BLOOD PRODUCTS ADVISORY COMMITTEE
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5630 Fishers Lane, Room 1066

Rockville, MD

Issue Summary

Topic III: Considerations for Options to Further Reduce the Risk of Bacterial Contamination in Platelets

I. Introduction

As the major viral threats to blood safety have come under control, the risk of bacterial contamination of platelets stands out as the leading infectious risk of blood transfusion. This risk has persisted despite numerous interventions including the introduction in the last decade of analytically sensitive culture-based bacterial detection methods, which are widely used to test platelets prior to their release from blood collection establishments. At this meeting, several potential strategies will be discussed for use of bacterial detection methods to further improve bacterial safety of platelets.

Pathogen reduction technologies are not approved for use in the U.S. For this reason they are not the focus of this meeting.

II. Background

Risks of Bacterial Contamination and of Sepsis from Platelet Transfusions

All blood components are susceptible to bacterial contamination. However platelet products, with storage at room temperature between 20°C-24°C, can support high titer bacterial proliferation and are associated with a higher risk of sepsis and related fatality than other transfusible components.

Skin bacteria are the most common source of contamination. Such contamination occurs at the time of collection and when present, produces an average bacterial load at collection estimated at < 0.1 CFU/mL[1, 2]. Bacteria may subsequently proliferate to clinically significant levels during

the 5-day room temperature platelet storage. Contaminating organisms may be fast or slow growers, Gram positive or Gram negative, aerobic or anaerobic, and may be more or less virulent.

A number of strategies have been implemented to mitigate the risk of bacterial contamination of platelet products including donor health screening, skin disinfection, diversion of an initial aliquot of whole blood at the start of collection, visual inspection, and bacterial detection.

About 2 million platelet transfusions are administered yearly in the U.S. Of those, about 1.75 million (88%) are apheresis platelets (i.e., single donor platelets or SDP) and 0.25 million are pools of whole blood-derived (WBD) platelets, with each pool composed, on average, of 5 single units of WBD platelets. WBD platelets are pooled either within 4 hours prior to transfusion (post-storage pooling), or pooled shortly after collection in a container cleared by FDA to store pooled platelets (pre-storage pooling).

Currently in the U.S. platelets are stored for a maximum of 5 days. In 1984 platelet storage was extended to 7 days, however two years later it was shortened back to 5 days based upon reports of increased septic transfusion reactions in the recipients.

An extension of the apheresis platelet shelf life to 7 days was introduced again from 2005-2008, as part of the PASSPORT clinical trial which was predicated on the assumption that the residual bacterial risk at 7 days would be no greater than that of day 5 untested (i.e. non-cultured) apheresis platelets (the standard product at the time) which was estimated at a minimum by results of a day 1 culture. Apheresis platelets stored in containers cleared by the FDA for storage to 7 days were tested by a standardized culture procedure on Day 1 (24 hours after collection) and then retested by culture at expiration. An interim analysis of the study suggested that the contamination rate at expiration was high enough (~ 3/5000 at the conclusion of the study) to fail the pre-specified end-point of the study (95% confidence of a contamination rate ≤1:5000), leading to an early termination of the study. This study indicated that an early culture at Day 1 did not improve safety of 7 day apheresis platelets compared to untested 5 day apheresis platelets and that a single culture on Day 1 is not sufficient to extend platelet storage from 5 to 7 days. Platelets stored for 7 days are not currently available in the US because of these study findings. Additionally,

the study demonstrated an estimated clinical sensitivity of only 26% for the culture on Day 1 to detect bacterial contamination in apheresis platelets.

Methods to Detect Bacterial Contamination in Platelet Products

Two culture-based systems (BacT/ALERT from bioMérieux and eBDS from Pall) and two non-culture-based rapid tests (PGD test from Verax, and BacTx from Immunetics) are cleared by the FDA for the detection of bacteria in platelets in the US.

