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

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Strategies to Control the Risk of Bacterial Contamination in Platelets for Transfusion

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The AABB, America's Blood Centers (ABC) and the American Red Cross (ARC) appreciate the opportunity to present this joint statement as the Food and Drug Administration (FDA) finalizes recommendations for bacterial risk control strategies for platelet transfusion.

This statement updates the FDA on the current thinking of our organizations since November 30, 2017, when this topic was last discussed by the Blood Product Advisory Committee. 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 current interventions which interdict about 30-50% of bacterially-contaminated platelet units, transfusion-transmitted sepsis remains the most common infectious cause of recipient mortality reported to the FDA. Nineteen fatalities have been recognized and reported in the past decade; but surveillance is passive, and the clinical burden is believed to be 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. While calibrating our efforts to enhance platelet bacterial safety is intrinsically difficult without an *a priori* threshold level of tolerable risk, we strongly endorse providing multiple options based on both demonstrable enhanced safety and operational considerations for collection facilities and hospitals across the US, dependent on their ability to implement one or more allowable interventions. This statement expresses and implies no preference for a specific mitigation option over others, nor does it commit any blood collector or hospital to a specific approach or combinations of interventions. That must be the result of consultation between the collectors and transfusion services.

The options available to achieve this goal include enhancing the sensitivity of testing for bacteria and the use of pathogen inactivation (PI). We favor making multiple approaches available while

surveillance data accrue on their relative clinical values. Regarding bacterial culture approaches, these include rapid, point-of-care tests on days 3 or 4 and beyond, reculturing during the shelf life of the product, and implementing changes in the approach to primary culture. Data are available for each of these approaches to support increased safety relative to the current intervention using early culture alone.

Increased sensitivity of primary culture may be achieved using 3 options: 1.) Increasing the inoculated platelet volume using aerobic culture only without increasing the platelet hold time or changing other parameters, 2.) Increasing the inoculated volume without changing the platelet hold time, but using both aerobic and anaerobic culture, the latter for detection of obligate anaerobes and enhanced growth for facultative anaerobes, and 3.) Increasing the inoculated volume using both aerobic and anaerobic culture, in addition to a longer hold time for platelets prior to culture (greater than or equal to 36 hours). Published data from the National Health Service Blood and Transplant in the United Kingdom, and emerging data provided by our Canadian colleagues suggest that the combination of large volume, delayed sampling (LVDS into both an aerobic and anaerobic culture media is effective.

Two culture approaches during platelet storage presented today have shown improved bacterial yield and, in one case, reduced septic transfusion events. The method described by the Hopkins group for 5-day platelets using secondary culture at day 3 describes improved yield and clinical outcomes (recognizing the limitation that only 5 mL was inoculated into a single aerobic bottle). The Irish Blood Transfusion Service has described improved yield during their experience with aerobic and anaerobic culture on days 1 and 4, with extension of platelet shelf life to 7 days.

Some enhanced testing options can be implemented with 5-day stored platelets, but with the extension of storage to 7 days all enhancements improve operational efficiency and platelet availability. This is particularly true with the LVDS option, which results in the additional loss of up to one day of cumulative shelf life that is mitigated when product expiration is extended to 7 days.

Based on published reports and hemovigilance data from outside of the US, PI has been shown to provide bacterial safety for platelets while also effectively reducing the risk of transmitting other blood-borne pathogens. In the US, the capacity to produce PI platelets is limited by the restrictive guard bands 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. In order to overcome limitations to the PI platelet supply, we urge the manufacturer and FDA to collaborate aggressively in pursuit of the goals of expanding guard bands and providing data in support of treating triple collections. Further, we ask the FDA to make the regulatory process more conducive to timely implementation of this technology. We understand the limitations of the data for evaluation of the clinical efficacy of US licensed PI platelets. 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.

In summary, morbidity and deaths due to transfusion-transmitted bacterial infection still occur

and it is necessary to pursue enhanced safety to protect patients. The allowance for multiple approaches that enhance bacterial safety balances the need to improve safety with economic and logistic considerations that may influence decision-making in different institutions.

Thank you for the opportunity to offer these comments.

AABB is an international, not-for-profit association representing individuals and institutions involved in the fields of transfusion medicine and cellular therapies. The association is committed to improving health through the development and delivery of standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership includes physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries and AABB accredits institutions in over 50 countries.

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 US, 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' US members are licensed and regulated by the US 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.