Guidance for Industry and FDA Review Staff

Collection of Platelets by Automated Methods

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I. INTRODUCTION

This guidance provides you, blood establishments, and FDA staff with revised recommendations for the collection of Platelets by automated methods (plateletpheresis). This guidance is intended to help you ensure donor safety and the safety, purity, and potency of Platelets collected by an automated blood cell separator device. For the purpose of this document, Platelets collected by automated methods and resuspended in plasma will be referred to by the product name "Platelets, Pheresis." We consider the recommendations in this guidance document to provide appropriate criteria for a biologics license application or supplement for manufacturing Platelets, Pheresis, and provide guidance on preparing a manufacturing supplement for Platelets, Pheresis under Title 21 Code of Federal Regulations 601.12
(21 CFR 601.12).

This guidance applies only to the following Platelets, Pheresis components:

- Platelets, Pheresis (single, double, and triple collections);
- Platelets, Pheresis Leukocytes Reduced (single, double, and triple collections); and
- Platelets, Pheresis or Platelets, Pheresis Leukocytes Reduced collected concurrently with Plasma, Red Blood Cells (RBCs), and/or Source Plasma.[1]

This guidance replaces FDA's "Revised Guideline for the Collection of Platelets, Pheresis" dated October 1988. Also, this guidance finalizes the draft guidance, "Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods" dated September 2005.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

[1] This guidance does not apply to plateletpheresis components collected concurrently during apheresis granulocyte collection procedures or plasma reduced apheresis platelets, which are not currently licensed products, or to platelets prepared from plasmapheresis as described in 21 CFR 640.22(b).

The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

If you have any questions about the effect of any portion of this guidance on a regulatory requirement, contact the Center for Biologics Evaluation and Research (CBER), Office of Blood Research and Review, Division of Blood Applications, at 301-827-3524.

II. DISCUSSION

A. Background

Plateletpheresis is the routine collection of platelets using an automated blood cell separator device, which results in the product Platelets, Pheresis manufactured from a high yield of platelets from a single donor. Transfusion of Platelets, Pheresis is effective for treating patients with platelet related insufficiencies, while limiting the recipient's exposure to platelets from multiple donors. In recent years, many improvements have been made in automated blood cell separator device technology, platelet storage stability, and blood cell counting methods, including:

- collection process efficiency;
- storage container characteristics; and
- accuracy of methods for determining a donor's pre-donation platelet count and component yields.

Automated blood cell separator devices are now capable of various plateletpheresis collection procedures including but not limited to the following:

- collection of double and triple platelet components obtained during a single procedure;
- use of in-process leukocyte reduction (Ref. 1);
- collection of concurrent plasma components (Ref. 2); and
- collection of concurrent RBC components (Ref. 3).

This document includes the following recommendations:

- Published research indicates that there is poor recovery of viable platelets stored at a pH of less than 6.2 (Refs. 4 and 5). Therefore, your process validation and quality control (QC) testing for Platelets, Pheresis should assure a pH at or above 6.2, to rule out a pH less than 6.2 on the date the product is issued or on the date the product expires (outdates). Note that we recommend that you adopt a stricter pH standard than that currently specified in 21 CFR 640.25(b)(2).
- You should include additional deferral criteria for donors of Platelets, Pheresis who have taken certain medications (see section III.A.) (Refs. 6, 7, and 8).

- To protect the safety of the donor, seven days should elapse after collection of a double or triple Platelets, Pheresis before the donor is eligible to donate Platelets, Pheresis again. In addition, first-time donors without a pre-donation platelet count should not undergo collection of a triple Platelets, Pheresis.
- Because of similarities between plateletpheresis and Source Plasma donation, you should follow the donor weight provisions for Source Plasma donors under 21 CFR 640.63(c)(6) (see Section III.A.).
- QC testing, as prescribed in 21 CFR 640.25(b)(1) through (3) requires that, each month, four units prepared from different donors be tested at the end of the storage period for platelet count, pH of not less than 6.0 when measured at the storage temperature of the unit, and volume. In addition, 21 CFR 211.160(b) requires that laboratory controls include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity.

We also note that bacterial contamination of blood components and associated transfusion risks is a continuing problem (Refs. 9 and 10). Bacterial contamination testing is a necessary part of process validation and quality assurance monitoring for Platelets, Pheresis.