A. Culture-based devices

BacT/ALERT and eBDS devices have been cleared by FDA for the quality control (QC) of apheresis platelets, single units of WBD platelets and pooled platelets. Each of these clearances was based on spiking studies in which platelet products were intentionally contaminated with a series of bacterial organisms commonly associated with platelet contamination, and subsequently tested with the device to determine its analytical sensitivity. BacT/ALERT and eBDS devices have similar analytical sensitivity, about 1-10 CFU/mL. The BacT/ALERT system consists of two distinct growth media bottles (one aerobic and one anaerobic bottle) with a sampling volume in each bottle ranging from 4 to 10 mL. The eBDS system detects only aerobic and facultative anaerobes and uses a product sampling volume of ~ 3 mL.

In accordance with AABB standards, these devices are currently being used by most blood collection centers *de facto* as release tests on platelet products destined for transfusion. This means that the bacterial culture test is performed prior to platelet distribution as a routine procedure. However, the exact sampling and culture procedures vary considerably among blood collection centers.

A sample from the platelet component is inoculated in the culture-based device at least 18 hours post-collection (commonly at 24 hours). Products are made available for transfusion after a variable hold period (from < 6 hours to > 24 hours) to allow any bacteria present in the sample to proliferate in the culture medium to levels that may be detectable based on the sensitivity of the device. Products tested by the BacT/Alert system are distributed as "negative-to-date" based on the status of the culture at the time

the unit is released by the collection center. The culture may turn positive after distribution of the unit triggering notification of the transfusion service.

The rate of bacterial contamination in apheresis platelets as determined by sampling of platelets 24 hours after collection for inoculation in culture-based devices (also referred to as Day 1 or early culture) is estimated at about 1/5000 (0.84/5000[3]-1.16/5000[4]). However studies have shown that the residual risk of bacterial contamination on the day of transfusion, or at outdate, in apheresis platelets that had tested negative by early culture is 1/1,500[4] – 1/2,300[5]. A number of studies have shown that the sensitivity of the early culture varies between 22% and 40%[1,4,6].

Based on published studies the false positive rate of culture-based devices range from ~1/4400[7] to 1/550[4] and the false positive to true positive ratio from ~ 2[7] to ~ 8[4].

For pre-storage pooled platelets that had tested negative in early culture, the residual risk of bacterial contamination at the time of transfusion varies between 1/6000 and 1/1000[8].

Passive reporting (i.e., reporting initiated by the transfused patient's clinical team) reveals rates in distributed apheresis platelets of about 1/107,000 for sepsis, and 1/1.01million for sepsis-related deaths[9]. However active reporting (i.e., as part of a study with active monitoring) of transfusion-associated septic reactions at a single institution has shown a rate about 10 times higher compared to passive reporting[10] (1/6400 vs. 1/66,000).

Based on published studies, both the rate of bacterial contamination[10] and that of septic transfusion[11] reaction is about 5 times higher in pooled platelets than in apheresis platelets, consistent with the number of units in WBD derived pooled platelets and the absence of pooling in apheresis platelets.

B. Non-Culture-Based Rapid bacterial detection tests

Two rapid non-culture-based bacterial detection tests are cleared by the FDA for the U.S. market for the detection of bacteria in platelet products: The PGD test by Verax, and the BacTx by Immunetics.

1. The PGD (Pan Genera Detection) test from Verax

The Verax PGD test is a rapid, single use, lateral flow immunoassay that detects surface bacterial antigens, lipoteichoic acid (LTA) and lipopolysaccharide (LPS), found on Gram-positive and Gram-negative organisms, respectively. A visual read-out can be obtained 20 to 60 minutes after the preparation and application of the sample to the test device. For apheresis platelets, the Verax PGD test was initially cleared in 2007 as an adjunct QC test following testing with an FDA-cleared culture-based test. The adjunct labeling was based on the relatively low analytical sensitivity (limit of detection) of the device (8.6×10^5 CFU/mL) compared to the culture-based devices (1-10 CFU/mL).

