



Advancing Transfusion and
Cellular Therapies Worldwide

ASSOCIATION BULLETIN

#04-07

Date: October 14, 2004
To: AABB Members
From: Kathleen Sazama, JD, MD - President
Karen Shoos Lipton, JD - Chief Executive Officer
Re: Actions Following an Initial Positive Test for Possible Bacterial Contamination of a Platelet Unit

Summary

This Association Bulletin is intended to provide additional guidance to supplement Association Bulletins #03-12 and #03-10. In particular, this Association Bulletin provides standardized definitions for test results, addresses investigation of units identified as positive by a bacteria detection test and discusses the management of other components (“co-components”) associated with the same donation. Furthermore, guidance is provided to address situations in which 1) a positive test result is encountered only after the transfusion of the unit, and 2) a recipient develops culture-proven posttransfusion sepsis after receiving platelets that have all tested negative.

Please consult previous Association Bulletins for references to scientific articles on the subject of bacteria detection.

In compliance with standard 5.1.5.1 of the 22nd edition, *Standards for Blood Banks and Transfusion Services*, collection facilities and transfusion services are using various methods to detect bacterial contamination of platelets. Culture-based systems, cleared by the Food and Drug Administration for quality control, and surrogate methods (e.g., glucose and pH measurement) have been implemented in AABB-accredited facilities.

Recommendations

Standardized definitions

It is strongly recommended that the standardized definitions provided in the appendix to this document be used consistently by all facilities in their reporting of bacteria detection test results. Pertinent definitions excerpted from the appendix are used in several sections of this Association Bulletin.

A “test” is defined as any method implemented to comply with the AABB standard, whether by a culture-based or non culture-based method. If the initial test is positive (or, for surrogate tests, gives an abnormal result as defined by the facility's Standard Operating Procedure) it should be termed an initial positive. A **culture-based** test should be performed to confirm this initial positive result. In situations in which the platelet component has not been transfused, and in which there are no data available from an evaluation of the recipient,* the final result can then be classified as true positive, false positive, or indeterminate, according to the following definitions:

- Initial positive – positive or abnormal (out-of-range) initial test.
- True positive – positive on both initial and confirmatory test.**
- False positive *** – positive on initial test, negative on confirmatory test.*
- Indeterminate – positive on initial test with no confirmatory test performed or confirmatory test performed but cannot be interpreted.

* If data are available from confirmatory culture-based testing and recipient evaluation, the definition under Identification of a Suspect Unit (After Its Transfusion), *infra*, then applies.

** It is required that the confirmatory test be culture-based and be performed on a different sample than the blood culture bottle or other sample used for the initial test. For example, a sample source for the confirmatory test could be the original platelet component. A subculture of the initial positive culture is not an adequate sample for this purpose. If initial testing was culture-based, the confirmatory test can use the same method applied to the alternate sample source.

*** False-positive results may occur for several reasons, including contamination during inoculation and machine or reading error.

Evaluation of a Platelet Unit with an Initial Positive Result on a Culture-Based Test (Platelet Unit Not Transfused)

When the initial bacterial culture of a platelet unit is found to have a positive result, the unit and all co-components should be quarantined immediately. If a co-component (such as a Red Blood Cell (RBC) unit or the split of an apheresis platelet) has been transfused, the transfusing physician should be notified immediately so the patient can be monitored appropriately. It should be noted that organisms isolated from whole-blood-derived platelets may or may not be present in the associated RBC unit.

All initially positive units should be recultured in order to determine whether the initial result was a true positive. If the second culture is not positive, the presence of bacteria is not confirmed, and the test result is false positive. RBCs, Fresh Frozen Plasma, or Cryoprecipitated, anti-hemophilic factor, from the same donation may be released from quarantine. However, due to the greater risk of bacterial growth in platelet units, it is recommended that platelet units that are initial positive (and any associated split apheresis units) should not be transfused, even if the second culture is negative. If the second culture is positive, all co-components should be discarded; however, before discard, facilities could also consider culturing the co-component to obtain data for research purposes. If a co-component has been transfused, the second culture results for

the platelet unit (e.g., true positive or false positive) should be reported to the transfusing facility and the transfusing physician as soon as possible.

If not already identified from the initial isolate, the microorganism should be identified at the time of second culturing. Isolates should be saved for potential further investigation. The identity of the microorganism is important in assisting the blood collecting organization to understand the source of the bacterial contamination (skin contaminant vs donor bacteremia) and determine if improvements need to be made in its practices. Identification of the organism may also be important in determining whether donor notification will be required.

