Blood Bulletin
Carter BloodCare
America's Blood Centers
It's About Life

The Case for Transfusion of Low Yield Platelets

By Nancy Van Buren, MD, Medical Director at Innovative Blood Resources, a division of New York Blood Center, Richard Gammon, MD, Medical Director at OneBlood, Kip Kuttner, DO, Medical Director at Miller-Keystone Blood Center, & Susan Rossmann, MD, PhD, Chief Medical Officer at Gulf Coast Regional Blood Center; The authors disclose no conflicts

Key Points

- Platelet shortages are anticipated due to strategies necessary for implementation of the FDA's September 2019 final guidance for mitigation of platelet component bacterial contamination due to fewer single donor apheresis platelets meeting the FDA minimum content of 3.0×10^{11}/unit.
- Low (variable) yield single donor platelets have fewer than 3.0×10^{11} should be labelled with the actual platelet count per FDA requirements.
- Use of low yield platelets is an important strategy for optimizing the use of available platelet resources.
- It is time to consider integrating low yield platelets into the platelet inventory in the United States, which is already the standard of practice in other countries.

Background: Platelets are cells in your blood that form clots to help stop bleeding. They are used to stop or avoid massive bleeding for cancer patients, patients undergoing major surgery, and trauma victims. Currently, most blood suppliers collect them through platelet apheresis, the use of a special machine that filters platelets to allow a donor to keep red and white cells and plasma. They may also be collected as a part of whole blood donation. When apheresis technology was initially adopted in 1972, the Food and Drug Administration (FDA) set the minimum platelet content requirement (PCR) of 3×10^{11}/unit; however, there is no restriction on transfusing units with lower platelet yields. The 2007 FDA guidance states that apheresis platelet components for transfusion containing less than 3×10^{11} platelets should be labelled with the actual platelet count.[1] In comparison, whole blood-derived platelet concentrates (often referred to as random-donor platelets) should contain at least 5.5×10^{10} platelets,[2] which continue to account for less than five percent of transfusions in the United States (U.S.).[3] In fact, the U.S. has a minimum PCR higher than Canada and the majority of European Union (EU) nations (which range from 2.0 to 2.5×10^{11} platelets).[4]

Anticipated shortages due to FDA guidance: Strategies for implementation of the FDA's September 2019 final guidance for mitigation of platelet component bacterial contamination[5] all adversely impact platelet component dose and split rate of apheresis platelet collections, which are typically maximized to collect two to three platelet doses. It is estimated that 20-25 percent of single donor platelets (SDPs) may be produced with lower yields due to the burden of additional sampling required for bacterial cultures.[6] Pathogen reduction (PR) technology is an alternative choice for complying with FDA's September 2019 final guidance. This process can also decrease the yield of apheresis platelet units below what was stated in the 2007 FDA Guidance[1,6] leading to low (also called variable) yield platelets. This will further impact platelet availability, which is already challenged by factors such as limited shelf-life (5-7 days), a rising demand as the population ages, increasing prevalence of hematological malignancy, and the impact of the COVID-19 pandemic (as well as future events) on platelet inventory and blood donation. Donor age is beginning to affect the platelet supply. From 2001 and 2017, the peak age of platelet donors increased from 41-45 years to 56-60 years, respectively.[7] In one medium size blood center, 65 percent of platelet donors are 50 years of age or older.[8] Younger donors are often less able or unwilling to make the 2-3-hour commitment required of platelet donation, and older donors are more likely to develop medical conditions or be receiving medications that prohibit them from giving blood or platelets.[7]

Transfusion of low yield platelets as a strategy for optimizing the use of available resources: Low yield platelets (apheresis platelets with PCR less than 3×10^{11}/unit) generally do not correlate with more platelet transfusions. Clinical trials in the U.S., including the Platelet Dose Study (PLADO), have demonstrated acceptable clinical effectiveness of a lower PCR for the prevention of bleeding in thrombocytopenic hematology-oncology patients (patients who do not produce enough platelets because of their cancer or its treatment).[9] In the PLADO study, patients receiving the lower (50 percent) dose did not manifest more bleeding, which should alleviate concerns about the efficacy of the platelet dose in low yield platelets, i.e. between 2.5 and 2.9×10^{11}. Specifically, more frequent transfusions observed in the PLADO low dose arm would be an unlikely result from a product with only 10-15 percent fewer platelets. Finally, harmonization of the U.S. with EU minimum PCR will increase the number of platelet units available.[10]

Recommendations: It is time to consider integrating low yield platelets into the standard platelet inventory. These have already been accepted in other countries as standard of care and is an important measure to optimize the use of available platelet resources which will be impacted by implementation of FDA's September 2019 final guidance for mitigation of platelet component bacterial contamination. Research should be sponsored to identify optimal platelet transfusion thresholds and dosing strategies for non-hospitalized patients for prophylactic use, in the presence of congenital or acquired platelet dysfunction, and for bleeding patients in surgical and trauma settings.[11]

References

1. Food and Drug Administration. *Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods*. 2007. [https://www.fda.gov/regulatory-information/search-fda-guidance-documents/collection-platelets-automated-methods].
2. Gammon RR, ed. Standards for blood banks and transfusion services. 32nd ed. Bethesda, MD: AABB, 2020.
3. Jones JM, Sapiano MRP, Savinkina AA, et al. Slowing decline in blood collection and transfusion in the United States-2017; *Transfusion* 2020;60: S1-S9. Doi: 10.1111/trf.15604.
4. EDQM. Guide to the preparation, use and quality assurance of blood components. 19th ed. Available at https://www.edqm.eu/en/blood-guide. Accessed 23 Nov. 2020.
5. Food and Drug Administration. Guidance for Industry: *Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion*. 2019.[https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bacterial-risk-control-strategies-blood-collection-establishments-and-transfusion-services-enhance].
6. Paradiso S. Implementing the FDA Guidance for Industry of Platelets: Bacterial Risk Control Strategies from a Blood Bank Perspective. AABB 2020 Annual Meeting.
7. Stubbs J, Homer M, Silverman T, Cap A. The current state of the platelet supply in the U.S. and proposed Options to decrease the risk of critical shortages. *Transfusion*. 2020;1-10. Doi: 10.1111/trf.16140.
8. Kuttner K, personal communication. November 2020.
9. Slichter SJ, Kaufman RJ, Assmann SF, *et al*. Dose of prophylactic platelet transfusions and prevention of hemorrhage. *N. Engl. J. Med*. 2010; 362:600-13. Doi: 10.1056/NEJMoa0904084.
10. Benjamin RJ, Katz L, Gammon RR, Stramer SL, Quinley E. The argument(s) for lowering the U.S. minimum required content of apheresis platelet components. *Transfusion*. 2018; 59: 779-88. Doi: 10.1111/trf.15036.
11. Gammon RR, Devine D, Katz LM, *et al*. Buffy coat platelets coming to America: Are we ready? *Transfusion*. 2020. Doi: 10.1111/trf.16184.

Blood Bulletin is issued periodically by America's Blood Centers. Publication Editor: Mack Benton. The opinions expressed herein are opinions only and should not be construed as recommendations or standards of ABC, ABC SMT Committee, or its board of trustees. Publication Office: 1717 K St. NW, Suite 900, Washington, DC 20006. Tel: (202) 393-5725; Fax: (202) 393-1282; E-mail: memberservices@americasblood.org.