In 2011, the Verax PGD test was cleared for testing apheresis platelets as an added safety measure following testing with an aforementioned FDA-cleared culture-based test. The 'safety measure' indication was granted to the Verax PGD test based on a clinical field study[12] in which 27,620 apheresis platelets that had screened negative by Day 1 culture were retested, on the day of transfusion, with the Verax PGD test which registered a true positive bacterial detection rate, on that day, of 1/3069 (0.033%). Thus the Verax PGD test would further detect some contaminated platelets that had been missed by the Day 1 culture method. However, the false positive rate (i.e., repeat reactive PGD not confirmed by culture) was 0.51% when the recommended strategy of repeat PGD testing of an initial reactive result is carried out (a repeat reactive PGD test being defined as at least 2 reactive PGD tests of 3 total tests) and was 0.91% based on an initial reactive result without repeat testing. Non-reactive PGD tests were not retested by the PGD test. Based on a subset of 10,724 units in which both repeat reactive and non-reactive units were cultured, the false negative rate was about 1/5000, and the approximate sensitivity and specificity were 60% and 99.3%, respectively.

The relatively high false positive rate of the Verax PGD test compared to its true positive rate (0.51% or 0.91% vs. 0.033% respectively leading to a false positive to true positive ratio of about 16 when the false positive rate based on a repeat reactive result is considered) could lead to the discard of a

number of otherwise suitable platelet products, and potentially limit the availability of HLA-, or ABO-matched platelets, or of fresh platelets. Platelet inventories in facilities where platelet transfusions are administered infrequently would be particularly impacted by a high false positive rate, as discussed in more detail below.

No data currently exist that indicate how long after a Verax PGD non-reactive result is obtained can a platelet component be issued without risk to the patient. A proliferating organism may reach the limit of detection of the device after the test is performed, and this may take minutes or hours. Based on the design of the Verax PGD field study, most participating centers conducted their platelet testing in batches once every 24 hours, to fit into their daily operational routine. Accordingly, and reflecting these experimental conditions, the package insert states that testing with Verax PGD may be conducted on apheresis platelets within 24 hours prior to transfusion. This instruction, however, is accompanied by recommendations to test as closely as possible to the time of transfusion, and by a discussion of bacterial doubling time between sampling and transfusion. The package insert additionally includes data on breakthrough clinical bacteremia or sepsis in the face of a negative Verax PGD test with time interval between testing and transfusion, and a statement that the true false negative rate or the clinical sensitivity of the Verax PGD test were not established by the study.

As a case in point, an instance has been described[13] of a bacterially contaminated platelet unit that tested positive on culture within 24 hours after it was determined to be non-reactive by the Verax PGD test.

In a separate field study[14] conducted by the Canadian Blood Services, the Verax PGD test true positive detection rate on outdated pooled buffy-coat platelets (day 7- day 10 platelets) that had tested negative by early bacterial culture was 1/4000 (0.025%). The false positive rate was 0.27% and 1.15% based on repeated versus initial reactivity in PGD testing, respectively. Therefore the ratio of false positive to true positive results in that study was at least 10.

The Verax PGD test has also been cleared for QC testing of WBD platelets, pooled within 4 hours prior to transfusion based on spiking studies.

