

**STATEMENT OF THE AMERICAN ASSOCIATION OF BLOOD BANKS
BEFORE THE BLOOD PRODUCTS ADVISORY COMMITTEE**

Leukocyte Reduction Guidance

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The American Association of Blood Banks (AABB) is the professional society for over 8,000 individuals involved in blood banking and transfusion medicine and represents approximately 2,000 institutional members, including blood collection centers, hospital based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.

At this time, the AABB is not proposing specific quality assurance measures. Instead, we would like to highlight some parameters that the AABB believes must be considered by the FDA before arriving at recommendations for leukoreduction.

First, terminology must be clearly defined. In discussions between experts in statistical evaluation on the AABB Standards committee and the FDA, it is clear that the blood banking community did not understand certain terminology contained in the draft FDA guidance. The FDA guidance discussed use of 'tolerance bounds,' but the blood banking community generally interpreted this as a confidence interval. There is a great deal of difference between these two parameters, including the number of leukocyte-reduced units that would require direct quality control testing.

Second, requirements should be set based on clinical relevance of requirements, not process capability. FDA must evaluate the available clinical data for the intended use of the product. Three leading benefits for the use of prestorage leukocyte-reduced blood products are the reduction of risks of febrile non-hemolytic transfusion reactions, alloimmunization to platelets, and transfusion-transmitted CMV. There are numerous studies of these indications that may be interpreted to achieve these benefits at a cutoff of $<5 \times 10^6$. There is little clinical evidence that the proposed reduction of the specification limit or standard for WBC residual content in blood products to $<1 \times 10^6$ WBC would have measurable benefits with regard to these endpoints.^{1,2,3,4,5,6}

Third, technological capabilities for measurement methods must be considered. For example, manual counting methods are widely used for determining the number of residual WBCs in a leukocyte-reduced product. Unless automated methods are widely available, direct quality control of large numbers of units may not be practical. Even when automated counting methods are available, the additional steps involved in collecting the sample for counting, and the necessary record keeping will introduce additional complexities. Measurement of red cell recovery is even more difficult.

Fourth, the technical ability to achieve the proposed endpoints must be considered. In the recently published VATS (Viral Activation from Transfusion Study), Figure 22 and Table 2 demonstrate that 1-22% of filters currently used for prestorage leukoreduction would not have met the proposed standard.⁷ In light of the markedly increased number of QC measures that would be required upon encountering each failure to achieve the $<1 \times 10^6$ cutoff, these data predict that the resultant QC requirement increase could be truly massive.

Fifth, requirements should not be set based on comparison to tests that are not clearly considered to be a “gold standard.” There are numerous tests for CMV and the true sensitivity and specificity of these assays is not known. The use of various tests across the US is also not known and is not easily determined. The rate of transfusion-transmitted CMV is reported to be 1-4% in antibody screened units.^{8,9,10} Thus, requiring CMV testing for all leukoreduced units will not eliminate CMV transmission. BPAC should also be aware that the use of leukoreduced units to prevent CMV transmission is already a standard of practice in a number of facilities.

The AABB encourages the FDA to continue to evaluate the use of statistical quality control in blood and blood components, and will assist the FDA in any way possible. However, we anticipate that the FDA will consider the impact on both the blood collection facility and the transfusions service, and will set requirements that will not be unnecessarily burdensome, will be technologically feasible, and will contribute to the effectiveness and safety of blood components. We must not lose sight of the ultimate goal — to provide the patient with the needed transfusion component that is safe and effective.

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