Blood Bank
of San Bernardino
and Riverside Counties

December 21, 2005

1341 5 DEC 28 P 1:14

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

RE: Docket 2005D-0330

Thank you for the opportunity to submit comments regarding the September 2005 draft guidance titled "Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods." These are submitted for consideration from the Blood Bank of San Bernardino and Riverside Counties, a licensed blood center that annually performs approximately 8500 platelet apheresis collections at 4 fixed site locations in southern California and distributes approximately 11,300 units of apheresis platelets to any of 33 hospital customers.

General Comments

The proposed guidance calls for more testing and expanded qualification criteria for plateletpheresis donors, new limitations on collection frequency and volume, requirements for medical director access that could necessitate recentralization of collections, new labeling requirements, and expanded process validation and quality control. It is difficult to imagine that, if implemented, the guidance requirements would not result in appreciably increased cost and reduced availability of apheresis platelets which have the potential to result in platelet shortages and increased use of whole blood-derived platelets as the alternative preparation. Since manufacturers do usually not culture whole blood-derived platelets for bacteria, such a shift could have the unintended negative consequence of increasing the likelihood of septic reactions following platelet transfusion. We are not aware of case reports or published experience from plateletpheresis programs that indicate that current practices have been unsafe for donors or produced unsuitable or ineffective products, so the impetus for introducing these new requirements and restrictions is not apparent.

Specific Comments on Sections as They Appear in the Draft Guidance

On DONOR SELECTION AND MANAGEMENT

Donor Selection

WBC Count. The guidance document requires that the WBC count be checked on a donor prior to the first donation, and the donor accepted according to the manufacturer's directions for use. However, our manufacturers do not have specific requirements on this parameter.

Drugs affecting platelet function. The 5-day waiting period after aspirin ingestion is longer than the waiting period endorsed by the AABB Uniform Donor History Task Force and accepted by FDA. We are unaware of any clinical experience that indicates that the 3-day waiting period has resulted in the collection of ineffective or sub potent product.

Deferral of donors who have taken Plavix or Ticlid for 5 and 14 days respectively appears to be based on the comments in the Physicians Desk Reference of the duration of time the clinical bleeding time is prolonged in patients taking therapeutic doses of these medications. If so, it

2005D-0330

C 14

384 Orange Show Road, P.O. Box 5729, San Bernardino, CA 92412-5729 • Tel. 909-885-6503 • Fax: 909-381-2036

should be appreciated that the bleeding time is known to be a poor reflection of the integrity of platelet function. A more scientific basis for deferral might be some multiple the half-life clearance of the drugs, which are respectively 8 hours and 4 days.

Most non-steroidal anti-inflammatory drugs have no effects on platelet function at all, and there is currently no requirement for deferral of donors who have taken these medications; we are unaware of any clinical experience that indicates that this practice has resulted in the collection of ineffective or sub potent product that would require the implementation of a 3 day waiting period for what will be a substantial fraction of potential donors.

Donor Management

Platelet count. The guidance states that, in the absence of a pre-donation platelet count on the day of donation (such as at a mobile site), a post-donation count from a previous donation may be used to set the target platelet yield. However that post collection platelet count is expected to be at the lowest point since it reflects donation loss before full splenic mobilization and re-equilibration after dilution. If this low, non-representative value is used to set the target platelet yield on a subsequent collection, the probable result will be an over-collection. We'd recommend use of historic pre-counts as a more accurate alternative if a same day pre-count is not available.

Donation frequency. In the preamble its state that the revised guidance is intended to incorporate information learned since the previous guidance. However the recommendation in the 1988 guidance allowed up to 24 donations in a 12-month period, and many of these donations resulted in double or triple collections using current instrumentation set in compliance with the manufacturer's guidelines. We are unaware of any data indicating that the current practice has resulted in any donor harm. It would seem that the recommended limit of 24 platelet components each 12-month period is unfounded.

Total volume loss per collection procedure. What is the rationale for limiting the total volume of all blood components to 500 (600 mL for donors weighing 175 lbs or greater), even if the device labeling allows more than this volume to be collected? Why would the volumes approved for each device not be sufficient to protect the safety of the donor?

Previously, similar volumes were listed as limits on plasma losses. Please clarify whether the entire volume of red blood cells, collected concurrently with a plateletpheresis product or products, is to be included in this total volume loss limit.

