

# COALITION FOR REGULATORY REFORM

American Association of Blood Banks - America's Blood Centers -  
American Blood Resources Association

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September 15, 1998

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

**Re: Docket No. 98N-0359 – Comments on Section 406(b) of the Food and Drug Administration Modernization Act of 1997**

Dear Sir or Madam:

The Coalition for Regulatory Reform (CFRR or the Coalition) is pleased to have this opportunity to comment on the important information gathering objectives outlined in Section 406(b) of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The CFRR was formed in 1994 at the request of FDA, to bring the blood and plasma industries together to jointly explore ideas for a more efficient regulatory system for blood and plasma products. The Coalition is composed of the American Association of Blood Banks (AABB), (which includes the American Red Cross and the Armed Services Blood Program Office), America's Blood Centers (ABC), and the American Blood Resources Association (ABRA). This organization represents the entire spectrum of blood and plasma collection and transfusion interests. The comments outlined below reflect the collective view of these industry segments.

## **Agency Communication**

Recently, FDA's communication with industry has improved greatly. The agency has published proposed rules in a timely fashion, given industry an adequate opportunity to comment, disseminated draft guidance early in the process, and conducted more frequent agency workshops to address important regulatory changes. CFRR applauds FDA's improved communication and encourages further steps in this regard.

More specifically, CFRR encourages FDA to strictly adhere to its Good Guidance Practices (GGP) document and broaden the document's scope of application. The greatest effect in terms of regulatory efficiency is seen when industry is given an opportunity to meaningfully participate in the regulatory process. Thus, FDA should solicit input from and collaborate with industry early in the development of agency guidance.

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Involving industry early in the guidance drafting process will likely result in more relevant guidance and more efficient guidance-drafting practices. This means not waiting for industry input until a draft guidance is available for distribution, but rather, partnering with industry at the initial stages of development to gain a better understanding of what is practicable and feasible. Groups like CFRR and others stand ready to work with FDA in this regard.

One example where early industry input has worked is with the chemistry manufacturing and control (CMC) guidance for the blood and blood products industries. CFRR participated early in the development of this guidance and was pleased to see that many of its suggestions were incorporated into the draft document circulated for comment. Another area where this approach would likely be effective is with regard to proposed donor screening questions. Dissemination of such questions on a pilot basis would yield important information about how the questions are likely to be asked, interpreted and answered. This type of early information acquisition from industry is essential to developing appropriate guidance.

Other ways in which agency communication can be improved include using plain language in guidance and regulations and acknowledging receipt of industry correspondence to the agency. The use of jargon is pervasive in the biologics industry. Notwithstanding this, every effort should be made to make pronouncements of agency policy as simple as possible. Complex language and use of jargon often serves to confuse the meaning and intent of agency policy statements.

Acknowledgement of industry correspondence will also serve to make industry-agency communication more effective. While it may not be feasible to acknowledge all correspondence it would be appropriate to acknowledge certain classes of correspondence such as those pertaining to compliance issues or specific regulatory initiatives. An acknowledgement letter would set forth the question raised or issue presented, as the agency understands it, and a timeframe for responding to the question or issue. An acknowledgement procedure such as this would add certainty to the industry's communications with the agency.

Finally, rapid communication can be enhanced by continuing to post information in a timely manner on publicly available resources. The agency's use of the internet and CBER FAX are good examples of FDA reliance on technologies that provide for fast access to important information. Increased use of the resources available through the Office of Communication, Training, and Manufacturer's Assistance (OCTMA) would also be valuable. For example, an OCTMA automated message system to notify registered entities of newly released guidance, regulations or other classes of agency communications would be extremely helpful in speeding public access to agency information.

### **Improve the Review Process**

In the last year the Center for Biologics Evaluation and Research (CBER) has made great strides toward improving the licensure process. The proposed rule to replace the Product License Application and Establishment License Application (PLA/ELA) has been published and the Biologics License Application (BLA) process shows great promise. The guidance document that implements the BLA, the so-called CMC Guidance, also was recently published. CFRR strongly encourages CBER to ensure that the paperwork reduction and regulatory efficiency goals of the BLA are maximized with its implementation. Further explanation of these BLA issues can be found in the CFRR comments to the dockets for the proposed rule and guidance implementing the BLA procedures.