B. Definitions

For purposes of the terms used in this guidance, the following definitions apply:

Actual platelet yield – The total platelet yield in the component, calculated by multiplying the platelet count of the sample times the volume of the component (platelet count x component volume = actual platelet yield).

Apheresis – Automated blood collection in which a device continuously or intermittently removes a small volume of whole blood, separates the components, collects certain components, and returns to the donor the uncollected remainder.

Automated blood cell separator – A device that uses a centrifugal or filtration separation principle to automatically withdraw whole blood from a donor, separate the whole blood into blood components, and return to the donor the remainder of the whole blood and blood components. The automated blood cell separator device is intended for routine collection of blood and blood components for transfusion or further manufacturing use.

Bacterial contamination testing – Testing conducted to determine whether a product contains viable contaminating bacteria.

Component – A part of a single donor's blood, such as platelets, separated from whole blood by physical or mechanical means. For Platelets, Pheresis, a component is a

transfusable product that may result from a single collection (resulting in one component), a double collection (resulting in two Platelets, Pheresis components), or a triple collection (resulting in three Platelets, Pheresis components).

Concurrent component – When a blood component, such as Platelets, is being collected during an apheresis procedure, a concurrent component is a different blood component (i.e., Plasma, RBCs) collected at the same time.

Dedicated donation – Platelets, Pheresis donated for a specific recipient.

Devices cleared or approved – Describes a device that has been cleared or approved by FDA pursuant to a 510(k) Premarket Notification (cleared device) or Premarket Approval Application (approved device). (See Title 21, United States Code, section 360c; Federal Food, Drug, and Cosmetic Act (FDCA), section 515 – Premarket Approval; and, FDCA, section 510(k)).

Donation frequency – Interval between a donor's collection procedures.

Process validation – Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality characteristics.

Qualification – A part of process validation that establishes confidence that a manufacturing device is capable of operating consistently (equipment installation qualification) and can be performed effectively and reproducibly (process performance qualification), and that the finished product meets all of the release requirements for functionality and safety (product performance qualification).

Residual White Blood Cell (WBC) count – The number of WBCs remaining in a Leukocytes Reduced component, calculated by multiplying the WBC count from a sample of the component times the volume of the component. In this document:

- references to residual WBC count testing apply when the Platelets, Pheresis will be labeled as Leukocytes Reduced.
- references to percent platelet retention apply to leukocyte reduction by filtration, provided there is access to a pre-filtration sample.

Rolling 12-month period – Continual assessment of a donor over a 12-month period. This is not a set 12-month period (i.e., calendar year).

Target platelet yield – The intended platelet yield programmed into an automated blood cell separator device, which may be based on the donor's platelet count and other factors.

Tolerance values – Minimum and maximum values (i.e., container volume; platelet concentration) described by the manufacturer as being acceptable. These values may also be described as specifications.

Weight/volume conversion – The total weight of the component minus the tare weight of the empty container divided by the specific gravity of the component equals volume of the component.

III. DONOR SELECTION AND MANAGEMENT

A. Donor Selection

Under 21 CFR 640.21(c), plateletpheresis donors must meet donor suitability criteria described in the biologics license application or supplement. These typically conform to donor suitability requirements (21 CFR 640.3) and recommendations applicable to donors of Whole Blood. In addition, we recommend:

- donor weight of at least 110 pounds (currently required for Source Plasma donors under 21 CFR 640.63(c)(6))
- Prior to the first donation, collect a sample for a platelet count.
- If you cannot test a sample for a platelet count prior to the first donation (for example, because the donor presents at a mobile collection site), you should collect a pre-donation sample and evaluate the donor's platelet count after the first collection.

You should not collect Platelets, Pheresis from donors who have ingested platelet inhibitory drugs recently enough to adversely affect platelet function in the product, or the safety of the donor. These recommendations include, but may not be limited to:

- Aspirin (ASA)/ASA-containing drugs/Feldene – two full medication free days prior to donation (Refs. 6 and 7)
- Plavix (Clopidogrel) and Ticlid (Ticlopidine) – 14 full medication free days prior to donation (Ref. 8).

