



A Joint Statement to the Food and Drug Administration's Blood Product Advisory Committee

November 30, 2017

“Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion; Draft Guidance for Industry,” March 2016

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America’s Blood Centers (ABC) and the American Red Cross (ARC), responsible for more than 90% of blood collection and distribution in the United States, appreciate the opportunity to present this joint statement as FDA considers revisions to the draft recommendations in the March 2016 draft guidance, “Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion.”

This statement is intended to update FDA on the current thinking of our our organizations. We believe these comments will assist FDA in evaluating the multiplicity of effective approaches that are available to enhance the safety of the blood supply and, ultimately, the care and safety of the patients we serve.

Despite the current interventions, which interdict about 30-50% of bacterially infected platelet units, transfusion-transmitted sepsis remains the most common infectious cause of recipient fatalities reported to the FDA. Currently around 5 fatalities/year are recognized and reported, but surveillance is passive and the clinical burden is believed to be substantially greater. Hence, our organizations support a need to enhance bacterial safety of transfused platelets using measures beyond the current approach of initial bacterial culture performed on apheresis platelets at approximately 24-hours post-collection. We strongly endorse the availability of multiple options to achieve this goal based on operational considerations in collection facilities and hospitals across the US that affect their ability to implement one or more of the allowable interventions.

The options currently available to achieve this goal include enhancing the sensitivity of testing for bacteria and the use of pathogen inactivation (PI). The data support the conclusion that

pathogen inactivation (PI) is the intervention that will provide the maximum bacterial safety for platelet products. While PI using an FDA licensed technology is being implemented throughout the US, current demand exceeds supply and the capacity to produce PI platelets is not sufficient for their universal use. Reasons limiting availability include the restrictive guardbands for qualifying apheresis products as eligible for PI, and the lack of a licensed system for triple apheresis products or for whole blood-derived platelets. A contributing factor is the length of time it has taken FDA to review and approve blood center license applications allowing for interstate shipment of PI-treated platelets. Thus far, the only approved license applications took 1 year to be approved by FDA and older completed submissions still await decisions. In addition, FDA has made changes to the validation and QC data requirements while submissions have been in progress. Such a long review cycle should not be necessary given that the format for each blood center submission has been standardized and the processes under review already have been in common use in blood center component manufacturing. A number of process changes to increase the percentage of products eligible for PI have been proposed, guided by the PI sponsor and standardized between blood centers. However, each of these requires yet another round of submissions and FDA review, further delaying the ability to increase the supply of PI platelets. In order to overcome these limitations to the PI platelet supply, we urge the FDA to do its part pursuing the goal of extending the guardbands, allowing triple collections to be treated, and most importantly to make the regulatory process more conducive to timely implementation of this technology.

We have discussed the clinical efficacy of the U.S. licensed PI platelets and understand the limitations of the data. Robust data on their effectiveness are derived largely from hematology-oncology patients, and patients with active hemorrhage from trauma and other conditions may be underrepresented. We are, however, encouraged by evolving hemovigilance data, especially from the European Union, that are not suggestive of material issues with the product, but surveillance clearly must continue.

With regard to enhanced sensitivity testing for bacteria, we favor making multiple approaches available including point-of-care tests on day 4 and beyond, reculturing during the shelf life of the product, and delayed primary culturing (at 36-48 hours) with higher input volume using both aerobic and anaerobic bottles. Data are available for each of these approaches to support increased bacterial safety relative to the current intervention using early culture alone. An alternate approach involving increased platelet culture volume at  $\approx 24$  hours after collection, combined with the use of both aerobic and anaerobic bottles, may increase sensitivity and should be considered.

Although these enhanced testing options can be implemented with 5-day stored platelets, they become much more realistic with the extension of platelet storage to 7 days. This is particularly true with regard to both reculture during storage and the delayed primary, high-volume culture option, which each result in the additional loss of  $\frac{1}{2}$  to one day of cumulative shelf life, unless product expiration is extended to 7 days. Currently the FDA has proposed that 7-day dating be restricted to the use of tests that have a "safety measure" claim. We agree with application of this requirement for point-of-care tests that were validated against culture, but do not think it is

necessary either for secondary cultures, or for the approach of delayed primary culture at 36-48 hours. Of note with regard to inventory management and platelet availability, since PI platelets which are currently restricted to 5-day storage do not need to undergo primary culture, these platelets are available to transfusion services up to 24 hours sooner than conventional platelets; thus, these products already have a longer interval of functional availability.

As you have heard today, the AABB surveyed its member hospitals regarding plans to implement additional bacterial interventions. Of those responding most (59%) report that they anticipate challenges in meeting the guidance requirements and many prefer their provider perform the additional mitigation steps. The survey indicated that demand for PI-platelets is expected to exceed 1.25 million units per year. In the absence of an intervention by the blood collector, the hospital survey suggests that some hospitals will attempt to avoid secondary testing and only transfuse platelets that have been stored for 3 days or less. This will likely decrease the number of collection facilities willing to distribute platelets on consignment and rotate stock between hospitals to avoid outdating. The result is decreased platelet availability and increased waste through outdate.

In summary, deaths due to transfusion-transmitted bacterial infection still occur and hence it is necessary to provide enhanced safety to protect patients. The allowance for multiple approaches to enhance bacterial safety recognizes balancing the need to improve safety with economic and logistic considerations that may influence decision making in different institutions. Finally, our request to FDA to simplify the regulatory framework for wider PI availability is based on concerns for patient safety rather than decreasing the regulatory workload on blood centers.

Thank you for the opportunity to offer these comments.

Founded in 1962, America's Blood Centers is North America's largest network of community-based, independent blood programs. The network operates more than 600 blood donor centers providing over half of the U.S., and a quarter of the Canadian blood supply. These blood centers serve more than 150 million people and provide blood products and services to more than 3,500 hospitals and healthcare facilities across North America. America's Blood Centers' U.S. members are licensed and regulated by the U.S. Food and Drug Administration. Canadian members are regulated by Health Canada.

The American Red Cross shelters, feeds and provides emotional support to victims of disasters; supplies about 40 percent of the nation's blood; teaches skills that save lives; provides international humanitarian aid; and supports military members and their families. The Red Cross is a not-for-profit organization that depends on volunteers and the generosity of the American public to perform its mission. About 5.6 million units of whole blood are collected from roughly 3.3 million Red Cross volunteer donors, separated into 8 million transfusable blood products and supplied to approximately 2,700 hospitals and transfusion centers across the country for patients in need.