

January 3, 2006

Division of Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Reference: "Collection of Platelets by Automated Methods" Docket No. 2005D-0330.

While we agree with many of the proposed recommendations for collection of platelets by automated methods, we feel there are some specific issues that need to be re-evaluated. We have initiated collecting data to support some of our proposed changes; however the data is not yet available. We will submit a summary of the data as soon as we are completed with the collection and analysis. Thank you for your consideration of our comments in formulating the final requirements.

III. Donor Selection and Management (A. Donor Selection)

1. Please clarify the intent of the requirement to obtain a pre-donation WBC count. The document states that the collection facility should evaluate the donors WBC count to ensure that the "laboratory values are acceptable under the manufacturer's directions for use" however we are unaware of any manufacturer's directions related to a pre-donation WBC count. For example, Gambro BCT does not define a maximum WBC for the Trima Accel.
2. Please ensure consistency between the proposed recommendations, the AABB Standards, and the uniform Donor History Questionnaire (DHQ). Medications and the length of deferral listed are inconsistent as follows:
 - Aspirin (ASA) / ASA containing drugs are currently 36 hours which is inconsistent with the 5 day deferral listed in the document.
 - Non-steroidal Anti-inflammatory Drugs (NSAIDS) are no longer a concern per the AABB which is inconsistent with the 3 day deferral listed in the document.

In addition, we recommend that both Plavix and Ticlid be added to the uniform medication deferral list.

III. Donor Selection and Management (B. Donor Management: 2. Donation Frequency)

3. We agree that a donor should undergo no more than 24 Platelet, Pheresis collections in a 12-month period; however we disagree with the limitations imposed on the total number of platelet components collected in a 12-month period. The collection of a single, double, or triple component should be based on the instrument settings and the donor's pre-donation platelet count. To our knowledge there is no published data to support limiting the number of double and

triple components collected from a donor. If there is data please provide references. Donors must undergo either pre or post collection platelet counts with deferrals in the counts are less than 150,000. This protects the donors from developing thrombocytopenia. Arbitrary limits on the number of products collected and arbitrary deferrals without evidence do not add to the safety of this approach of qualifying donors based upon their platelet count.

III. Donor Selection and Management (B. Donor Management: 4. Total Volume Loss)

4. We recommend the statement on the total volume be changed to the following:

The total volume (excluding anticoagulant) of all blood components retained per collection of Platelets, Pheresis should not exceed 500 mL (600 mL for donors weighing 175 lbs or greater) or 15% the volume described in the labeling for the device, whichever is less.

III. Donor Selection and Management (D. Medical Coverage)

5. We feel the recommendation for requiring a qualified physician to arrive at the premises within 15 minutes is too restrictive. Current industry practice allows emergency medical care personnel to provide support to whole blood donor establishments and blood mobiles. Based on the current data, adverse reactions related to an apheresis platelet collection are less frequent than those experienced by whole blood donors. The Journal of Clinical Apheresis will publish a review article by Dr. Jeffrey Winters entitled "Complications of Donor Apheresis". This article addresses specific data related to the issue of donor complications. Attached is a link to the document <http://www3.interscience.wiley.com/cgi-bin/fulltext/110489478/PDFSTART>.

V. Component Collection and Management (B. Target Platelet Yield)

6. We disagree with establishing specific target yields. The requirements should require each establishment to validate their collection and component manufacturing procedures and establish acceptable targets based on their validation.

VI. Process Validation (B. Validation Protocol)

7. The performance qualification criteria stated is too prescriptive. For example, testing of 60 consecutive units seems excessive for a small donor center collecting less than 5,000 components annually; whereas, it might be appropriate for an establishment collecting more than 10,000 components annually.

The use of parametric measuring system (as recommended by Dumont, et al.¹) should be included as an alternative to the non-parametric method listed. The parametric measuring system allows less units to be counted (N=20 vs. 60) by using probability plots and confidence levels. These calculations can be done in computer-based programs. An excellent example of a customized program for platelet apheresis is the EZQC® program for statistical process control (Gambro-BCT, Lakewood, CO). The EZQC program allows non-statisticians to put their data from validation and quality control procedures into the program, and the program analyzes the capabilities of the system tested and process control after validation. Burgstaler, et al.², presents examples of its use. The use of parametric measurement systems would make universal leukoreduction far more feasible with less cost but still maintain assurance of compliance.

VII. Quality Assurance and Monitoring (A. SOPs and Recordkeeping: 1. Requirements)

8. Not all test or procedures used in donor acceptability have both a minimum and maximum value. For example, the donor's weight has a minimum however a maximum value is not defined.

Consider modifying the statement as follows:

Your written SOPs must include minimum and maximum values, where applicable for a test or procedure when it is a factor in determining donor acceptability (21 CFR 606.100(b)(2)).

VII. Quality Assurance and Monitoring (B. Donor Monitoring: 1. Platelet counts)

9. We agree that a pre-donation platelet count is critical to appropriate donor management. Consider modifying the requirements in this document to allow more flexibility for facilities that perform a pre-donation count and retain the restrictions (e.g. longer deferrals following double or triple product donation and elimination of the requirement for a post-donation platelet count) when a pre-donation platelet count is not available.

The statement, *You should review a donor's records before each donation to monitor the donor's ability to recover his/her baseline platelet count* is vague and unnecessary when a pre-donation count is performed. Define acceptance criteria for those who are able to perform a pre-count (150,000/uL).

VII. Quality Assurance and Monitoring (C. Component Testing: 2. QC Monitoring)

10. Describe the requirement for testing "different donors". Based on most component manufacturing processes, the identity of the donor is not used in selection of the component chosen for QC and is unknown to the component laboratory. Consider modifying the requirement to state:

Each month four units prepared from different donors must be tested at the end of the storage period for the platelet count, pH of not less than 6.0 measured at the storage temperature of the unit, and volume (21 CFR 640.25(b)(1)-(3)). We interpret four to be a minimum number to be tested, and testing "at the end of the storage period" to include testing at the time of issue.

X. Reporting Changes to an Approved Biologics License Application (BLA)

11. Consider eliminating this section from the document or simply reference the user to the current guidance document for reporting changes to an approved application. Duplicating this information is likely to cause confusion and can lead to errors when one document is updated and the other is not.

References:

1. (FDA advisory Committee on Blood Safety and Availability, ref. #31) Dumont LJ, Dzik WH, Rebullia P, Brandwein H and the members of the BEST Working Party of the ISBT. Practical guideline for process validation and process control of white-cell reduced blood components: Report of the Biomedical Excellence for Safer Transfusion (BEST) Working Party of the International Society of Blood Transfusion (ISBT). *Transfusion* 1995; 36:11-20.
2. Burgstaler EA, Pineda AA. Platelet apheresis: instrumentation validation. *Transfusion Science* 1999; 21:153-161.