When the drugs listed in this section are taken for a specific medical condition, donors should not discontinue taking drugs prescribed or recommended by their physicians in order to be eligible[2] to donate Platelets, Pheresis. However, we do not necessarily recommend deferral of such donors for all blood products, if the donors are in good health, and establishments may make eligibility determinations for donations of other products.

[2] We are using the terms "eligible" and "eligibility" in this guidance to refer to the donor suitability requirements described in 21 CFR 640.3 and 640.21(c).

B. Donor Management

1. Platelet Count

- You should collect a pre-donation sample from the donor for a platelet count. The device operator should enter that platelet count, or the one obtained immediately following initiation of the collection procedure, to more accurately set the target platelet yield parameters for each collection of Platelets, Pheresis. These steps should be consistent with the automated blood cell separator device manufacturer's directions for use.

- For any collection facility that cannot test a pre-donation sample for a platelet count (for example, a mobile collection site), you may use an average of previous historic platelet counts (as specified by the device manufacturer), or a default platelet count (either as recommended by the automated blood cell separator device manufacturer, or determined by using blood center specific values), to set the target platelet yield. You should not collect a triple Platelets, Pheresis from first-time donors who do not have a pre-donation platelet count available either prior to or immediately following initiation of the collection procedure. Concurrent components may be drawn if the donor meets eligibility requirements for those components.

- You should defer from donation donors whose platelet counts are less than 150,000 platelets/uL until a subsequent pre-donation platelet count indicates that the donor's platelet count is at least 150,000 platelets/uL.

2. Donation Frequency

To protect the safety of the donor:

- a donor should undergo no more than 24 Platelet, Pheresis collections in a rolling 12-month period.
- the interval between each collection of Platelets, Pheresis should be at least two days with no more than two procedures in a seven-day period.
- the interval between collection of a double or triple Platelets, Pheresis and any subsequent collection of Platelets, Pheresis should be at least seven days.
- the automated blood cell separator device should be set with a post-donation platelet count target of no less than 100,000 platelets/uL.

3. RBC Loss Prior to a Collection of Platelets, Pheresis

To protect the donor from significant RBC loss, we recommend that:

- you not allow a donor who has donated a unit of Whole Blood, a single unit of Red Blood Cells by apheresis, or a single unit of Red Blood Cells by apheresis concurrent with Platelets, Pheresis or Plasma in the previous 8

weeks to donate Platelets, Pheresis, unless the extracorporeal red blood cell volume during the Platelets, Pheresis collection is expected to be less than 100 mL (Ref 3).

- you not perform any collection procedure on a donor who has donated two units of Red Blood Cells by apheresis within the previous 16 weeks (Ref. 3).

4. Total Plasma Volume Loss Per Collection Procedure

The total plasma 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
- the volume described in the labeling for the automated blood cell separator device (this volume may be more or less than the 500 mL or 600 mL volume stated in the above bullet).

IV. INFORMATION PROVIDED TO THE DONOR

Under 21 CFR 640.22(c), the collection procedure must be as described in the biologics license application or supplement. As part of the collection procedure, Platelets, Pheresis donors should receive information about the collection procedure and its associated risks. You should provide Platelets, Pheresis donors with the same information that is provided to a Whole Blood donor[3], plus the following information specific to the platelet collection:

- a description of the procedure for collection of Platelets, Pheresis and its associated risks.
- information about potential side effects of the procedure including possible effects as a result of solutions and/or treatment to reduce side effects such as treatment with a calcium replacement. Examples of side effects include anticoagulant effects (tingling and/or nausea), hypovolemia (decreased blood volume), fainting, and any other side effect as described by the automated blood cell separator device manufacturer.
- information indicating that there are limitations to the number and types of components that can be donated per year.

V. COMPONENT COLLECTION

Improvements in collection of Platelets, Pheresis have enabled blood establishments to obtain from a single collection procedure one, two, or three Platelets, Pheresis component(s) (and concurrent collection of Plasma, Source Plasma and/or RBC components).

