American Red Cross

Together, we can save a life

October 14, 2003

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

RE: Safety Reporting Requirements for Human Drug and Biological Products; Proposed Rule.
[68 FR 36527, June 18, 2003; Docket No. 2000N-1484]

Dear Docket Officer:

The American Red Cross (Red Cross) appreciates this opportunity to provide public comments concerning the Food and Drug Administration's *Proposed Rule* on Safety Reporting Requirements for Human Drug and Biological Products (hereafter, referred to as *The Proposed Rule*). The Red Cross, through its 36 Blood Services regions, supplies approximately half of the nation's blood for transfusion needs.

The Red Cross is vitally concerned with the safety and welfare of the volunteer donors upon whom we depend to provide a ready supply of the "gift of life." Red Cross procedures for qualifying donors, collecting blood, and providing donor care are designed to ensure the maximum safety possible during and following donation. Red Cross would support any initiative that would contribute to continuous quality and safety improvement for blood donation. With more than 80% of Red Cross blood collections occurring on mobile collection operations with their attendant variety of challenging physical circumstances, Red Cross still has an excellent record for maintaining the safety of donors. Fewer than 5% of Red Cross donors suffer any adverse reactions to donation. This statistic includes donors who suffer only "very slight" reactions.

Likewise, Red Cross cares deeply about patients who receive blood and blood products. More than 3,000 hospitals nationwide rely on Red Cross regions to meet the daily needs of their patients for blood and blood products. While our regions do not directly

00N-1484

C 32

administer blood products, and therefore will not be involved directly in reporting adverse reactions in blood recipients, we recognize that successful outcomes of transfusion therapy depend on having the highest quality blood products possible to administer. Each step in our manufacturing processes is carefully performed and controlled so that the resulting blood products possess the safety, quality, identity, purity, and potency (SQuIPP) that patients deserve.

It is for these reasons that the Red Cross appreciates the opportunity to provide comments on *The Proposed Rule* that would enhance and extend the requirements for reporting adverse reactions in blood donors and transfusion recipients. **Red Cross supports FDA's efforts to improve knowledge about the seriousness and frequency of adverse events that occur in blood donors and patients, and to achieve consistency in reporting these events.** However, Red Cross questions whether the efforts, as outlined in *The Proposed Rule,* will efficiently and effectively achieve this objective. Specifically, the proposal as presented is focused on supplying large amounts of data to FDA without a guarantee of analysis and information feedback to the industry or the public-at-large. One-way activity, without feedback on industry-wide safety trends, only diverts the medical and technical resources of Red Cross regions away from core manufacturing activities and provides no opportunity to improve our processes, based on the data.

Red Cross provides the following specific comments with respect to *The Proposed Rule*:

1. **Confusing and Inconsistent Terminology:** FDA is proposing to amend 21 CFR §606.170 to require blood collection establishments to submit reports to the agency of all "serious suspected adverse donor reactions." The agency states that serious suspected adverse reactions (SARs) that require "immediate medical intervention" or "follow-up medical attention" should be reported. A list of reaction types to be included in the reporting is provided, however, the list contains such conflicting and confusing qualifiers as "requiring medical intervention," "requiring significant medical intervention," and "clinically significant" involvement. In practice, these terms could be interpreted in different ways across the industry. For example, does "medical intervention" specifically imply in-person attention from a licensed physician? Is slowing the infusion rate to correct a hypocalcemic arrhythmia a significant intervention? Without common definitions, comparisons between blood suppliers will be invalid and events of intermediate severity may not be reported. **Red Cross urges FDA to define or provide examples for these qualitative terms, so that the intended level of reporting will be achieved, and to use the same terms consistently throughout the Final Rule, so that meaningful information can be abstracted from the data.**

2. **Scope of Reporting:** The magnitude of reporting required in *The Proposed Rule* will place an enormous additional burden on both blood collection organizations

and blood transfusion services in hospitals. Red Cross currently logs about 200 reports monthly of wide range of donor complications, where outside medical care was either recommended by Red Cross or sought by the donor. Red Cross believes that at least this number of events would be considered reportable. Reporting these significant donor events to FDA is not an issue for Red Cross; however, if the Final Guidance does not clarify and limit the scope of reporting to these truly significant events, then the DRCP effort will need to be expanded to include many donor reactions of lesser magnitude. Red Cross believes that this will dilute the usefulness of the data, since it will include a range of donor complications of varying severity. Further, it will lessen the amount of attention paid to finding and correcting the problems causing the most significant donor reactions.

