Association Bulletin #10-05 - Suggested Options For Transfusion Services and Blood Collectors to Facilitate Implementation of BB/TS Interim Standard 5.1.5.1.1

Date: August 19, 2010
To: AABB Members
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Re: Suggested Options For Transfusion Services and Blood Collectors to Facilitate Implementation of BB/TS Interim Standard 5.1.5.1.1

Summary

This bulletin was developed by the AABB Bacterial Contamination Task Force, in cooperation with the Blood Bank/Transfusion Service Standards Program Unit. It provides updated information about bacterial contamination in whole-blood-derived (WBD) platelets and options for detection that are in compliance with the BB/TS Interim Standard 5.1.5.1.1.

Association Bulletins, which are approved for distribution by the AABB Board of Directors, may include announcements of standards or requirements for accreditation, recommendations on emerging trends or best practices, and/or pertinent information. This bulletin contains recommendations, some of which support existing standards requirements.

Background

Association Bulletin 09-04 reviewed efforts to mitigate bacterial contamination in platelets and alerted the membership to the status of new assays designed, in part, for point-of-issue testing of WBD platelets.[1] It acknowledged that new approaches were required to address the recognized sensitivity and specificity limitations of then-currently used testing methods — primarily microscopic staining methods or measurement of pH or glucose. Association Bulletin 09-04 also stated:

"...At this time, transfusion services using uncultured WBD platelets should begin to consider their options. Transfusion services may consider working with their blood provider on the provision of pre-pooled WBD platelets tested with culture-based methods. Transfusion services may also want to consider new alternative methods under development (such as noted above)."

The requirement for bacteria detection in WBD platelets was explained as follows:

"...to promulgate an interim standard to require enhanced methods of bacterial detection in WBD platelets—either by specifically prohibiting the use of less sensitive methods such as pH or glucose, or by establishing a minimum sensitivity level for methods used to detect bacteria."

In January 2010, an interim standard was published for public comment. On May 3, 2010, Association Bulletin 10-02 was published to notify the membership of Interim Standard 5.1.5.1.1, with an effective date of January 31, 2011.[2] The new standard is as follows:

> **5.1.5.1** The blood bank or transfusion service shall have methods to limit and to detect or inactivate bacteria in all platelet components. Standard 5.6.2 applies.
> **5.1.5.1.1** Detection methods shall either be approved by the FDA or validated to provide sensitivity equivalent to FDA-approved methods.

This bulletin provides further information to facilitate implementation of Interim Standard 5.1.5.1.1.

Rationale

It is widely believed that septic reactions caused by bacterial contamination of platelets remain one of the most common serious infectious complications of transfusion.[3] Standard 5.1.5.1 requires efforts to limit and detect bacterial contamination in all platelet components. To meet this standard, apheresis platelets, constituting the large majority of platelets used in the United States, are nearly universally tested in collection facilities using culture-based quality control (QC) assays. In the last published National Blood Collection and Utilization Survey Report, 17% of platelet doses in the United States were from WBD platelets.[4] Until now, management of approaches to detect bacterial contamination in uncultured WBD platelets has been problematic because of the limited sensitivity of non-culture methods. A recent study has demonstrated that culture-based testing of prepooled WBD platelets manufactured from platelet-rich plasma using sample diversion have a bacterial contamination rate of 1:1036, 5.8 times higher than the rate for apheresis platelets prepared by the same collection organization.[5] This difference may be less apparent in some blood collection organizations, perhaps associated with the method by which WBD platelets are prepared.[6]

In November 2009, Verax Biomedical received clearance from the US Food and Drug Administration (FDA) to market its PGD® test to detect bacteria in WBD platelets prior to transfusion. The device was cleared previously for testing leukocyte-reduced apheresis platelets as an adjunct QC test. The current FDA-approved indication for the Verax PGD® test for WBD platelets includes detection of aerobic and anaerobic gram-positive and gram-negative bacteria in...

