



Stop Bugging My Platelets

Bacterially contaminated platelets pose the greatest risk of transfusion-transmission infection (TTI) in comparison with other blood products. The rate of adverse reactions resulting from transfusion of contaminated platelets is extremely low with between 1 and 5 reported instances from approximately 2 million platelet transfusions per year^{1,2}. However, this low rate is attributed to underreporting so that contaminated platelets remain a significant TTI risk. The FDA addressed this issue in September of 2019, in a final guidance with steps that blood centers must take in the 18 months following the release of the guidance. Bacterial risk control mitigations set forth by FDA in this guidance are secondary rapid testing, sampling and culture strategies, and pathogen reduction (PR). This brief discussion will only address platelets with a 5-day shelf-life, stored at room temperature.

Rapid (point of issue) tests such as the Verax Pan Genera Detection (PGD) test³ may be part of a two-step safety strategy. This handheld immunoassay, which costs ~\$30 per test, is designed to detect a broad spectrum of both aerobic and anaerobic bacteria with a sensitivity as low as 103 to 105 CFU/mL. Limitations and challenges of the PGD test include implementation, the need for additional testing to confirm an initial positive result, and a significant false positive rate (0.51%).

A recently published article investigated the number of PGD-positive test results between 2013 and 2018 using the Red Cross hemovigilance database; a total of 475 initially reactive PGD tests were identified of which only 1.5% turned out to be true positives.⁴ Despite the increasing number of initially reactive PGD tests reported by hospitals to the Red Cross in five years' time the total number of reports remains low (Chart 1). Notably, a disproportionate number of positives were reported when testing whole blood-derived platelets. The article stated that in 2018 alone, 93 presumed positive PGD tests were reported and the estimated cost to the Red Cross as calculated from the investigations of 64 hospital reports was \$87,000. This figure includes the cost of the platelets, any non-platelet co-components, the labor involved in managing the positive cases, and the 'loss' of units not collected due to the resulting donor deferral that is applied while investigating for bacterial contamination. Based on their analysis the authors conclude that initially reactive PGD test results have an adverse impact both on platelet inventories and blood center costs. The authors note that the test may have been more widely adopted by hospitals not served by the Red Cross.

The strategy of large-volume delayed sampling (LVDS) involves taking larger volumes from each platelet unit and inoculating the sample into aerobic and anaerobic culture media 36-48 hours after collection, rather than 24-hour interval that is now widely used. The greatly increased sample volume of at least 16 mL per unit, and additional time prior to sampling may coax any bacteria present to grow. LVDS is a single-step strategy as no other steps need to be taken prior to transfusion.

In another option, if the first (primary) culture is taken and inoculated into aerobic and anaerobic media no sooner than 24 hours, the product may be transfused up to three days (even though it is a 5-day product) after which time a secondary culture must be taken prior to transfusion. Please refer to



Chart 1. Reactive PGD Tests Reported to Red Cross 2013-2018

the FDA guidance for additional details.

As an alternative to the measures discussed above, the FDA recognizes the use of pathogen inactivation technology to produce pathogen reduced (PR) platelets. This method, developed by Cerus Corporation, exposes an apheresis collected platelet to an amotosalen compound and UV light to virtually eliminate most infectious agents, which obviates the need for any additional bacterial testing. The safety of PR products

In summary, FDA considers LVDS (no sooner than 36 hours after collection) and PR to be single-step strategies as no other steps must be taken prior to release for transfusion. All work is performed by the blood center which simplifies the process for the blood bank or transfusion service. Two-step strategies involve a primary culture at the 24-hour mark followed by a rapid test prior to transfusion; or, a primary culture taken at the 24-hour mark followed by a secondary culture at the 3-day mark. Two-step strategies may need to be performed both at the blood center and at the blood bank or transfusion service.

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References

- Ramirez-Arcos S, DiFranco C, McIntyre T, et al. Residual risk of bacterial contamination of platelets: six years of experience with sterility testing. *Transfusion* 2017; 57:2174-81.
- Katus MC, Szczepiorkowski ZM, Dumont LJ, et al. Safety of platelet transfusion: past, present and future. *Vox Sang.* 2014; 107:103-13
- Bacterial risk control strategies for blood collection establishments and transfusion services to enhance the safety and availability of platelets for transfusion: guidance for industry. 2019. Available from: <https://www.fda.gov/media/123448/download>.
- Rios J, Westra J, Dy B et al. Adoption trends of point of issue Verax PGD rapid test for bacterial screening of platelets between 2013 and 2018 among hospitals supplied by the American Red Cross and impact on platelet availability. *Transfusion* 2020; 60: 1364-72.

Links to Additional Resources/Information

FDA Bacterial Risk Control Strategies, 2019 Guidance: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bacterial-risk-control-strategies-blood-collection-establishments-and-transfusion-services-enhance>
 Verax Pan Gera Detection Test (corporation website): <https://www.veraxbiomedical.com/approach/risk/>