Culture-based methods are unlikely to be applied routinely to pools of whole-blood-derived platelets because of the current requirement that each unit be cultured prior to pooling, that each unit be leukoreduced, and the current storage limitation of the pool. However, if culture-based methods are widely adopted for this component in the future, all co-components associated with all of the donations in a positive pool should be quarantined until further culturing of the individual platelet units can be performed. A positive culture on an individual platelet unit would identify the contaminated unit, whereas negative cultures of individual units would be helpful in identifying those units not responsible for the pool's contamination.

Evaluation of a Platelet Unit with a Positive Result on a Staining Test

If staining techniques are used for bacteria detection, a positive result should trigger quarantine of co-components. The transfusing facility and the transfusing physician should be notified if a co-component has been transfused. The unit should be cultured to confirm the initial screening results, and the culture results should be used to classify the unit as true positive or false positive. Subsequent management of the unit and related components should proceed as indicated in the previous section of this bulletin.

Evaluation of a Platelet Unit with an Abnormal Result on a Surrogate Test for Bacteria Detection

Because no pH or glucose value can be established as an absolute determinant of platelet bacterial contamination, each transfusion service will need to validate its own cutoff level. Many factors affect the cutoff level, including the type of component, the preparation method, the concentration of platelets and leukocytes expected in the unit, the storage container, and the length of storage before transfusion. Because the specificity of these surrogate tests is poor, there is no recommendation to quarantine the co-components associated with platelet units that give abnormal results; this is left to the discretion of the individual facility. It is recognized that many facilities may elect to perform such quarantine.

If a platelet unit is found to have reduced pH and/or glucose, the unit should be cultured. If the unit has been received from an outside supplier and the surrogate testing is performed at the transfusing facility, the supplier and the transfusing facility will need to agree on who will perform this culture. If culturing is performed at the transfusing facility, positive results will need to be communicated to the supplier.

If the culture result is negative (i.e., no growth), no action need be taken on co-components (and any co-components quarantined at the discretion of the facility may be released). If the culture is positive, all co-components should be retrieved and discarded. However, before discard, facilities may also want to consider culturing the co-component to obtain data for research purposes. If a co-component has been transfused, the transfusing facility and the transfusing physician should be notified as soon as possible. The microorganism should be identified, and isolates should be saved for potential further investigation. As previously stated, identification is important for an understanding of the source of the bacterial contamination and for donor management decisions.

Identification of a Suspect Unit (After Its Transfusion)

On occasion, a patient will receive an apheresis or whole-blood-derived platelet unit or a pool of whole-blood-derived platelets subsequently found to be positive on initial bacterial screening. The appropriate medical management of these patients is viewed as the practice of medicine. The physician's management of the patient will depend on the underlying clinical status of the patient transfused, the response of the patient to the suspect transfusion, and the clinical judgment of the transfusing physician. At a minimum, prompt notification of the transfusing physician with all available information must be made according to local operating procedures either by the transfusion service or the facility performing the testing. A Gram's stain should be performed immediately on any retained portion of the unit to provide additional information about the nature of the contaminating microorganism. The microorganism should be identified and susceptibility testing performed promptly. All additional results should be reported to the transfusing facility and the transfusing physician as soon as possible. Additionally, the transfusing physician should assess the recipient and report findings to the transfusion service which, in turn, should report this information to its blood supplier. Direct communication between the medical director of the testing facility and the transfusion service medical director, and between either of these individuals and the transfusing clinician, is important to allow for optimal patient management decisions. Communication can facilitate appropriate clinical responses by providing basic information regarding the spectrum of microorganisms previously identified in positive platelet cultures to the clinician.

The minimal evaluation of an initially positive test result from a transfused platelet unit should include culture of any residual component, if available, to confirm the initial result. The evaluation should usually include blood cultures of the recipient, even in the absence of apparent sepsis, to be certain that clinically silent infections are not missed. The initial isolate, any microorganisms obtained from the residual component, and from the recipient, should be retained until the case investigation is completed. This permits detailed studies to determine if the micro-organisms are linked, should that be deemed necessary. Results of the recipient workup should be communicated to the medical director of the collection facility; these data will help determine the significance of the initially positive test result.

