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American Red Cross

April 12, 2017

Division of Dockets Management (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Submitted via http://www.regulations.gov

Re: Docket No. FDA–2014–D–1814, "Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services To Enhance the Safety and Availability of Platelets for Transfusion" draft guidance, 15 March 2016.

Dear Dockets Manager:

AABB, America's Blood Centers (ABC) and the American Red Cross (ARC) appreciate the opportunity to provide additional comments to the Food and Drug Administration (FDA) on the draft guidance titled "Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services To Enhance the Safety and Availability of Platelets for Transfusion." Our recommendations have been drafted by member experts, including those with relevant experience in implementation and use of technologies recommended in the draft guidance. These members serve on AABB's Bacterial Contamination Work Group, Regulatory Affairs Committee, and Transfusion-Transmitted Diseases Committee.

After submitting comments to the draft guidance in May 2016, we are now updating FDA with additional important information based on implementation experiences. These comments are intended to reinforce positions stated in the May 2016 comments, as well

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as identify specific critical concerns impacting both blood collection establishments and transfusion services. We strongly encourage FDA to consider these comments before issuing a final guidance. We believe these comments will alert FDA to adverse, unintended consequences expected to impact the blood supply and ultimately, patient care.

Loss of inventory during manufacturing

Currently, the ability to inactivate bacteria using pathogen reduction (PR) technology for all platelet products is not possible. Therefore, multiple options to protect platelets from bacterial contamination are needed. Currently, no complete solution exists because all pathogen inactivation (PI) methods have content and volume limitations for effective treatment. There is a well-documented decrease in the split product rate associated with approved PR technology using stringent guardbands. Split rates decline about 15% in the hands of experienced users. Currently, triple collections remain ineligible for PI. Early implementers are able to treat a maximum of 75-85% of optimized single collections, but no more than 40-45% of doubles. Even with approval of a triple kit, it remains unclear as to what proportion of those collections will be suitable for PR technology and therefore the impact to supply unknown. Blood collectors may be required to retool apheresis collections in order to qualify more products and this can significantly impact blood collection facilities' ability to to meet the current need for platelet products.

Impact on transfusion services

FDA must recognize burgeoning concerns from transfusion services were not well represented in initial comments to the docket. Transfusion services are only now beginning to recognize the consequences of bacterial contamination mitigation efforts on their operations. Since implementation has occurred, transfusion services have observed firsthand the consequences of not being able to maintain an adequate inventory. Transfusion services have traditionally relied upon blood collection establishments, as their blood supliers, to address FDA's manufacturing recommendations. Transfusion services are also challenged to implement unfunded testing and relabeling of platelets beyond day 3 of dating. Compliance with FDA's draft recommendations will significantly push the scope of manufacturing responsibilities into transfusion services, which, in some cases, are not able to meet these requirements. The personnel, training, equipment, and information technology adjustments required for compliance can result in major expenditures for most transfusion services. Transfusion services face difficulties justifying the organizational and financial changes necessary to support these recommendation before publication of the final guidance. Therefore adequate lead time between issuance of final recommendations and its required implementation is imperative.

Many blood collection establishments are able to meet the demand for platelets by allowing the return of platelets from hospitals on a "consignment basis" (for distribution elsewhere) to maximize use of this critical product and minimize outdating. There is now strong indication that the consignment model is likely unsustainable with a functional 3-day inventory or after further manufacture using point-of-issue (POI) testing and

relabeling procedures outside a cGMP environment. A March 2017 survey of ABC members provides a snapshot of the impact of the recommendations on the management of inventory. Eighty one percent (42 of 52) of respondents distribute some or all of their platelets on consignment. Three of those blood centers have determined it woud be necessary to discontinue this practice, with an additional 50% (21 of 42) currently considering discontinuing consignment, if the recommendations in the final guidance remain similar to those in draft. The resultant increase in outdating is one of the unintended consequences that could lead to severe platelet shortages while precluding availability of emergency stock in remote healthcare facilities previously able to rotate inventory.

A decision by FDA to finalize any of the recommendations as currently written, in the face of uncertainty about compliance capacity, would be premature. Additional important information is needed to address the limitations of bacterial inactivation methods, POI testing and unintended consequences of a functional 3-day platelet in the absence of the ability to fund or implement either of these alternatives.

In summary, FDA should issue final guidance only after the following considerations are fully addressed. FDA should:

- Consider potential unintended consequences of efforts to mitigate bacterial contamination risks, as identified by the blood community.
- Consider the results of a large AABB survey of transfusion services, to be deployed imminently, since hospitals are understandably reluctant to submit public comments predicting that their transfusion service may be unable to implement the FDA's recommendations.
- Consider an expedited review and approval of triple collections for use with pathogen inactivation, including more permissive guardbands, to allow more units to qualify.
- Consider accelerated review and approval of the Biologic License Application (BLA) submitted by blood collectors for licensure of pathogen reduced products.
- Consider revisiting the current definition of a dose of apheresis platelets. This definition has evolved over time, and it might be prudent to consider an evidence-based decision to lower the minimum content of at least the prophylactic dose to minimize the loss of inventory associated with the current approved methods for bacterial inactivation.
- Recognize that most transfusion services will not undertake the necessary changes to the blood establishment computer systems, transfusion service computer systems and quality systems until the final receommendations are issued. As such, transfusion services will require an extended timeline for effective implementation.
- Release final recommendations in December 2017 and employ an 18-month timeline for implementation because the proposed 12-month timeline is not reasonable with existing options and models that must mature.

In the face of new data and growing experience, we strongly recommend additional time for both FDA and the blood community to prepare for an effective implementation. Only with a full understanding of implementation options, selection of approved methods for use in various transfusion services and clinical settings for inactivation of bacteria in platelet products, and the maturation of manufacturing processes will we be able to achieve the intended goals of the guidance.

AABB is an international, not-for-profit association representing individuals and institutions involved in the field of transfusion medicine and cellular therapies. The association is committed to improving health by developing and delivering standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB membership consists of nearly 2,000 institutions and 8,000 individuals, including physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers. AABB members are located in more than 80 countries.

Founded in 1962, ABC 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.

ARC 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.

Thank you for the opportunity to provide additional comments. We look forward to continuing to work with the FDA on patient and donor safety initiatives. Questions concerning these comments may be directed to SCarayiannis@AABB.org.

Sincerely,

Sharon Carayiannis
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Director, Regulatory Affairs