> *...(P)ools of up to six (6) units of leukocyte reduced and non-leukocyte reduced whole blood derived platelets that are pooled within four (4) hours of transfusion as a quality control test".*[7]

The test requires a minimum of approximately one half hour to complete, starting with setup and the initial reading after a 20-

minute incubation period. The instructions for use allow repeated reexamination within 60 minutes of sample addition for completion of a valid test. Data in the product information suggest this device can detect a broad range of contaminating bacteria in the range of 10^4-10^5 CFU/mL, with *Serratia marcescens* the outlier at 8.2×10^5.[7]

Due to the absence of suitable methods available at the time of adoption of Standard 5.1.5.1, detection methods such as pH or glucose testing and microscopic methods (eg, Gram's stain) had been accepted to meet Standard 5.1.5.1 for WBD platelets, despite sensitivity and specificity limitations. However, with the approval of the Verax PGD® test, a suitable method is now available. Therefore, the use of currently available methods for microscopy or measurement of pH or glucose no longer meets the requirements of the revised standard.

Options

Recommended options to meet the intent of Interim Standard 5.1.5.1.1 include the following:

- Point-of-issue use of Verax PGD® test on pools of up to 6 units of leukocyte-reduced and non-leukocyte-reduced WBD platelets that are pooled within 4 hours of transfusion.
- Use of prepooled WBD platelets tested with an approved culture-based QC test by the supplier.
- Use of apheresis platelets tested with an approved culture-based QC test by the supplier.
- Culture of aliquots from individual WBD platelet units destined for pooling.
- Use of approaches or methods that are not FDA-cleared but have been validated to be of equivalent clinical sensitivity to an approved assay may be an alternative to an approved test. Validations will be subject to review at the time of accreditation assessments.

The use of pools of WBD platelets within 3 days of collection of the oldest unit in the pool has been suggested as an alternative to testing. Validation of the clinical sensitivity of such an approach would be necessary to meet the requirements of Standard 5.1.5.1.1. However, because such a method would not constitute a method to "detect" bacteria, such a method also requires a variance approval from the Blood Bank/Transfusion Service Standards Program Unit.

The Verax PGD® test package insert indicates that the optimal time for sampling bacteria in leukocyte-reduced apheresis platelet units or WBD pools begins 72 hours after collection. However, testing earlier than 72 hours may also result in the detection of contaminated units if the bacteria have grown to sufficient levels. Therefore, early testing should be considered when another alternative is not available. In WBD pools that will be leukocyte reduced using a leukocyte reduction filter, optimal performance may be achieved if the Verax PGD® test is performed on the pool prior to filtration. However, if workflow or clinical constraints make testing before leukocyte reduction difficult, testing after filtration should be considered.

Implications for hospital transfusion services

Transfusion services that are currently distributing for transfusion platelets that have been tested using less sensitive methods of bacteria detection (including pH, glucose, or microscopy) will need to implement one of the above options to be in compliance with Standard 5.1.5.1.1. In other words, blood transfusion services will need either to obtain their platelets from a blood supplier who performs the testing required by Standard 5.1.5.1.1 or to perform suitable testing themselves to ensure adherence to this standard.

Urgent issuance or dispensing of platelets without a test for bacterial contamination, or while the test is in progress, remains acceptable as the "practice of medicine" if addressed in the facility's emergency release procedures.

The College of American Pathologists is considering similar recommendations for the transfusion services they accredit.

Agreements between hospital transfusion services and blood collection facilities

Because WBD platelets will have associated co-components (eg, red cells and possibly transfusable plasma), testing facilities using the Verax PGD® test should have policies to address notification of the collection facility in the event of a positive test result, so that the blood collector can make decisions in an expeditious manner as to whether to recall and quarantine co-components. To assist with these decisions and to fully characterize the result as true or false positive, testing facilities should also have policies for addressing whether confirmatory cultures will be performed on the pool and/or on individual residual platelet concentrate containers if available. These policies should be shared and a communication plan between the testing facility and the collecting facility should be formalized.

Agreements between transfusion services and collection facilities should contain language about whether or not bacterial contamination testing of platelets is performed by the collection facility. As a part of supplier qualification, transfusion services should obtain documentation regarding the bacterial contamination testing methods used by their supplier. The same also applies to collection facilities importing platelets from other facilities.

References

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