In addition, FDA has a host of new tools for effecting modifications or changes to approved applications. These include the prior approval supplement (PAS), the Changes Being Effected (CBE30), and Annual Report (AR) submissions. These are important milestones; however, much work remains to be done in the area of biologics applications. FDA should utilize these tools to the greatest possible extent; the onerous PAS process should be used only for novel products or for a first-time request to license an establishment or product.

Areas where the agency has promised guidance and which industry desperately needs, include guidance specific to blood for changes to an approved application which includes guidance on how and when to submit prior approval supplements, changes being effected and annual reports. Guidance on comparability protocols is also needed. These are tools that may yield the greatest regulatory efficiencies but remain untapped. Many companies already have been required to submit annual reports without clear guidance on what the reports are supposed to contain or how the agency will use this information. Comparability protocols offer the promise of a standardized method for effecting certain application changes without the need for prior agency approval, but the scope of eligible changes and protocol contents remain undefined. These tools and others if used as intended, can relieve the agency's application review burdens for non-user fee industries.

### **Blood Action Plan**

The Blood Action Plan holds promise for better communication of agency product quality expectations to industry. Based on FDA's public statements, the Blood Action Plan calls for a rewrite of the blood and plasma regulations. This includes updating requirements, eliminating obsolete requirements, and formalizing requirements published through guidance and memoranda into regulations. CFRR applauds these efforts and hopes to work with the agency in achieving these goals.

It is important to note, however, that no publicly available documents currently exist to describe the Blood Action Plan, time frames for achieving the plan objectives have not been publicly announced and industry input has not been sought. One initiative of the

plan is to develop a pilot program for approval of certain blood and plasma products through a monograph system. While this program holds promise for both FDA and industry in terms of the application process, without an industry-FDA dialogue this program may never get off the ground and an important opportunity may be lost.

### **Product Quality**

Although GMPs are the cornerstone of quality products, the blood and plasma industries have lacked clear GMPs. Instead, the current GMPs contain many references to biologics that often do not directly bear on the blood and plasma industries. The current GMPs applicable to blood and plasma products span three sections of the Code of Federal Regulations – 21 C.F.R. §200, §600 and §800. A comprehensive rewrite of the GMPs is needed to incorporate these important requirements into one set of unified regulations for blood and plasma products.

Other regulatory requirements that bear on product quality include error and accident reporting, adverse event reporting, and product recalls and withdrawals. These tools are underutilized. Although industry expends vast resources submitting error and accident reports, FDA has failed to use this information as a quality assurance tool. Quarterly reports of errors and accidents are published but no meaningful analysis or trend reporting of submitted errors and accidents has ever been made publicly available. This is a missed opportunity. FDA can help industry better itself by making this kind of information available. Furthermore, error and accident reporting should not be extended to other industry segments without careful consideration.

Recalls and withdrawals are intended to help ensure that only quality products reach patients. However, the current recall regulations are not appropriate for blood and plasma products. Many if not most blood and plasma recalls involve only hypothetical risks, expired products or already transfused products. Other tools such as recipient notification may be more appropriate in such circumstances. A more rational recall and withdrawal policy would save agency resources and permit industry to concentrate its resources on delivering high quality products.

### **Closing**

In closing, CFRR recognizes the magnitude of FDA's task – ensuring that only safe and effective products are made available to consumers. Without adequate funding CBER cannot carry out this mandate. Furthermore, this important mandate requires that the agency retain individuals with extensive skills and technical expertise. As such, CFRR fully supports CBER-based research needed to maintain an appropriate scientific infrastructure.

Thank you for the opportunity to comment. CFRR looks forward to working with the agency on current and future regulatory initiatives. If you have questions about these comments or wish to contact CFRR, please contact Christopher P. Healey, Director of Government Affairs at the American Blood Resources Association (410) 263-8296.

Sincerely,

A handwritten signature in black ink that reads "Roger Brinser / C.F.R.R." The signature is written in a cursive style.

Roger Brinser  
Co-Chair  
Coalition for Regulatory Reform