whole, the regulatory burden through increased training and time in reporting would likely be very significant.

The Preamble and the regulatory language of the Proposed Rule do not describe how the required data will be used. Generally, we understand that this would allow an early warning system. However, methods for data storage or actions which would be taken on the basis of the data collected are not described. In short, while there are specific time periods and methods of reporting placed upon industry, the data to be provided would not meet the goals of the Rule as we understand them.

Because of the human resources burden, the substantial costs of training personnel, upgrading systems and licensing MedDRA, and the lack of a clear public health benefit, PPTA asks that provisions of this Proposed Rule that would require the reporting of plasma donor adverse reactions be withdrawn or, in the alternative, have its areas of ambiguity clarified prior to finalization.

PPTA appreciates the opportunity to comment on this Proposed Rule. Should you have any questions regarding these comments or would like additional information, please contact PPTA. Thank you for your consideration.

Respectfully submitted,

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