

BLOOD PRODUCTS ADVISORY COMMITTEE
86th Meeting – March 9-10, 2006
Gaithersburg, MD

Issue Summary

Topic II. Public Comments on “Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods (Draft)”

Issue:

On September 30, 2005 FDA published a draft guidance entitled “Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods” which, when finalized, will supersede “Revised Guideline for the Collection of Platelets, Pheresis” dated October 7, 1988. FDA seeks advice from the Committee and public comment on several specific proposals in the document to which there have been comments to the docket.

Background:

This draft guidance is being developed to provide blood establishments and FDA staff with updated recommendations for the collection of Platelets, Pheresis by automated methods (plateletpheresis), to help ensure donor safety, and the safety, purity, and potency of Platelets collected by an automated blood cell separator device. The recommendations consist of a consolidation and clarification of relevant existing recommendations, and the introduction of several new recommendations to address the current technology. We are seeking the scientific advice of the Committee on FDA’s proposed recommendations in regard to 1) validation of microbial safety of blood collections; 2) the deferral period for platelet collection in donors who have taken platelet function inhibitors; and 3) the number of platelet components that may be collected safely from an individual donor within one year.

Discussion:

Item 1: Process Validation for Bacterial Safety

Process validation data establishes documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics. It is only upon acceptable completion of process validation that routine production and quality assurance (quality control testing and monitoring) begins. One element of process validation is the determination qualification of the product integrity, which includes bacterial testing to ensure adequacy of an aseptic process for blood collection and component processing. FDA’s draft guidance recommended that that process validation for microbial safety should include culture-based testing of 500 consecutive collections for bacterial contamination, with no more than one positive

test result. The rationale for this sample size is to assure with >95% confidence that the true bacterial contamination rate is less than 1%. Based on published literature (ref 1), the bacterial contamination rate for a conforming process should not exceed 1:3,000. At this level, the proposed validation test would be expected to yield a false result of non-conformance in fewer than 3% of determinations.

Comments to the docket indicate that blood centers consider the recommendation to test 500 consecutive collections to be excessive. The presenter will discuss the rationale for recommending that blood establishments test 500 consecutive plateletpheresis components during process validation.

Item 2: Duration of Medication Deferral for Platelet Inhibitors

Current industry practices have permitted platelets to be collected from donors with recent exposure to platelet function inhibitors. FDAs draft guidance contained recommendations that proposed limitations for collection of Platelets, Pheresis from donors taking medications that are platelet function inhibitors in order to ensure potency of platelets. As proposed, Platelets, Pheresis may be collected from donors:

- o 5 days from the last dose of aspirin (ASA) or aspirin containing drugs. ASA results in irreversible damage to the platelets. It is the position of the FDA that donors should be deferred for 5 days after the last dose of ASA in order to allow for ~60% replacement of normal platelets.
- o 3 days from the last dose of non-steroidal anti-inflammatory drugs (NSAIDs). It is the position of FDA that while NSAIDs are reversible platelet function inhibitors with a short-lived effect on the platelets, a conservative deferral is needed to address the fact that there are some NSAIDs which have a serum half live of 50 hours.

Comments to the docket recommend shorter deferral periods based on certain published literature. The presenter will discuss the information found in available published literature about the duration of effect of platelet function inhibition and the half-life of the drugs.

Item 3: Number of Platelet Components Collected per Year

The current guidance “Revised Guideline for the Collection of Platelets, Pheresis” dated October 7, 1988” allows for a maximum of 24 collections of Platelets, Pheresis per donor per year. However, this recommendation was implemented before the advent of double and triple component collections. Currently FDA believes that there are insufficient data to address safety concerns that are raised by large volume collections at the presently allowed frequency. With the goal of further protecting the safety of the donor in the absence of adequate safety data, FDA’s draft guidance recommended that:

- o A donor should undergo no more than 24 Platelet, Pheresis collections in a 12-month period

- The blood establishment should collect no more than 24 total Platelets, Pheresis components in a 12-month period. Two components collected from a double collection of Platelets, Pheresis and three components collected from a triple collection of Platelets, Pheresis would be counted as two components and three components respectively.
- The interval between each collection of a single Platelets, Pheresis should be at least two (2) days with no more than two procedures in a 7-day period
- The interval between collection of a double Platelets, Pheresis and any subsequent collection of Platelets, Pheresis should be at least 7 days
- The interval between collection of a triple Platelets, Pheresis and any subsequent collection of Platelets, Pheresis should be at least 14 days.
- A post-donation platelet count should be performed after each collection.

Comments to the docket suggest that the proposed criteria are too restrictive in that they will have a negative impact on component availability. The comments also state that more aggressive collection strategies have been utilized for years without evidence of adverse events.

Questions to the Committee:

1. Do BPAC members agree that bacterial testing of 500 consecutive collections is appropriate for validation of the aseptic process?

1a. If not, what sample size and acceptance criterion does BPAC suggest?

2. Do BPAC members agree that the information presented on the duration of effect of platelet function inhibition and half-life of the drug, support limiting collection to 5 days from the last dose of aspirin (ASA) or aspirin containing drugs, and 3 days from the last dose of non-steroidal anti-inflammatory drugs (NSAIDs)?

2b. If not, please comment on deferral periods that would be more appropriate.

3. Do the BPAC members agree that the proposed recommendations on donation frequency, interval between donations, and number of components collected per year are appropriate to protect the safety of the donor pending the availability of additional safety data on larger annual volumes of collection?

3b. If not, please comment on limits that would be more appropriate.

References

1. Blajchman MA. Incidence and significance of the bacterial contamination of blood components. Dev Biol 2002; 108: 59-67.