

Date: August 25, 2008  
Reference No.: FDAA08014

**VIA WEB & USPS**

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

**SUBJECT:** Agency Information Collection Activities; Proposed Collection; Comment Request; Current Good Manufacturing Practices and Related Regulations for Blood and Blood Components; and Requirements for Donor Testing, Donor Notification, and ``Lookback' '[Docket No. FDA-2008-N-0345]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA's) Comment Request on the proposed collection of certain information, specifically Current Good Manufacturing Practices (cGMP) and Related Regulations for Blood and Blood Components; and Requirements for Donor Testing, Donor Notification and "Lookback," [hereinafter, referred to as "Comment Request"]. 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 appreciates the opportunity to comment on these data collection activities, which fall within the scope of the Paperwork Reduction Act (44 U.S.C. 3501 – 3520). The Comment Request includes data collection pursuant to multiple regulations and requests that comments be provided on four topics: 1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; 2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; 3) ways to enhance the quality, utility, and clarity

of the information to be collected; and 4) ways to minimize the burden of the collection of information on respondents, including through use of automated collection techniques, when appropriate, and other forms of information technology. While the Comment Request addresses a comprehensive list of regulations within cGMP and related regulations as well as “Lookback,” PPTA is limiting its comments to activities associated with “Lookback.”

Title 21, Code of Federal Regulations, Part 610.46 – 610.47, addresses activities related to “lookback” for HIV and HCV. These activities include consignee notification to quarantine products collected prior to a donor’s testing reactive or the establishment’s obtaining other information indicating evidence of HIV or HCV in a donor. These activities include establishing a system for such notifications and notifying consignees in the appropriate amount of time and for the appropriate “lookback” periods. Although not a part of this Comment Request, PPTA views it necessary to discuss other “lookback” activities that are addressed in FDA guidance, specifically the December 10, 1993, recommendation memorandum to all blood establishments entitled, “Guidance Regarding Post Donation Information Reports.” This long-standing memorandum provides guidance, including the notification of consignees when information is obtained following a donation that would have deferred the donor had it been known at the time of the donation. Due to the regulatory requirements cited in the Comment Request and the guidance on post-donation information, collecting establishments have developed elaborate and far-reaching systems to identify donations for “lookback” and perform notifications for both test results and other situations addressed in the post-donation guidance. Below PPTA addresses the specific questions posed in the Comment Request in regards to “lookback” regulations. PPTA’s comments reflect the additional reporting necessitated by the referenced FDA guidance.

**Topic 1: whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility**

The collection of information under 21 CFR § 610.46 – 610.47 is not necessary for the proper performance of FDA’s function and adds no additional level of safety and efficacy to final fractionated therapies. Over the past several years, PPTA has examined ways to improve the overall effectiveness of these specific reporting requirements. PPTA discovered that most of the reporting requirements provide little additional information to FDA that assists with its duty of “ensuring the safety, purity, and potency”<sup>1</sup> of plasma protein therapies. PPTA purports that lookback requirements should only be maintained for those reports to consignees that truly may impact the safety and efficacy of final products.

In 2006 and 2007, PPTA conducted a survey of fractionators to determine the burden of “lookback” and its utility in enhancing safety. Of the tens of thousands of “lookbacks” performed each year by collectors, very few unpooled plasma units are available at the

---

<sup>1</sup> Federal Register; Vol. 73, No. 122, June 24, 2008, p. 35695

time of the “lookback” notification to retrieve.<sup>2</sup> Fractionators stated that one of the few scenarios where a lookback report would cause action to be taken on the pool would be if it were found that a donor contracted variant Cruetzfeld-Jacob Disease (vCJD). Under this scenario, fractionators would destroy pools and consider final product recalls. There is no connection between the regulatory requirements and guidance on consignee notification and the value of these notifications to the fractionators. This apparent disconnect is related to the failure of FDA to appropriately distinguish plasma for manufacturing use from blood for transfusion. Furthermore, these requirements fail to recognize advances in testing technology over the past fifteen years and are no longer based on scientific evidence.

For instance, the introduction of nucleic acid amplification testing (NAT) reduces the risk that a previously collected unit is infectious. Moreover and most important is that plasma intended for further manufacturing use is subjected to a robust pathogen clearance process during fractionation that removes infectious particles from the manufacturing pool. These clearance steps enhance the safety of the final product. “Lookback” can truly only add a level of safety to blood used for direct transfusion, whereby prior collected units may carry risk when transfused without being subjected to pathogen clearance procedures. For the fractionation industry, “lookback,” with the exception of vCJD in a donor, has limited utility in terms of final product safety. Therefore, the “lookback” activities are not necessary for the “proper performance of FDA’s functions” and have little “practical utility.”

**Topic 2: The accuracy of FDA’s estimate of the burden of the proposed collection of information, including validity of the methodology and assumptions used**

In regards to this topic, FDA’s estimates for burden hours per response to 21 CFR §§ 610.46 & 610.47 are low. For one, the estimates fail to reflect the relationship between a Source Plasma collection center and its corporate office in “lookback” activities. Generally, the collection center notifies the corporate office of an event. The corporate “lookback” function is responsible for consignee notification. Also, not taken into account is the amount of time required by the consignee, usually a fractionator, to address the “lookback” notification. The degree of automation of record keeping is an important factor in determining the reporting burden. Below are estimates from PPTA member companies on the amount of time it takes to respond to the “lookback” requirements.

<b>Responses per Location</b>	<b>Burden Hours per Response</b>
Source Plasma Center Level	0.50 – 1.00 hrs
Corporate Level	2.0 hrs
Fractionators/Final Manufacturer Level	0.50 – 1.00 hrs

<sup>2</sup> For example, one PPTA member fractionator, for the year 2006, received approximately 48,000 notices. Of those 48,000 notices, no information contained in the reports warranted pool interdiction or a final product withdrawal. Another company, a collector, issued consignee notifications for 47,000 Source Plasma units in 2007 and surpassed that number in the first half of 2008.

**Topic 3: Ways to enhance the quality, utility, and clarity of the information to be collected**

The “lookback activities” are not necessary for the proper performance of FDA’s functions and have little practical utility, therefore this topic is moot.

**Topic 4: Ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology**

With respect to topic 4, since the “lookback” activities are not necessary for FDA’s proper performance and have little practical utility, this topic does not need to be addressed.

Respectfully submitted,



Mary Gustafson  
Vice President, Global Regulatory Policy  
Plasma Protein Therapeutics Association