When data from the confirmatory culture-based testing of the transfused platelet unit and from the evaluation of the recipient are available, the following definitions should be used to classify the test results.

- Initial positive – positive or abnormal (out-of-range) initial test.
- True positive – positive on initial test **and either**: 1) the remaining available sample of the unit is positive by confirmatory test* **or** 2) the recipient has posttransfusion sepsis verified by positive culture.
- False positive – positive on initial test **and both** 1) the remaining available sample of the unit is negative by confirmatory test* **and** 2) the recipient **has no** clinical or microbiological evidence of posttransfusion sepsis.
- Indeterminate – other combinations of component and recipient results.

* It is required that the confirmatory test be culture-based and performed on a different sample than the blood culture bottle or other sample used for the initial test. For example, a sample source for the confirmatory test could be the original platelet component. A subculture of the initial positive culture is not an adequate sample for this purpose. If the initial testing was culture-based, the confirmatory test can use the same method applied to the alternate sample source.

Posttransfusion Sepsis in Recipient(s) from Units that Are Negative by Bacteria Detection Tests

Transfusing physicians should continue to evaluate all transfused patients with onset of signs or symptoms consistent with bacteremia or sepsis for septic transfusion reactions. This evaluation should occur even in the absence of notification of a positive initial bacteria detection test result because the rate of false-negative results for each of the various testing methods is not known. If the recipient is proven to have bacteremia, the residual volume from the transfused platelet unit(s), if available, should be cultured (or cultured a second time, if the initial test was culture-based). Results should be classified as follows:

- False negative – negative on the initial test but the remaining available sample of the unit is positive by confirmatory test. The same microorganism should be isolated from the component and the recipient. To the extent possible, other sources of bacteremia (e.g. infected indwelling catheter) should be excluded.
- Indeterminate – negative on the initial test and no confirmatory test obtained on the transfused platelet component.
- True negative – negative on the initial test and the remaining available sample of the unit is negative on confirmatory culture-based test.

If a false negative result is documented, co-components from the same donation should be retrieved. If a co-component has been transfused, the transfusing physician should be notified.

Appendix 1: Surveillance Case Definitions (Incorporated in Text)

A “test” is defined as any method implemented to comply with the AABB standard, whether by a culture-based or non-culture-based method.

These definitions apply in any of the following circumstances:

- ✓ When the component has not been issued.
- ✓ When the component has been issued and transfused.
- ✓ When the component has been issued based on a negative initial test and the recipient developed posttransfusion sepsis confirmed by a positive culture.

1. Initial positive

- Positive or abnormal (out-of-range) initial test.

2. True positive

- Positive on both the initial test and a confirmatory test.*
- Positive on the initial test, the unit was transfused **and** *either of the following occurs*:
 - The remaining available sample of the unit is positive by confirmatory test*
 - The recipient has posttransfusion sepsis verified by positive culture.

3. False positive**

- Positive on the initial test, negative on a confirmatory test.*
- Positive on the initial test **and** *both of the following occur*:
 - The remaining available sample of the unit is negative by confirmatory test*
 - The recipient **has no** clinical or microbiological evidence of posttransfusion sepsis.

4. Indeterminate

- Positive on the initial test and either no confirmatory test was performed or the confirmatory test results could not be interpreted.
- Negative on the initial test, no confirmatory test was performed on the transfused platelet component, and recipient shows evidence of posttransfusion sepsis.
- Other combinations of component and recipient results in situations where the component has been transfused.

5. False negative

- Negative on the initial test but the remaining available sample of the unit is positive by confirmatory test* after the component has been transfused to a recipient who develops culture-proven posttransfusion sepsis. The same microorganism should be isolated from the component and the recipient. To the

extent possible, other sources of bacteremia (e.g., infected indwelling catheter) should be excluded.

6. True negative

- As part of an investigation of reported posttransfusion sepsis, the unit tests negative on the initial test and the remaining available sample of the unit is negative by confirmatory culture-based test.

* It is required that the confirmatory test be culture-based and be performed on a different sample than the blood culture bottle or other sample used for the initial test. For example, a sample source for the confirmatory test could be the original platelet component. A subculture of the initial positive culture is not an adequate sample for this purpose. If the initial testing was culture-based, the confirmatory test can use the same method applied to the alternate sample source.

** False-positive results may occur for several reasons, including contamination during inoculation and by machine or reading error. All are included under this heading for the purposes of these definitions.