Harm et al. screened 70,561 nonleukoreduced whole blood-derived platelet pools with the PGD test. There were seven true-positive PGD tests and 242 false-positive tests (positive predictive value of PGD test, 2.81%).[15] The overall contamination rate was 99 per 10^6 WBP pools (1:10,080; 95% confidence interval [CI], 40-204), and the false-positive rate was 3430 per 10^6 WBP pools (1:292; 95% CI, 3011-3890). All seven bacterial isolates were Gram positive. The median age of the individual WBP units in the seven contaminated pools was 5 days (range, 3-5 days) compared to 4 days (range, 1-5 days) in the false-positive pools (p = 0.0012). In this study, there were about 35 false-positive test results for every true-positive. (The definition of a false-positive result varied by time and site in the study.) In the report by Jacobs et al.[11] discussed above, in which apheresis platelets were studied, there were about 16 false-positives for every true-positive when the recommended strategy of repeat PGD testing of an initial reactive result was carried out (a repeat reactive PGD test being defined as at least 2 reactive PGD tests out of 3 total tests). A relatively high false-positive rate can pose a particular challenge in the many hospitals that transfuse only a few platelets per week and that maintain a small inventory or may receive platelets on demand from their blood supplier. Another way of looking at this is that there were 1:3069 true positives and 1:195 false positives in the Jacobs et al. study, with an overall positive rate of 1:183. At these rates a hospital using 4 units/week (200/year) would likely find one positive test per year and one true positive result every 15-16 years. A hospital using 100 units/week (~ 5,000/year) would likely find ~ 25 positive tests per year and 1-2 true positive results a year.

Other studies using traditional plate culture have shown a contamination rate of 1/400[5] on WBD platelets pooled just prior to transfusion.

Published studies[14, 16-18] have reported an analytical sensitivity of the Verax PGD test that is lower than that stated in the Verax PGD package insert, especially for Gram-negative organisms. Spiked *E. coli* and *K. pneumoniae* organisms were detected only at levels 100 times higher than those stated as the manufacturer's limit of detection (LOD), and *S. epidermidis* detection required levels 10 times greater than those cited in the package insert. In one inter-laboratory comparison study of 12 spiked samples, the Verax PGD test detected 4 of 12 samples. Of the 8 samples that were missed, 4 were below the manufacturer's LOD, and 4 were above the manufacturer's LOD including *E. coli*, *K. pneumoniae,* and *S. aureus* organisms. This discrepancy with the test package insert may be related to the variability in

the bacterial surface antigens (LTA or LPS) that the test detects. Additionally, the difficulty of some operators in reading and interpreting the test has been documented[14, 16].

At a recent July 17, 2012 AABB Workshop on secondary testing (i.e., day of issue bacterial testing following an early culture) of platelet products, transfusion services shared their experiences on the use of the Verax PGD test. Some services are using the test on pooled platelets just prior to transfusion; others services either never adopted, discontinued, or plan to discontinue the use of the test on apheresis platelets based on a determination that the benefits of the test do not outweigh the challenges of implementation; and a medical director of one transfusing facility recommended the use of the test in his facility, however, the test was not implemented due to a perceived lack of need as no transfusion-related septic reactions were diagnosed at that facility.

2. BacTx from Immunetics

In June 2012, FDA cleared the BacTx test for QC testing of WBD platelets pooled within 4 hours prior to transfusion. Clearance was based on spiking studies. BacTx technology detects peptidoglycan, a ubiquitous component of bacterial cell walls, using an enzymatic colorimetric reaction detected by a photometer. The instrument read-out occurs within 30 minutes of sample application. In spiking studies the analytical sensitivity of the BacTx was determined to be 5.8×10^4 CFU/mL, and specificity was 99.8%. No data are available yet on the performance of the BacTx in clinical use.

III. Discussion of potential strategies to mitigate the residual risk of bacterial contamination of platelets

FDA is presenting options to consider to improve the safety of platelets from bacterial contamination including shortening of platelet products shelf-life to 4 days following sampling and culture on Day 1 unless additional testing is performed, and shelf-life extension beyond 4 days based on secondary testing of the product, either by using a repeat culture on day 4 of storage, or else testing with a rapid bacterial detection device no more than 4 hours prior to transfusion.

A. Shortening of platelet product shelf-life

As stated above, room temperature platelet storage can result in the proliferation of bacteria. It has been additionally shown that the percent of detectably contaminated units directly correlates with the length of platelet storage[19]. Transfusion-associated septic reactions that were analyzed by storage day of transfused apheresis platelets previously screened as negative by early culture demonstrated that 5% of septic reactions were associated with day 2 platelet transfusions, 10% with day 3, 20% with day 4, and 65% with day 5 platelet transfusions[20]. As expected the longer the storage of the platelets, the greater the risk of sepsis.