[3] Refer to FDA regulations and guidance developed by FDA on this topic and available on the FDA website. http://www.fda.gov/cber/blood/bldpubs.htm

Under 21 CFR 640.22(c), the collection procedure must be as described in the biologics license application or supplement. In addition, the phlebotomy must be performed by a single uninterrupted venipuncture with minimal damage to, and minimal manipulation of, the donor's tissue (21 CFR 640.22(d)). A sterile connecting device may be used as described in the manufacturer's directions for the apheresis collection set. The automated blood cell separator device must perform in the manner for which it was designed (21 CFR 606.60(a)). Accordingly, your collection procedures should be consistent with the Operator's Manual, directions for use, and/or manufacturer's specifications. Specifications identified by the manufacturer may include, but not be limited to, the donor's platelet count, weight, height or hematocrit; the minimum/maximum volume of the storage container; platelet concentration per uL in the storage container, or actual platelet yield. In addition, supplies and reagents must be used in a manner consistent with instructions provided by the manufacturer (21 CFR 606.65(e)).

VI. VALIDATION OF THE COLLECTION PROCESS

The Current Good Manufacturing Practice (CGMP) regulations described in 21 CFR Parts 210 and 211 contain the minimum requirements for methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing or holding of a drug to assure that the drug meets the requirements of the FDCA as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess (21 CFR 210.1(a)). These CGMP regulations also apply to Whole Blood and blood components (21 CFR 210.2(a), 211.1(b)) and supplement the CGMP regulations for blood and blood components contained in 21 CFR Part 606. As an element of CGMP, process validation "establishes documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality characteristics" (Ref. 11).[4] We recommend that establishing documentation of process validation include, but not be limited to, validation protocol development, installation qualification, process operator performance qualification, and product performance component qualification (Ref. 11).

Each device intended for the routine collection of Platelets, Pheresis must be cleared or approved by FDA for this purpose (see 21 CFR 864.9245). You should conduct validation of the collection process using each type of device used in your establishment prior to implementing routine collections.

In addition, your validation efforts should include the following manufacturing steps:

- cell counting
- pH measurement: we recommend that a pH meter or gas analyzer be routinely used rather than pH (nitrazine) paper.
- component weighing

[4] The requirement for process control is set forth in general terms in 21 CFR 211.100.

- sterile connecting method (Ref. 12)
- storage
- shipping

A. Equipment Installation Qualification

21 CFR 606.60(a) requires that equipment be observed, standardized and calibrated on a regularly scheduled basis as prescribed in the Standard Operating Procedures Manual and must perform in the manner for which it was designed. Upon initial installation, the automated blood cell separator device should be qualified as described in the Operator's Manual or manufacturer's directions for use.

B. Validation Protocol

An integral element of the performance and documentation of process validation is the development of a validation protocol. You should refer to FDA's "Guideline on General Principles of Process Validation" (Ref. 11) as an outline for developing your validation protocol. The validation protocol should include at least the following:

- a description of the equipment to be used
- minimum/maximum acceptable values for the Platelets, Pheresis collection and/or component as specified by the automated blood cell separator device manufacturer
  - total volume (after removal of samples for hematological testing and bacterial contamination testing), including per component (container) from double and triple collections
  - actual platelet yield
  - residual WBC count (if Leukocytes Reduced) for the collection and components (if multiple components are collected), and percent platelet retention when applicable
  - concurrent component volume (Plasma or RBC), if applicable
  - pH measurement
- manufacturer's specifications or recommendations for processing parameters (i.e., actual platelet yield and concentration, weight or volume collected)
- description of supplies used in the collection (e.g., collection/storage containers, anticoagulants, etc.)
- failure investigation criteria
- personnel training criteria
- standard operating procedures for performing each element of the collection process
- documentation of the validation protocol criteria (all of the above)

C. Process Performance Qualification (Operator)

Each person engaged in the collection of Platelets, Pheresis must have adequate education, training, or experience to assure competent use of the automated blood cell separator devices involved (21 CFR 211.25(a)). Establishments must maintain applicable proficiency test results (21 CFR 606.160(b)(5)(v)).

We recommend that personnel training include the successful, consecutive, performance under supervision of an appropriate number of procedures, as defined by your facility. These procedures should result in the collection of Platelets, Pheresis meeting relevant component specifications.

