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December 15, 2005

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

RE: Draft Guidance for Industry and FDA Review Staff. Collection of Platelets by Automated Methods

Dear sirs:

We are one of the world's leading academic institutions providing research-based clinical patient care. Each year we transfuse more than 180,000 units of blood components, of which approximately 40,000 are red blood cells, 130,000 are platelets and the remainder a mix of granulocytes, cryoprecipitate and fresh frozen plasma. Approximately 5,000 apheresis platelets, representing about 30% of all platelet transfusions, and 42,000 whole blood donations are collected in our donor center annually.

We offer the following comments/suggestions regarding the proposed guidance for collection of platelets by automated methods.

1. Page 3, line 2, and page 5, II. A. second paragraph and bulleted items. The deferral period for ASA-containing drugs is not based on current practice in any of the major US blood collection facilities and the reference is not from transfusion literature. In addition, the deferral interval stated for NSAIDS references the military listing of medications, Reference 9, which is not a peer-reviewed publication and does not represent an expert consensus. The suggested time intervals for donor deferral are much longer than the standard of practice. We use 48 hour deferral for both ASA-containing medications and for NSAIDS. This is the time interval approved by the FDA in the Uniform Donor History Questionnaire.
Requiring a longer deferral time for platelet donation will adversely impact our patients. We have observed no adverse patient effects from use of apheresis platelets collected 36 to 48 hours after ASA or NSAID ingestion. In addition, because of chronic platelet shortages, we have for years used no more than one platelet concentrate collected from a donor with ASA or NSAID ingestion within the past 36 hours per pool of platelets (7-10 concentrates) and have had no adverse patient outcome.
Most days, we struggle to provide the number and quality of platelets required by our cancer patients. Extending the deferral interval by even 12 hours will make the availability of platelets critical.
2. Page 6, first bullet. What is the reference for recommending a deferral of any platelet donor whose count is <150,000/ul?

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3. Page 6, item 2, second bullet. What is the scientific basis for recommending that the number of components collected (as opposed to number of collections performed) be limited to 24/year?
4. Page 6, item 2, fourth and fifth bullets. What is the scientific basis for recommending a prolonged interval between platelet apheresis procedures when a double or triple component collection has occurred?
In our donor population (frequently family members and friends), due to travel difficulties, we often find donors willing to donate 3-4 times in a 10 day period while they're in town to see their loved one/friend. Then the donors do not donate again for several weeks or months. Is there any data to suggest that collections must occur at fixed intervals throughout the year to protect donor safety?
5. Page 6, item 2, last bullet. What is the basis for the prolonged deferral time of 16 weeks for apheresis platelet donations from a donor who has donated double RBCs?
6. Page 7, item D. Medical Coverage. All staff are trained in CPR and must be ACLS certified to provide on-site emergency treatment for donors who experience reactions. Requiring that a physician be [constructively] on site at every location where apheresis platelets are being collected is simply not practical and may provide a false sense of security. Very few transfusion medicine physicians practice resuscitation skills on a regular basis. None to my knowledge have access to emergency transport vehicles.

We collect platelets on mobiles that may be as far away as 3 ½ hours from our center. At every site where apheresis collections are occurring, there are CPR-trained technical staff and/or nurses who are experienced and able to provide immediate interventions. There is a physician on call 24/7/365 who can be contacted by phone within 5-10 minutes to provide instructions for the uncommon situation when a donor is having a serious reaction. (This is very similar to in-patient care on nights and weekends.) With the network of EMTs and first responders throughout our region, they are much better prepared and equipped to deal with the serious reactions and are available much more readily than any single physician would be. It simply doesn't make sense to require the personal presence of a physician (who may exercise his/her ACLS skills once a year or less often) when trained technical and nursing staff and/or EMTs (or first responders) can handle the situation much more appropriately. EMTs arrive with resuscitation equipment and transport capabilities, and, more importantly, with daily exercise of the skills necessary to address the donor's needs.

7. Page 8, top of page, bullet 3. While it is probably a 'good idea' to inform donors about the matrix of donation (which products can be donated with what frequency over the course of a year), we would like to know the rationale for why this should be part of the donor education materials for Platelets, Pheresis (and not for whole blood or plasmapheresis donors).
8. Page 8, V. B. Although this section seems to be well-intentioned, an argument can be made that double components can be correctly collected with a target yield setting of 6.1, 6.2, 6.3, 6.4, ... 9.9 x 10¹¹; and triple components by settings of 9.2, 9.6, 11.5, etc. x 10¹¹. We request that this section be deleted from the final guidance document.
9. Page 8, V. C. Every device manufacturer has specific instructions regarding possible hemolysis. Requiring that an evaluation be done every time the tech sees "A red tinge to the plasma (prior to re-infusion to the donor)..." is too vague a criteria and may unnecessarily disrupt collections. We respectfully request that this section be removed from the final guidance document.
10. Page 9, VI. 3rd paragraph, 2nd bullet. What is the basis for requiring use of a pH meter when the requirement is only to show that the pH is >6.2?