Shortening of the shelf-life of platelets to 4 days would eliminate platelet products deemed most likely to be associated with septic transfusion reactions. 4-day platelets would still be tested early in storage by FDA-cleared culture-based devices to intercept the fast growing organisms which are considered the most pathogenic to patients.

Other countries have used similar strategies to limit the septic transfusion rates. The Paul-Ehrlich-Institute (FDA's counterpart in Germany) recently reduced the shelf life of platelets from 5 to 4 days because the majority of severe cases of transfusion-associated sepsis occurred with day 5 platelets[21]. Japan has had a 3-day shelf life for platelets for a number of years.

B. Retesting with a rapid test after product expiration

Another option for both improving platelet safety and extending storage of apheresis platelets, is to retest (i.e., in addition to early culture) apheresis platelets with a suitably labeled rapid test after the expiration of the 4-day platelet product shelf-life. After Day 4, the platelets may be transfused if found negative by a rapid test conducted no more than 4 hours prior to transfusion.

In Germany where platelet shelf-life is currently limited to 4 days, a strategy of testing uncultured platelets with rapid tests (flow cytometry or PCR) on samples drawn on days 3 through 5 enabled a storage extension for up to 5 days[22].

C. Retesting with a culture-based device during storage

As stated above, the risk of bacterial contamination on the day of transfusion for apheresis platelets previously screened as negative by an early culture is $1/1,500^4$ – $1/2,300^5$; and the risk of platelet transfusion-associated septic reactions is estimated to be at least $1/107,000^9$. As a path to both improving the safety of platelets and extending the platelet shelf-life to up to 7 days, one option to consider is to retest (i.e., in addition to the early culture) of in-date platelets on Day 4 using an FDA-cleared culture-based device. Positive units would be discarded and negative units would have their storage period extended to five days or seven days depending on the clearance specification of the storage container. A similar strategy has been implemented by the Irish Blood Transfusion Service (IBTS) for both apheresis and platelet pools in which platelets were tested by culture on Days 1, 4, and at outdate (i.e. days 6 and 8). Bacterial detection rates (combined apheresis and platelet pools) were as follows in a 2008 publication[1] from IBTS: 1.5/5000 on day 1, 1.5/5000 on day 4, and 4.2/5000 at outdate, with no septic transfusion reaction observed after culturing 43,230 platelet units. Updated data[23] from IBTS showed a very low day 4 bacterial detection rate for apheresis platelets (no confirmed positives detected in ~ 12,000 units tested). The current practice of IBTS is to culture platelets after one day of storage and expire them at 5 days unless recultured on day 4. A negative culture result on day 5 permits extension of dating to day 7. From 2010 onwards the IBTS no longer re-tests expired units a second time (or a third time in the case of day 4 retested units) to determine the false negative rate for early culture(s) due to cost constraints. There have been no septic transfusion reactions reported in the comprehensive Irish hemovigilance system since testing was introduced, with approximately 120,000 units tested.

However, important differences exist between the above mentioned option and the IBTS testing strategy. The latter tested a combination of apheresis platelets and buffy-coat platelet pools and these were tested with both aerobic and anaerobic BacT/ALERT bottles on days 1, 4, and at outdate with the associated higher sampling volumes, whereas in the U.S., apheresis platelets would be tested on day 1 with an aerobic culture only, and on day 4 with both aerobic and anaerobic cultures.

