

January 3, 2006

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

**RE: Docket No. 2005D-0330, *Guidance for Industry and FDA Review Staff.*  
*Collection of Platelets by Automated Methods***

Dear Docket Officer:

Thank you for the opportunity to provide comments concerning the Center for Biologics Evaluation and Research draft guidance on the collection of platelets by automated methods. We wish to bring the following to your attention.

**ITEM III (A)**

The guidance lengthens the eligibility timeframe for aspirin to 5 days from the last dose and adds other platelet active drugs. However, the cited reference provides no peer reviewed scientific literature to support these suggested medication deferral changes. Please provide a more comprehensive rationale in the guidance or allow the current deferral timeframe to remain in place.

**ITEM III (B) 2**

The draft guidance establishes the donation frequency for plateletpheresis to be 24 individual components within a 12 month period. There is no explanation or rationale as to why this is a donor "safety" issue. Our center has years of cumulative experience that demonstrates donors can contribute single and multiple products 24 times per year with little or no effect on their qualifying platelet count, which is the primary qualifying parameter. Any donor who continues to present with an acceptable count should be permitted to undergo up to 24 plateletpheresis procedures without regard to the number of components. Even if the (unexplained) safety issue is intended to prevent excess plasma loss, the total loss for 24 collection events, in our experience, has only been approximately 7,200 ml for single SDPs and up to 12,500 for triples. This is far from the 14,000 ml loss permitted by regulation.

NYBC analyzed data for a donor base of 14,778 for a recent 12 month rolling period. We classified donors into 3 categories of high frequency defined > 24 products per year, intermediate frequency defined as 12 to 24 products per year, and first time donors. We compared their last platelet count of the 12 month period with their first count on record. There were no significant changes to the average predonation platelet counts for each grouping.

(2)

The guidance is unclear as to whether FDA will require both a pre and post count for each donation. To require a post donation platelet for every donation is a duplication of process and unnecessary since the apheresis device donation software “prevents” the collection from exceeding certain parameters that assure an adequate post donation count.

**ITEM III (B) 4**

The total volume loss is inconsistent with current plasma loss guidance and device manufacturer’s instructions. This restriction could unnecessarily restrict the ability to collect multiple apheresis products (triples, concurrent plasma, and red cells). There are a number of references (*see attachment 1*) that demonstrate sequential daily removal of significant plasma volume over weeks of time has no significant effect on the donor. Please explain the rationale for this restriction.

**ITEM III (D)**

This requirement appears to be based on a mistaken premise that the mere presence of a physician reacting within some timeframe will have a positive effect on donor safety. Apheresis is a safe, experience-rated procedure carried out by knowledgeable staff who are aware of the potential for donor reactions and carefully monitor donors in this regard. Apheresis staff are trained in CPR and will administer this procedure if required. Knowledgeable physicians are available at all times, via telephone, to provide advice on donor management. In the event a donor requires emergent care within an arbitrary 15 minute time span, emergency care workers (911) have a better chance than a blood center physician of arriving quickly, rendering appropriate care with the required devices/medications and will be in a position to provide subsequent care/transport should this be necessary. To presume otherwise is contrary to reality. Please delete this unnecessary requirement which will severely compromise our ability to collect apheresis products with no improvement in donor safety.

**ITEM IV**

This section (last bullet point) requires that the donor be presented with *a description of the number of Whole Blood, apheresis Red Blood Cells or plateletpheresis collection procedures and/or components that may be collected per year, and the donation interval for each*. Please clarify and indicate if a summary (overview) document will be acceptable. The extensive mix of potential procedures/frequencies is complex and may result in donor confusion over a subject that they trust blood center staff to administer and monitor.

(3)

**ITEM V (B)**

This section establishes target yields for double and triple products. While this suggestion is helpful, please explain why FDA is seeking to establish these specific limits as part of the guidance. There are multiple donor and machine variables, including historic data for each repeat donor, which will result in a successful double/triple product even if the target is lower than the one(s) specified in the guidance.

**ITEM V (D)**

Bullet point one establishes various performance qualification criteria. The description is confusing. Does the criterion apply to technology utilized throughout an organization, or must it be applied to each specific collection site? Please clarify and also explain why (given the subsequent requirement to sample all aliquots of double and triple units) testing 30 triple units could not, for example, provide PQ for all single/double/triple products. Reference is also made to 500 bacterial contamination tests with 0 “failures”. What constitutes a “failure”? Finding a (+) screen result is not a failure, especially if subsequent confirmatory testing is negative or the organism identified is not a skin contaminant. It is also unclear as to which 500 collections must be tested or if this is PQ for the bacterial testing process itself or for collections at each donor center.

**ITEM VI (D)**

Bullet point one establishes various performance qualification criteria. Please clarify the intent of validation by machine type and sample size for centers with multiple collection sites. Does the criterion apply to the organization as a whole or to each registered collection site? If this were to apply to individual collection sites in a complex multi-site organization this would become a difficult, error-prone task to coordinate within the laboratories serving the sites.

