America's Blood Centers®
It's About Life.

1717 K Street NW, Suite 900, Washington, DC 20006
Tel: 202-393-5725 | Fax: 202-899-2621
www.AmericasBlood.org

December 13, 2024

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

Submitted via https://www.regulations.gov

Re: Docket No. FDA–2024–D–2732, "Recommendations for the Development of Blood Collection, Processing, and Storage Systems for the Manufacture of Blood Components Using the Buffy Coat Method."

Dear Dockets Manager:

America's Blood Centers (ABC) is the national organization bringing together community-based, independent blood centers. Our member organizations operate more than 600 blood collection sites providing close to 60 percent 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. All ABC U.S. members are licensed and regulated by the U.S. Food and Drug Administration (FDA).

ABC appreciates the opportunity to provide feedback on FDA's draft guidance on Recommendations for the Development of Blood Collection, Processing, and Storage Systems for the Manufacture of Blood Components Using the Buffy Coat Method. ABC strongly believes in feasible solutions to the implementation of the Buffy Coat Method and recognizes FDA's work to provide "recommendations on the development of blood collection, processing, and storage systems (e.g., blood bags with anticoagulant and additive solutions, empty bags for platelet pooling) intended for the manufacture of blood and blood components for transfusion using the buffy coat (BC) method." As FDA notes in the draft guidance, "blood establishments in the U.S. are interested in using the BC method to manufacture blood components for transfusion…In addition, use of the BC method may offer logistical advantages, which could result in higher plasma and platelet recovery and increased platelet availability, when compared to the [platelet rich plasma] (PRP) method." Unfortunately, significant operational issues would impair implementation of the buffy coat method in the United States under the proposed draft guidance.

I. Manufacturers are unlikely to seek to obtain FDA approval for use of the BC method, until implementation of the European Union's (EU) ban on di(2-ethylhexyl) phthalate (DEHP) in medical devices.

ABC is pleased that FDA is providing guidance to assist manufacturers on the pathway to manufacturing blood components for transfusion using the BC method. However, FDA should be aware that, at this time, manufacturers are unlikely to seek to obtain FDA approval or clearance to market blood collection, processing, and storage systems intended for the manufacture of blood components for transfusion using the BC method, until they have implemented the EU's ban on di(2-ethylhexyl) phthalate (DEHP) in

medical devices, effective in 2030. Any changes in the materials used in manufacturing the bags and/or the additive solutions in the bags would trigger a new validation to demonstrate that the new ingredients do not adversely affect the blood products. The data from the new validation would need to be submitted to and reviewed and approved by the FDA. Due to the costs associated with FDA approval, manufacturers will likely wait until they have fully transitioned to DEHP-free bags.

II. ABC recommends that FDA adopt alternate acceptance criteria for red blood cell (RBC) components to accommodate outlier events.

The draft guidance states "manufacturers should use standard summary statistics…to report the results of the in vitro studies." For RBCs, the draft guidance states that the primary endpoint for RBCs is "95% confidence that greater than 95% of components show ≤1.0% hemolysis at the end of storage." However, hemolysis failures are donor-dependent outlier events.[1,2,3] The potential increase in hemolysis with DEHP-free bags may also pose a delay for manufacturers to seek FDA approval for BC collection and storage bags. ABC recommends that FDA adopt alternate acceptance criteria for RBC components to accommodate outlier events.

III. ABC strongly recommends that FDA approve holding whole blood for 24 hours at room temperature.

Currently, to make platelets from whole blood, FDA requires the platelet concentrate to be separated within 4 hours of collection or within the timeframe that the blood bag's package insert indicates. In the U.S., the FDA has given clearance for up to 8 hours from collection (8 hour-hold) for the separation of platelet concentrates from whole blood.[4] Without FDA allowing 24 hours from collection for separation (24-hour hold), there will be significant operational issues that will impair implementation of the BC method in the United States.

Europe allows for a 24-hour hold (as does Canada), resulting in 50% or more transfusions of BC whole blood derived leukoreduced platelet concentrate in European countries.[5] In addition to the extensive real word data from Europe and Canada, studies show there is no significant issue with overnight hold of whole blood.[6,7] Additionally, as FDA notes in the draft guidance, "studies demonstrate that blood components prepared by using the BC method are comparable to blood components prepared using the [platelet rich plasma] (PRP) method, in terms of biochemical and physiological characteristics." For

---

[1]McAteer M, Dumont LJ, Cancelas J, et al Multi-institutional randomized control study of haemolysis in stored red cell units prepared manually or by an automated system. Vox Sanguinis (2010) 99, 34–43.

[2]Hess JR, Sparrow RL, van der Meer PF, et al. Red blood cell hemolysis during blood bank storage: using national quality management data to answer basic scientific questions. Transfusion 2009;49:2599-2603.

[3]Sparrow RL, Payne KA, Adams GG. Higher donor body mass index is associated with increased hemolysis of red blood cells at 42-days of storage: A retrospective analysis of routine quality control data. Transfusion. 2021;61:449–463. DOI: 10.1111/trf.16203.

[4]21CFR640.24(b), CFR - Code of Federal Regulations Title 21, accessed Nov. 5, 2024.

[5]Gammon RR , Devine D, Katz LM, Quinly E, Wu Y, Rowe K, Razatos A, Min K, Reichenberg S, Smith R. Buffy coat platelets coming to America: Are we ready? Transfusion. 2021; 61:627-633.

[6]Lu FQ, Kang W, Peng Y, Wang WM. Characterization of blood components separated from donated whole blood after an overnight holding at room temperature with the buffy coat method. Transfusion 2011; 51: 2199-2207.

[7] van der Meer, P.F., Cancelas, J.A., Cardigan, R., Devine, D.V., Gulliksson, H., Sparrow, R.L., Vassallo, R.R., de Wildt-Eggen, J., Baumann-Baretti, B., Hess, J.R. and (2011), Evaluation of overnight hold of whole blood at room temperature before component processing: effect of red blood cell (RBC) additive solutions on in vitro RBC measures. Transfusion, 51: 15S-24S. https://doi.org/10.1111/j.1537-2995.2010.02959.x

blood centers in the United States to practically implement alternative strategies for platelet collection, FDA must approve a 24-hour hold, as has been safely done in other jurisdictions.

IV. ABC applauds FDA's acceptance of the use of international data.

ABC is pleased that FDA is requiring manufacturers to "conduct appropriate clinical studies *or submit existing clinical data* to demonstrate the safety and efficacy of blood components prepared using the BC method." (emphasis added). There are numerous existing clinical studies that have been performed outside of the United States that demonstrate the safety and efficacy of blood components prepared using the BC method,[8] since the BC method is widely accepted and used in other countries, as noted above. FDA's acceptance of international data for use in the approval of new products or technologies reduces unnecessary and burdensome regulation to support innovation and blood product availability.

****

ABC appreciates the opportunity to comment on the draft guidance. If you have any questions or require additional information, please contact Justine Coffey, Director of Regulatory Affairs and Public Policy (jcoffey@americasblood.org).

Thank you for your collaborative work to ensure a safe, adequate, and available blood supply.

Sincerely yours,

Kate Fry, MBA, CAE
Chief Executive Officer

[8]Levin, E., Culibrk, B., Gyöngyössy-Issa, M.I.C., Weiss, S., Scammell, K., LeFresne, W., Jenkins, C. and Devine, D.V. (2008), Implementation of buffy coat platelet component production: comparison to platelet-rich plasma platelet production. Transfusion, 48: 2331-2337. https://doi.org/10.1111/j.1537-2995.2008.01836.x