D. **Culture a proportional volume**

Tomasulo and Wagner[24] modeled an intervention in which a fixed proportion of the collection volume from single, double, and triple platelet

collections would be cultured instead of a fixed volume as typically done. They applied a Poisson model to blood center data to calculate weighted average detection. Model 1 consisted of inoculating 3.2% of the collection volume from single, 1.6% from double, and 1.2% from triple collection procedures (8 mL in each case). Model 2 consisted of inoculating 3.8% of the collection volume from all platelet procedures. Volume-related and non–volume-related contamination mechanisms were evaluated. Testing constant proportions of the collection volume (Model 2) increases percent detection over testing constant volumes (Model 1) (68% vs. 41% detection if contamination is 30 colony-forming units (CFUs)/collection bag and 17% vs. 9% detection if contamination is 5 CFUs/collection bag). At low levels of contamination (approx. 5 CFUs/bag), the intervention might double the number of contaminated units detected. They concluded that based on the application of the Poisson model to detection of bacteria in platelet concentrates, inoculating cultures with overall consistent proportions of the collection volume should lead to a reduction in false negative tests and in the number of contaminated units transfused.

Since the proportional sampling volume approach is based only on theoretical modeling, it is considered as an adjunct option for options A, B, and/or C.

Table 1   Summary of Options Presented Above

A	Outdate platelets at Day 4 based on a negative culture on Day 1
B	Extend shelf life of platelets negative on Day 1 culture to Day 5 or Day 7 (depending on the storage container) if negative by a rapid test and transfused within 4 hours of rapid testing
C	Additional culture on Day 4 to extend dating of negative units to 5 days or 7 days (depending on the storage container)
D.	Option A, B, and/or C with proportional sampling volume

IV. Questions to the Committee

1. Does the Committee find that additional measures are necessary to decrease the current risk of transfusion of bacterially-contaminated platelet products?

2. If yes to Question 1, please discuss whether:

    A. Reduction in platelet product shelf-life from 5 to 4 days, and early culture would decrease the risk of transfusion-associated septic reactions sufficiently to obviate the need for additional testing;

    B. The available data are sufficient to support extension of platelet shelf-life up to 7 days if otherwise expired 4-day platelets (with negative day one cultures) are re-tested with an FDA-cleared rapid test and released within 4 hours of a negative test result.

    C. The available data are sufficient to support extension of platelet shelf-life up to 7 days if otherwise expired platelets (with negative day one cultures) are retested on Day 4 with an FDA-cleared aerobic and anaerobic (10 mL/bottle) culture-based method.

    D. For options A, B, and/or C the bacterial culture should be conducted using a proportionate sampling volume

    E. There are other test-based options that FDA should consider.

3. Please discuss whether, alternatively, for platelets limited to 5 days of storage, the available data support a strategy to culture platelets after the first 24 hours of storage and then retest just once with a rapid test on the day of transfusion.

4. Please discuss the role of surveillance for any of the options listed above in determining the effectiveness of any new strategies implemented by blood collectors or transfusion services (e.g., culture testing of the platelet product at the time of transfusion or at product outdate to determine the residual contamination rate, and/or active monitoring of septic transfusion reactions).

References

1. Murphy WG et al. Screening platelet concentrates for bacterial contamination: low numbers of bacteria and slow growth in contaminated units mandate an alternative approach to product safety. Vox Sanguinis 2008;95:13–19.

2. Richard Benjamin, American Red Cross, AABB 2008 Annual Meeting, Montreal, Canada.

3. Eder AF et al. Limiting and detecting bacterial contamination of apheresis platelets: inlet-line diversion and increased culture volume improve component safety. Transfusion 2009;49:1554-1563.

4. Dumont LJ et al. Screening of single-donor apheresis platelets for bacterial contamination: the PASSPORT study results. Transfusion 2010;50:589-599.

5. Michael Jacobs, AABB workshop on secondary testing of platelet products, North Bethesda, July 2012

6. Pearce S, et al. Screening of platelets for bacterial contamination at the Welsh Blood Service. Transfusion Medicine 2011;21:25-32.

