



Advancing Transfusion and
Cellular Therapies Worldwide

Rapid Tests for Detection of Bacterial Contamination of Platelets

Blood Products Advisory Committee, March 9, 2006

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AABB strongly supports development of rapid, sensitive and specific non-culture assays to detect bacterial contamination of platelets, using an approval scheme that does not unduly delay their licensure. Our most urgent need is for technology(ies) to replace the insensitive, non-specific and unregulated surrogate methods such as pH and glucose dipsticks, being used to test platelets from whole blood. Second, we must agree on an estimate of the sensitivity required to prevent or substantially reduce residual episodes of clinical sepsis and infection that continue to occur even after implementation of the AABB *Standard* requiring methods to detect and prevent bacterial contamination.

There is no agreed upon sensitivity standard for rapid tests performed shortly before platelets are issued for transfusion, but there is informed opinion that, when used as a pretransfusion test in the hospital blood bank for the goal of preventing clinical sepsis, the benchmark should be in the range of 10^3 – 10^4 CFU/mL.

There is broad understanding that rapid tests now in development will not have analytic sensitivity equivalent to culture-based tests if the new assays are used early during storage before time for bacterial proliferation sufficient for detection. When used later, especially in the transfusion service at the time of distribution for transfusion, rapid tests should be able to identify units in the target range and prevent adverse clinical events.

The FDA must find a regulatory scheme that is not unreasonably constrained by consideration of the current culture-based tests as “predicate devices.” It is known that some bacterially contaminated platelet units may be culture negative (i.e. false negative) using approved quality control devices; some estimates suggest that such negative culture results may occur in up to 25% of bacterially contaminated units. The initial utility of rapid tests will be for use just prior to transfusion to detect units falsely negative or untested by culture. Furthermore, as surrogate testing methods may detect only a minority of contaminated units (perhaps as few as one-third: *Transfusion* 2005;45:1133-7.) licensure of rapid tests for use immediately before transfusion will improve transfusion safety in comparison to current insensitive and nonspecific approaches to testing platelet pools derived from whole blood. Reasonable sensitivity and the expected

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specificity of rapid tests would, we suspect, represent a marked improvement for prevention of clinical events.

A kinetic approach as outlined by FDA can be reasonable if a developer seeks approval for a QC indication similar to the current culture based systems, but emphatically not for an indication as an adjunct to culture to be used near the time of issue for transfusion. The suggested approach seems likely to hamper development of the latter approach, resulting, for example, in unneeded delay in implementation of methods to test platelets from whole blood. We recommend that the FDA seek an alternate route to labeling rapid tests for this specific indication. A possible approach can be to establish the performance characteristics of a rapid test based on serial dilutions of a spiked unit.

For the standard quality control indication, demonstration in a parallel clinical study that the applicant test(s) can detect contaminated or spiked units that are identified by currently licensed systems at a given time point seems a reasonable criterion. For example, if a unit is spiked with 1 CFU/mL at collection, stored for 24 hours, inoculated into the predicate and applicant systems and detected after 24 hours in both systems, they might be considered equivalent.

In summary, the most urgent uses for the kind of assays under consideration are to replace current surrogate approaches widely used for testing platelets derived from whole blood and known to be both insensitive and nonspecific. Approval of rapid tests offers the opportunity for pretransfusion testing of platelets from whole blood to prevent a proportion of residual platelet associated sepsis. Accordingly the approval criteria should not require equivalence of the new approaches to culture based testing, but rather should be based on an agreed upon sensitivity that will accomplish the clinical goal. Approval for a more standard quality control indication should likewise demonstrate focus on the prevention of clinical sepsis without necessarily insisting on a single approach.

AABB is an international association dedicated to advancing transfusion and cellular therapies worldwide. Our members include 1800 hospital and community blood centers, transfusion and transplantation services and 8000 individuals involved in activities related to transfusion and transplantation medicine. For over 50 years, AABB has established voluntary standards and inspected and accredited institutions. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. AABB's highest priority is to maintain and enhance the safety and availability of the nation's blood supply.

The AABB Interorganizational Task Force on Bacterial Contamination of Platelets is composed of experts representing both transfusion services and donor collection facilities from AABB, America's Blood Centers (ABC), American Red Cross (ARC), and DoD, with liaisons from various government agencies. This task force has been instrumental in providing guidance concerning the implementation of AABB's Standards with regard to bacterial detection.