D. Product Performance Qualification for Component Collection Process

Various mechanical and biological factors may influence the plateletpheresis collection process (i.e., the optical qualities of a donor's plasma, the donor's platelet count and platelet size, vascular access, and procedure duration) (Ref. 14). The objective of collection performance qualification is to verify that the automated blood cell separator device performs according to the manufacturer's claims when used, and through appropriate testing establishes confidence that the finished product produced by the specified process meets all release requirements for functionality and safety (Ref. 11). All components collected during the validation process can be released for transfusion provided that they meet minimum specifications as defined by the manufacturer, are labeled appropriately, and are otherwise suitable.

Process performance qualification should include testing for the actual platelet yield, pH, and volume; residual WBC count and percent platelet retention (for Leukocytes Reduced components) (See Table 1). We recommend that you assess the following at each collection site:

- **actual platelet yield** (platelet count multiplied by the volume):
  - determine actual platelet yield at collection.
  - follow the platelet pre-donation count recommendations in section III.B.1., and set an appropriate target platelet yield as recommended by the automated blood cell separator device manufacturer to maximize the likelihood that each transfusable component contains $\geq 3.0 \times 10^{11}$ platelets and the target collection type (single, double, triple) is achieved.
- **pH** as a measurement of quality after storage:
  - determine pH on the date the product is issued or on the date the product expires (outdates).
  - each transfusable component should have a pH ≥ 6.2
- **percent platelet retention**
  - perform when the automated blood cell separator device or filtration method is first put into use at an establishment and/or as recommended by the automated blood cell separator device manufacturer.
  - if leukocytes are reduced by filtration and there is access to both a pre-filtration and post-filtration sample, calculate percent platelet retention using pre- and post-filtration volume and cell content.
- **residual WBC count**:
  - perform when the automated blood cell separator device or filtration method is first put into use at an establishment and/or as recommended by the automated blood cell separator device manufacturer.

- perform within 48 hours of collection or per the manufacturer's directions for the cell counting methodology used (Ref. 15).
- conduct testing on the collection (parent container) and on the individual components from double and triple collections

- **volume**:
  - determine the volume after removal of samples for testing (i.e., cell count, bacterial contamination testing).
  - fill each storage container consistent with the manufacturer's minimum/maximum specifications.
  - equilibrate storage containers for double or triple collections $\pm$ 10 mL, or per the manufacturer's directions if different.

You also should qualify devices and perform failure investigations as follows:

- **Devices**:
  - complete product performance qualification for apheresis devices from different manufacturers, and for each model.
  - obtain data from all automated blood cell separator devices at each site for initial product performance qualification. If additional devices of the same model are added at the facility after qualification, include qualification data in monthly QC only.
- **Failure investigation**: Conduct an investigation for all component qualification failures, and when appropriate, initiate corrective action and follow-up measures (see 21 CFR 211.192; 606.100(c)). We understand that some failures may occur due to conditions **not** resulting from a failure of the process (e.g., automated blood cell separator device failures, donor reactions). In addition, you should:
  - investigate as qualification failures residual WBC counts that exceed the following:
    - single collection: $\geq 5.0 \times 10^6$ (collection)
    - double collection: $\geq 8.0 \times 10^6$ (collection), **and** $\geq 5.0 \times 10^6$ (either or both components)
    - triple collection: $\geq 1.2 \times 10^7$ (collection), **and** $\geq 5.0 \times 10^6$ (one, two or all three components).

  - However, each transfusable component from a double or triple collection of Platelets, Pheresis may be labeled as Leukocytes Reduced provided the residual WBC count on the component is found to be $< 5.0 \times 10^6$. investigate collections that fail to meet the percent platelet retention, if performed. However, the component may be transfused if the actual platelet yield is determined subsequent to filtration, and the component is labeled appropriately.

Variation in the actual platelet count might be due to the platelet counter used and the type of platelet count used at the time of collection (pre-donation or historic average). However, you should select a statistically sound sample size, based on 95% confidence that 75% of components (platelet yield) will meet the recommended results (see Table 1). For pH and recommended residual WBC count, you should select a statistically

sound sample size, based on 95% confidence that 95% of components (pH) or collections (residual WBC count) will meet the recommended results. Using the binomial statistic for example, a minimum of 60 components/collections should be tested, with zero process failures (93 tested with one process failure, 124 tested with two process failures, etc.) to qualify the process. Determine the sample size selection before starting the qualification process. For example, if you test 60 samples and encounter a failure, you should not continue with the testing of an additional 33 components. If you select a sample size of 93 and encounter a failure during testing, you may continue to test but there should be no additional failures. Similarly, if you select a sample size of 124 and encounter two failures, you may continue to test, but there should be no additional failures.

