December 16, 2024

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-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Blood Collection, Processing, and Storage Systems for the Manufacture of Blood Components Using the Buffy Coat Method; Draft Guidance for Industry

Dear Dockets Manager:

The Association for the Advancement of Blood and Biotherapies (AABB) and the American Red Cross (ARC) are pleased to submit joint comments to the U.S. Food and Drug Administration (FDA) in response to the recently released draft guidance entitled, Recommendations for the Development of Blood Collection, Processing, and Storage Systems for the Manufacture of Blood Components Using the Buffy Coat Method; Draft Guidance for Industry.

**COMMENT 1 – Support for draft guidance recommendations**

AABB and ARC commend FDA in providing draft guidance and recommendations to manufacturers on the development of blood collection, processing, and storage systems (e.g., blood bags with anticoagulant and additive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 components for transfusion using the buffy coat (BC) method.

FDA approval or clearance to market such blood collection, processing, and storage systems would provide U.S. blood collection establishments the option to manufacture whole blood-derived platelets using the BC method, providing an additional source of platelets to help meet the growing demand for platelet transfusion, and offset the declining apheresis donor base.

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**COMMENT 2 – European requirements for non-DEHP (di(2-ethylhexl) phthalate blood bags**

Many blood collection system manufacturers and healthcare providers have begun the transition to non-DEHP products in response to patient safety concerns and European Union Medical Device Regulations. We recognize FDA's ongoing efforts to ensure the safety, efficacy and sustainability of blood and blood related products.

**Request:**
As manufacturers of blood collection systems increasingly transition to non-DEHP bag production, the development of DEHP-based blood collection systems for use in the U.S. market may decline significantly. Introduction of BC platelets in DEHP bags for the U.S., only to subsequently shift production to non-DEHP bags for the European market, may diminish interest among manufacturers. We urge the agency to elaborate on this topic when developing future guidance.

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**COMMENT 3 – Guidance is silent on the option for overnight ambient temperature hold**

Current FDA regulations at 21 CFR 640.24(b) states:
*"…the platelet concentrate shall be separated within 4 hours or within the timeframe specified in the directions for use for the blood collecting, processing, and storage system."*

Currently in the U.S., FDA permits whole blood for component production to be held at ambient temperature (20–24°C) for no more than 8 hours post-collection, after which it must be cooled to 1–6°C.[1] This restrictive 8-hour timeline limits the number of whole blood units which can be processed into platelets due to logistical challenges with timely transportation, storage, and processing. This is one reason most U.S. blood collection establishments do not produce whole blood-derived platelets today.

As described in the draft guidance, "*Studies demonstrate that blood components prepared by using the BC method are comparable to blood components prepared using the PRP [platelet rich plasma] method, in terms of biochemical and physiological characteristics.*" Most countries allow ambient hold up to 24 hours, as described by the Council of Europe Guide to the Preparation, Use and Quality Assurance of Blood Components (EDQM).[2] This ambient hold up to 24 hours provides increased flexibility necessary for greater platelet production through BC, PRP, and single centrifugation methods.

To fully leverage BC manufacturing, the current requirement for separation of the platelet concentrate from red blood cells within 8 hours must be removed to permit BC platelet production from whole blood. The precedent has been established as the limit has already been extended for plasma products. It is worth noting that an overnight ambient temperature hold method is widely used internationally, with millions of patients receiving blood products manufactured via the BC method.

**Request:**

AABB and ARC request that FDA approve an overnight ambient temperature hold for whole blood while maintaining the 35- or 42-day red blood cell dating period to facilitate the manufacture of BC platelets, as supported by international data.

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**COMMENT 4 – Donor Specific Product Failures – Non-process Failures**

Product failures may occur as a result of donor specific traits. These types of donor related product failures adversely influence results and are not the result of a process failure.

**Request:**
Our organizations request that future FDA guidance specifically allow non-process failures due to non-controllable parameters (i.e., donor specific characteristics) be defined in the testing plan, and allow for their exclusion and replacement.

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**COMMENT 5 – Statistical Requirement - 95% Confidence that greater than 95% of red blood cell components show ≤1.0% hemolysis**

These stringent acceptance criteria have proven to be overly burdensome and a barrier for manufacturers to pursue an overnight hold at ambient temperature and differ from requirements outside the U.S., including Canada and Europe.

**Request:**
We request that FDA consider updated, less burdensome acceptance criteria better aligned with other countries. The updated criteria would increase the likelihood that manufacturers can meet this requirement. This approach would decrease the regulatory burden by enhancing the ability to leverage data generated outside of the U.S. Additionally, if the 95%/95% acceptance criteria is not updated, please provide FDA's justification for retaining the stringent criteria.

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**COMMENT 6 – Guidance clarification on the need for clinical trials**

We appreciate the FDA's stated plans to consider all existing clinical data. Additional U.S. clinical trials should not be required where robust clinical data have already been generated through trials conducted outside of the U.S.[3] We believe that high-quality data from international clinical trials adequately support the safety and effectiveness of the collection system and should satisfy FDA requirements for clinical trial data.

**Request:**
AABB requests that FDA clarify in final guidance that duplicative clinical trials in the U.S. are not necessary because high-quality data from international studies are available. This request aligns with FDA's commitment to facilitating efficient regulatory pathways that ensure timely access and patient safety.

**Member Statements**

AABB (Association for the Advancement of Blood & Biotherapies) is an international, not-for-profit organization representing individuals and institutions involved in the fields of transfusion medicine and biotherapies. Since its inception in 1947, AABB has worked collaboratively to advance the field through the development and delivery of standards, accreditation and education programs. AABB is dedicated to its mission of improving lives by making transfusion medicine and biotherapies safe, available and effective worldwide. AABB's 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 more than 50 countries.

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.

Thank you for the opportunity to offer these comments. Questions concerning these comments may be directed to Scarayiannis@aabb.org.

Sincerely,

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| [signature on file] | [signature on file] |
| Sharon Carayiannis | J. Chris Hrouda |
| Vice President, Science & Practice | President, Biomedical Services |
| AABB | American Red Cross |

References:


1. Currently Approved CBER NDAs/ANDAs by Applicant As of 31-OCT-2024. https://www.fda.gov/media/76386/download#:~:text=Trade%20Name:%20Adsol%20with%20ACD,Date:%2027%2DDEC%2D1991, accessed Nov 11, 2024.
2. European Directorate for the Quality of Medicines & HealthCare. (2020). Guide to the preparation, use, and quality assurance of blood components: Recommendation No. R (95) 15 (21st ed.). Council of Europe.
3. Gammon RR, Devine D, Katz LM, et al. Buffy coat platelets coming to America: Are we ready? Transfusion. 2021; 61:627–633. https://doi.org/10.1111/trf.16184