Medical Coverage

The donor reaction rates in the apheresis donation area are low, and no greater than in whole blood areas. We agree that a physician knowledgeable regarding the apheresis process should be available to provide detailed information about the collection procedure to those evaluating and treating apheresis donors who have had reactions. Blood center procedures should address accurate evaluation of complications to properly determine severity and emergency procedures must be sufficient to ensure transport and urgent medical care for potentially life-threatening injuries and reactions. But blood centers will not be equipped, staffed or have the necessary drugs to provide emergency medical care regardless of the level of skill of its physician. Requiring there to be a physician at or within 15 minutes of every building or mobile site would make 50 to 70% of our current apheresis collections locations unsuitable (an obvious impact on the availability of blood product).

On INFORMATION PROVIDED TO THE DONOR

Donation intervals. What is the purpose is requiring donors to be informed of the donation interval requirements? The information is complex and would require explanation of products and donation types that may not ever impact a particular donor (consider, for example, explaining that the waiting period after whole blood to donate platelets is 3 days and you can donate platelets again in another 3 days unless the first platelet collection turned out to be a double platelet in which case you would have to wait 7 days, but if the you had been redirected from whole blood to donate a double red cell, you would have had to wait 16 weeks to make the first platelet donation). We wish our donors to have the information necessary to assist us in determining their eligibility and to be informed when they are approaching the maximum numbers of components or loss volumes, but the information should be applicable to the situation and the donor.

On COMPONENT COLLECTION AND MANAGEMENT

Collection

Phlebotomy. The guidance requires that the "phlebotomy must be performed by a single uninterrupted venipuncture." Please clarify whether this is intended to limit the use of double needle kits, or if this would preclude a second phlebotomy using either an integral needle intended for this purpose, or a second phlebotomy using a needle attached via SCD after the initiation of the collection

On PROCESS VALIDATION

Product Performance Qualification (Component Collection)

Collection performance qualification criteria. Consecutive collections are not usually all singles, doubles or triples, but a mixture of these types of collections based on the donor eligibility criteria. Do we meet this requirement if we test all components from consecutive donations on each type of cell separator until a minimum of 60 platelet products have been tested with no failures?

Please clarify how to test "percent recovery" for methods of platelet leuko-reduction that do not involve filtration.

Testing throughout the dating period. What is the reason that product qualification at the beginning and middle of the dating period is written as a requirement, rather than an option? Since the white cell contamination is measured at the start of storage so that falsely low values due to cell deterioration are avoided, and other quality parameters (pH, platelet count, volume) become progressively worse during storage, there doesn't seem to be any value in testing throughout the dating period. In fact, the most rigorous confirmation of product integrity would be testing all components at the end of the dating period. Perhaps the intent was to require that *no more than* one third of collections were tested at the beginning of storage, or that *no less than* one third were tested at expiration?

On QUALITY ASSURANCE (QA) AND MONITORING

SOPs and Recordkeeping

Actual platelet yield. Saying that the platelet yield "should" be provided to the transfusion facility implies that the information should be on the label or a tie tag. Currently, transfusion facilities are invited to call for this information from our facility, but requests have been rare. What evidence is there that hospitals will use platelet content information with sufficient frequency to warrant labeling each component?

Labeling. The reference to 21 CFR 606.121 c 6 appears to apply to whole blood derived platelets (requiring that an acceptable volume range be added to every apheresis product label). Was this requirement intended? The current practice at this facility is to write the actual product volume on the product label.

Component Testing

QC Monitoring. Please specify that the term "at issue" means "issue" from a blood center to a transfusion service, and not "issue" from the transfusion service to the clinical care area. If this requirement is to be fulfilled by the manufacturer of the product (blood center), then the testing has to be completed at the end of the **blood center** storage.

Percent Component Retention. Please clarify how this requirement applies to "automated leukocyte reduced components."

Acceptance criteria. If a product is tested after expiration and found to be unacceptable, corresponding components from that unit will be unavailable for quarantine or testing. Are the corresponding components assumed to be non-conforming unless tested and if so, must their release be reported as BPD because of the possible (but not certain) non-conformance?

Thank you again for the opportunity to comment and request clarification on the draft guidance.

Sincerely,

Linda A. Chambers, MD

Linda A. Chambers, M.D.
Executive Vice President
Quality and Medical Affairs

LAC:lmr/8577