Table 1. Product Performance Qualification Criteria for the Platelet Component Collection Process

Test	Recommended Results	Target[1]	Allowable Process Failures[2] to achieve recommended results for a set of N tests[3]		
Actual platelet yield of transfusable component	$\geq 3.0 \times 10^{11}$	95%/75% *	N=11 **	N=18 **	N=23 **
			0	1	2
pH	≥ 6.2	95% / 95% ***	N=60	N=93	N=124
			0	1	2
Percent component retention	$\geq$ 85% component retention if performed ****	95%/95%	N=60	N=93	N=124
			0	1	2
Residual WBC count *****	Single collection: $< 5.0 \times 10^6$	95% / 95%	N= 60 collections	N=93 collections	N=124 collections
			0	1	2
	Double collection: Collection: $< 8.0 \times 10^6$ or Components: $< 5.0 \times 10^6$	95%/95%	N=60 collections	N=93 collections	N=124 collections
			0	1	2
	Triple collection: Collection: $< 1.2 \times 10^7$ or Components: $< 5.0 \times 10^6$	95%/95%	N=60 collections	N=93 collections	N=124 collections
			0	1	2

[1,2] Process failures only; non-process failures should be excluded.

[3] Corrective actions for exceeding allowable process failures

- if you select a sample size of 11 and find one failure, 17 additional samples would need to be tested with no additional failures.
- if you select a sample size of 60 and find one failure, 91 additional samples would need to be tested with no additional failures. If you select a sample size of 93 and find two failures, 157 additional samples should be tested with no failures. If you select a sample size of 124 and find three failures, 127 additional samples should be tested with no failures.

* 95% confidence that greater than 75% of the components meet the standard.

** The sample size numbers can be used in a sampling plan that should be representative of products collected on each machine type in each facility.

*** 95% confidence that greater than 95% of the components meet the standard.

**** Or per the container/automated blood cell separator device manufacturer's specifications

***** The stratified recommended results should ensure that the individual transfusable units will be $< 5.0 \times 10^6$ even with a 25% error in equilibration of the volume for double and triple collections.

E. Re-Qualification/Re-Validation

- Exceeding the allowable **process** failures of the collection process qualification may indicate that the process is not in control. You must investigate and correct the source of this failure (see 21 CFR 211.192, 606.100(c)) and should repeat validation.

- The manufacturer may provide re-qualification requirements for the automated blood cell separator device to be followed.

VII. QUALITY ASSURANCE AND MONITORING

Quality assurance (QA) is the sum of activities planned and performed to provide confidence that all systems and system elements that influence the quality of the component are functioning as expected (Ref. 13). When this is demonstrated, the process is considered to be in a state of control. Whether a process is operating in a state of control is determined by analyzing the day-to-day process and the data for conformance with the manufacturer's specifications and for variability.

You must have a quality control (QC) unit that has the responsibility and authority to approve or reject all components, containers, closures, in-process materials, packaging material, labeling and drug products and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated (21 CFR 211.22(a)). Thus, the QC unit's responsibilities include the review of production records, and the review of complaints involving the possible failure of a product to meet its specifications. (See, for example, 21 CFR 211.22, 211.192, 211.198, 606.100(c)). Please refer to FDA's "Guideline for Quality Assurance in Blood Establishments" (Ref. 13) for developing a QA and Monitoring program.

A. Standard Operating Procedures (SOPs) and Recordkeeping

1. Requirements for SOPs

- An automated blood cell separator device must "perform in the manner for which it was designed" (21 CFR 606.60(a)) during the collection or processing of apheresis components. Written SOPs must be maintained and must include all steps to be followed in the collection, processing, compatibility testing, storage, and distribution of blood and blood components (21 CFR 606.100(b)). Therefore, you must have written SOPs for each step in the collection of Platelets, Pheresis.

2. Additional Provisions Applicable to SOPs

- **Adverse reactions:** You must have a written SOP for investigating adverse donor and recipient reactions (21 CFR 606.100(b)(9)). In addition, you should have a written SOP for managing a cardiopulmonary emergency or