The product performance qualification also calls for testing a minimum of 60 consecutive single (30 for double and 20 for triple) collections. Please clarify the intent. Can the 60 consecutive products be any combination of the above, or do singles, doubles, and triples all need to be validated separately?

Reference is made to 500 bacterial contamination tests with 0 failures. What constitutes a “failure.” Finding a (+) screening result is not a failure, especially if subsequent confirmatory testing is negative or the organism identified is not a skin contaminate. It is unclear whether this validation is intended to be a validation of collection procedures or the bacterial testing methodology. Again, it is unclear which units should be tested

(4)

based on the validation intent and how this would apply to a large organization with multiple collection sites.

Bullet point six describes testing at specific times throughout the dating period. In combination with the requirement for the testing consecutive units, this requirement would remove significant sections of inventory without regard to available supply or demand and could significantly compromise the availability of product. It is again unclear how a large multi-site organization would be expected to perform validation, and would become a barrier to introducing valuable new technologies and software upgrades.

Bullet eight describes one clear non process failure. There are a number of factors that could cause product failure that are gray areas, i.e infiltration or the need to discontinue a procedure early could be a function of the phlebotomy, the donor's vein, or flow rates. Is this a process or non- process failure? If a first time donor presents and is run on a default setting which may result in a failure due to lack of an accurate count is this a process or non process failure?

Table 1. Collection Performance Qualification Criteria allows for no process failures within 60 units or 1 failure in 93. It is highly unlikely when implementing new technology that this can be accomplished for the platelet yield criteria. There are many factors that come into play for platelet yield and failures may occur that do not reflect either on the technology's ability to function or the operator's ability to operate the equipment. In addition, this requirement far exceeds the current QC criteria that 75% must be  $\geq$  or greater than  $3.0 \times 10^{11}$  and exceeds the current AABB standard that 90% meet the criteria. Although we agree that 75% is a low target, based on the precision of hematology equipment and the inability to always have a day of donation platelet count the criteria in Table 1 for platelet yield is problematic.

In several workshops an FDA representative has stated that if the nature of the failure is determined, even if it is a process failure, that QC could be accepted as passing. This is not reflected in the guidance document, and the current language suggests the opposite. This trend is disturbing and compromises the effectiveness of information presented at industry-attended workshops.

## **ITEM VII (A) 2**

This section indicates that the platelet yield from each collection should be "provided to the transfusion facility". The circular of information includes the minimum platelet count of  $3.0 \times 10^{11}$  for platelet apheresis. Therefore this requirement does not seem necessary. If this becomes a requirement would the labeling regulations be modified? Would we base the counts of the double and triple products on the parent bag product count or would we need to re-implement the testing of all split products? Please clarify the guidance if this is the intent.

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**ITEM VII (B) 1**

Please explain the rationale for selecting a platelet count <100,000/uL as a notification target. This value is not clinically significant in and of itself. Our center has accumulated data from apheresis procedures that shows no significant drop in counts over time utilizing 150,000/uL as a pre-collection criterion.

**ITEM VII (C) 2**

This section requires the monthly QC protocol to include testing of components *collected on each individual automated blood cell separator device*. This is unclear. Does it apply to each technology employed at a collection site or each individual device at a site? Individual devices are validated at the time of installation. Does the guidance refer to the fact that random monthly QC testing should ultimately cover all devices over the course of time? Please clarify, since a validated process should not require 100% testing each month.

Under *Acceptance Criteria*, reference is again made to a dual pH standard of > or = to 6.2 in the Guidance vs. the regulated criteria of > or = to 6.0. If there is compelling evidence to utilize the higher pH value please amend the regulation instead of recommending in a guidance document that does not have to be followed.

Thank you for the opportunity to comment on this docket. We have serious concerns that many of the proposed changes, while well intentioned, have no valid application to donor or product safety, will severely limit the availability of apheresis products and may cause a reversion to less efficacious random donor platelet products. In addition, the complexity of donor\donation requirements can not be supported by current computer tracking systems and would require manual work-around or significant reprogramming. Validation requirements seem excessive based on the fact all product for release must be qualified. This guidance will be an impediment to implementing new and valuable technology advances and the cost and disruption to industry is not supported by a demonstrated improvement in donor or product safety.

Sincerely,



Marvin Lessig, DO  
Medical Director  
New Jersey Blood Services

## Attachment 1

1. Transfusion 1980 20(4): 465-6
2. Transfusion 1981 21(3): 247-60
3. Transfusion Med 1993 3(1): 59-65
4. Vox Sang 1983 45(1):14-24
5. Vox Sang 1991 60(2):82-7
6. Vox Sang 2004 86(3):189-97
7. Vox Sang 2005 88(3): 189-95
8. Transfus Sci 1997 18(2):205-13
9. Dev Bio Stand 1980 48:279-86