7. Souza S *et al*. Improving the performance of culture-based bacterial screening by increasing the sample volume from 4 mL to 8 mL in aerobic culture bottles. Transfusion 2012:52:1576-1582

8. Yomtovian R, Jacobs M.R., Westra J. et al. Detection of Platelet Bacterial Contamination of Apheresis and Prestorage Pooled Whole Blood Derived Platelets Units at Blood Centers Prior to Release and at a Hospital Transfusion Service at Time of Issue. Transfusion 2011;51(s):197A.

9. Richard Benjamin, AABB workshop on secondary testing of platelet products, North Bethesda, July 2012

10. Jacobs et al. Relationship between Bacterial Load, Species Virulence, and Transfusion Reaction with Transfusion of Bacterially Contaminated Platelets. Clinical Infectious Diseases 2008;46:1214-1220

11. Ness P, Braine H, King K, Barrasso C, Kickler T, Fuller A, Blades N: Single-donor platelets reduce the risk of septic platelet transfusion reactions. *Transfusion* 2001; 41:857–861.

12. Jacobs MR, Smith D, Heaton AW, et al. Detection of bacterial contamination in prestorage culture-negative apheresis platelets on day of issue with the Pan Genera Detection test. Transfusion 2011;51:2573-2582.

13. Katharine Downes, AABB workshop on secondary testing of platelet products, North Bethesda, July 2012

14. Ramírez-Arcos S, Kou Y, Mastronardi C, et al. Bacterial screening of outdated buffy coat platelet pools using a culture system and a rapid immunoassay. Transfusion 2011;51:2566-2572.

15. Harm SK, Charapata M, AuBuchon JP, Triulzi DJ, Yazer MH. <u>Routine use of a rapid test to detect bacteria at the time of issue for nonleukoreduced, whole blood–derived platelets</u>. Transfusion. Published online: 31 JUL 2012 | DOI: 10.1111/j.1537-2995.2012.03818.x

16. Vollmer T, Hinse D, Kleesiek K, et al. The Pan Genera Detection Immunoassay: a Novel Point-of-Issue Method for Detection of Bacterial Contamination in Platelet Concentrates. J Clin Microbiol 2011:48; 3475–3481.

17. Raffaele L, Spreafico M, Foglieni B. Performance of the Rapid Pan Genera Detection (PGD) System For the Point of Issue Screening of Platelet Concentrates for Bacterial Contamination. Vox Sanguinis (2011) 101 (Suppl. 1), p 56

18. Vollmer T, Hinse D, Schottstedt V, et al. Inter-laboratory comparison of different rapid methods for the detection of bacterial contamination in platelet concentrates. Vox Sanguinis 2012;103:1–9.

19. Buchholz DH, Young VM, Friedman NR, Reilly JA, Mardiney MR., Jr Detection and quantitation of bacteria in platelet products stored at ambient temperature. Transfusion. 1973 Sep-Oct;**13**(5):268–275.

20. Eder AF, Kennedy JM, Beth DA, et al Bacterial screening of apheresis platelets and the residual risk of septic transfusion reactions: the American Red Cross experience (2004-2006). Transfusion 2007 Jul;47(7):1134-42.

21. Burger R, Offergeld R. Determining the shelf life of platelet concentrates with the aim of reducing life-threatening septic transfusion reactions due to bacterial contamination. Bundesgesundheitsbl Gesundheitsforschung Gesundheitsschutz 2008; 51:1484.

22. Ruester B, et al. Routine bacterial screening in platelets with a generic 16S DNA NAT System on Zelos x 100 Platform and Bactiflow. Vox Sang 2012: 103 (s1);177 Abstract P-344.

23. Tomasulo, Peter. AABB workshop on secondary testing of platelet products, North Bethesda, July 2012

24. Tomasulo, PA, Wagner SJ. Predicting improvement in detection of bacteria in apheresis platelets by maintaining constant component sampling proportion.Transfusion. Published online: 31 JUL 2012
DOI: 10.1111/j.1537-2995.2012.03821.x