11. Page 11, "Collection performance qualification criteria": Please clarify the following statements
 - a. "Perform bacterial contamination testing on 500 collections with 0 failures." What constitutes a bacterial contamination testing failure? Why 500?
 - b. "Determine the sample size selection before starting the qualification process. For example, if you test 60 and encounter a failure, you should not continue with the testing of an additional 33 components." What should we do?

Page 12, "Collection ..." continued

 - c. "Examples of non-process failures include positive bacterial contamination testing results from the collection from a donor with asymptomatic bacteremia." Why do you classify this as a failure?
 - d. Performance qualification for bacterial testing requires 0 failures out of 500, but Table 1 states a target of 99%/99% -- which would permit 4 failures out of 500. Please reconcile.
12. Page 14. The requirement for transfusing platelets within 4 hours after opening a container is predicated on the concern for bacterial contamination and contradicts the statement on page 22, Item C. which permits a 24 hour expiration "...if the integrity of the hermetic seal is broken after collection". Please reconcile.
13. Page 15, third bullet. pH measurement. Because the regulatory requirement is only that the pH be >6.0, why are you requiring that nitrazine paper should read in tenths of units? Isn't it more important that the paper accurately detect a pH of 6.0 or lower?
14. Page 17, B. 1. Second paragraph, last line. Because a post-donation platelet count can be used as the starting point for the next collection, the ability to review donor records before each donation to determine baseline platelet count recovery is problematic. Suggested rewording: "You should review a platelet apheresis donor's platelet count at least quarterly to identify any failure to recover his/her baseline platelet count."
15. Page 17, B. 2. The last sentence is redundant with the last statement in item B. 1. and can be deleted without losing any information.
16. Page 18. second bullet under Table 2. What is the basis for excluding a double RBC donor from apheresis platelet collection for 16 weeks?
17. Page 21, VIII. B., last paragraph. Please note that the 30-day rule may be inappropriate for WNV NAT (which probably should be performed on every donation because the mode of infection is by mosquito bite that can occur at any time).
18. Page 22. C. See item 14 above.

In addition, we have the following questions:

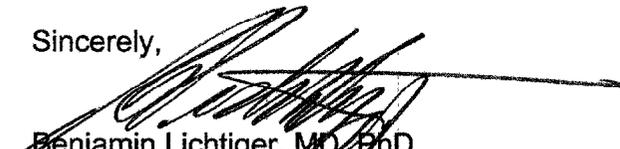
1. We are registered to produce Platelets, Pheresis. Will all currently licensed/registered establishments that have been approved for manufacturing of Platelets, Pheresis, be required to submit a BLA supplement upon finalization of this guidance?
2. Why are plasma-reduced apheresis platelets excluded from this guidance? What guidance should be followed in preparing such products?
3. Page 2, II. A. 3rd set of bulleted items: Why is concurrent collection of RBCs omitted?

We have the following comments regarding the document.

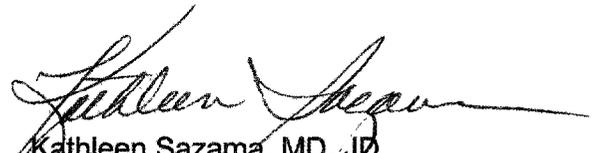
1. Page 2, II. A. paragraph 1, line 4. Platelets are used to treat patients who are not thrombocytopenic but in whom platelets may be being consumed at a rapid rate (e.g., disseminated intravascular coagulation) or are not functional for genetic or metabolic reasons. It is incorrect to state that platelets are only used in thrombocytopenic patients.
2. Page 2, II. A., last introductory paragraph states . "We have new information since the issuance of our previous guidelines". The first reference cited, Reference 5 (Murphy S. Platelet storage for transfusion. Seminars in Hematology), was published in 1985. Clearly the information in this publication was available at the time of the 1988 Platelets, Pheresis guideline. If the intent was to indicate that FDA has re-reviewed previously published data in light of the 2003 reference, then this statement could be revised to reflect that situation.
3. Page 3, II. B. Definitions: **Automated blood cell separator device** is defined as "A device operating on a centrifugal or filtration separation principle..." but **Apheresis** is defined as "Automated blood collection . . . [that] separates the components [only] by centrifugation . . ." This appears to be discrepant?
4. Page 3, II. B. Definitions: There is no FDA-approved device and no known method that can guarantee that a platelet product is "free from viable contaminating organisms." Please consider other language for the final guidance, such as "Testing intended to detect and identify bacteria present in platelets."
5. Wouldn't this be a good time to correctly identify these components as "Apheresis Platelets?"

Thank you for the opportunity to provide these comments. If any of these comments or suggestions are not clear, please contact us.

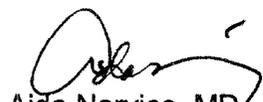
Sincerely,



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