Although FDA believes that the information needed for reporting is being captured by in-house reporting mechanisms already in place, this is not the case for donor reactions reported to Red Cross. The standard form to be used to submit reports to the FDA asks for information that is not routinely obtained from donors (for example, what medication they are taking or what diagnoses they have) and to which Red Cross does not have easy access.

Red Cross urges the FDA to consider whether this extensive reporting will produce useful data and whether the data collection effort should be focused more sharply on the most significant reactions. The human resources that will need to be dedicated to investigating, documenting, and submitting a greatly increased number of events could perhaps be better applied to other more vital activities that preserve the safety of the donation experience and ensure the SQuIPP of Red Cross blood products. The Final Guidance should be clear about what information must be included and what is optional for reports of donor SARs, especially with respect to information that is not routinely gathered as part of the pre-donation donor eligibility determination.

While Red Cross is most concerned about requirements for reporting donation-related serious SARs, we would also like to add a brief comment on behalf of our hospital customers. Hospitals will be impacted even more severely than blood collection organizations if the Final Rule issued is close to *The Proposed Rule.* Hospitals will be required to report recipient SARs if the association of a reaction with a transfusion is a "reasonable possibility" and that "relationship cannot be ruled out." Blood transfusion recipients are, as a group, the sickest patients in hospitals and are subject to a variety of severe medical problems, due to their underlying disease processes. These patients will exhibit signs and symptoms of conditions, such as congestive heart failure and sepsis, that could be indicative of adverse reactions, but that are not, in fact, causally related to their transfusion therapy. Hospitals will nevertheless be required to file reports on these very sick

patients when they are transfused, since they will be unable, in many cases, to differentiate transfusion-*caused* reactions, from manifestations of underlying disease.

Further Red Cross suggests that FDA not require the reporting of recipient "reactions" that are expected, due to the quantity of blood products given or the mode of administration, for example, iron overload, citrate toxicity and volume overload. FDA should focus the reporting of recipient reactions on those that are thought to be due to the quality or nature of the blood products.

Red Cross urges FDA to replace the terms "reasonable possibility" and "relationship cannot be ruled out" in the Final Rule with the current and more reasonable terms "confirmed" or "probable" in order to eliminate unnecessary reporting by the hospitals that use our blood products. Red Cross further encourages FDA to limit reporting of recipient reactions to those that are thought to be related to blood product quality.

3. **Utility of the information to enhance donor and recipient safety:**

   Red Cross supports the comment letter submitted by the American Association of Blood Banks (AABB) for *The Proposed Rule*, especially with regard to the need to obtain useful information from this program. The data reported to FDA must be analyzed with findings reported back to industry in order for effective quality improvements to occur. FDA might want to ensure that this will be possible, by securing appropriate resources and tools to complete its part of this program. There will be little ultimate value in generating a central repository of cases or a numeric tally of transfusion and donation complication events unless FDA is able to group reported events into meaningful categories, describe event rates as a function of collection or transfusion facility characteristics, and track and trend events. **Red Cross urges FDA to commit to specified periodic reporting of the results of the expanded safety reporting system at the same time that the reporting requirements for blood collection establishments and transfusion services are implemented.**

FDA is in an ideal position to establish a national blood donation and transfusion safety improvement initiative that begins with required reporting of specified events. The program however will not be effective unless the participants can reasonably meet the reporting workload, the event definitions are sufficiently standardized across all reporting facilities, and the submitted data are appropriately analyzed and reported back in such way that preventive and corrective actions can be implemented.

The Red Cross appreciates this opportunity to provide public comments on *The Proposed Rule.* If you have any further questions or require follow-up, please contact Barbara M. Peoples, Director, Technical Policy and Promotion at 202-303-5212 (phone), 202-303-0106 (fax) or peoplesb@usa.redcross.org (e-mail).

Sincerely,

Kathryn J. Waldman
Vice President
Regulatory Compliance & Quality Systems;
and Chief Compliance Officer