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

any other adverse reactions associated with donation, containing steps for contacting physicians, obtaining an emergency rescue squad response, and transporting the donor to the hospital.

- **Hematocrit**: If the final platelet collection contains more than 2 mL of packed RBCs, you should attach a sample of donor blood to the platelet storage container for compatibility testing to prevent the possibility of an adverse reaction during transfusion. In addition, you should hold the Platelets, Pheresis collection prior to distributing as Leukocytes Reduced until a residual WBC count of the transfusable component can be determined and found to be $< 5.0 \times 10^6$.

- **Component volume**: You should describe how to process components in the event the volume exceeds the automated blood cell separator device manufacturer's specifications. In addition, the volume in the storage containers from double or triple collections should be within ± 10 mL of each other or per the manufacturer's directions if different.

- **Samples for QC:** Containers for QC samples should be attached to the component/collection set using a sterile connecting device, to ensure the maintenance of the closed system.

- **Actual platelet yield**: The platelet yield from each collection of Platelets, Pheresis should be available to provide to the transfusion facility.

- **pH measurement**: Accurate pH measurement is time dependent, and samples should be tested within 1 hour of sampling, or as suggested by the manufacturer of the pH measurement system. We recommend that a pH meter or gas analyzer be routinely used rather than pH (nitrazine) paper. However, if you choose to determine pH measurements with nitrazine paper, the selected paper should read in increments of one-tenth units, or it may provide inaccurate measurements.

- **RBC loss**: You must have a written SOP for your collection procedure, including in-process precautions to measure accurately the quantity of blood removed from the donor (21 CFR 606.100(b)(5)). You should calculate the donor's RBC loss, which may include the residual RBCs remaining in the apheresis collection set after a collection of or discontinued collection of Platelets, Pheresis; the extracorporeal RBCs remaining in event of no RBC rinseback; the RBC loss from collection of tubes for testing; and/or collection of a concurrent RBC. You should record such RBC loss in the donor's record, in a manner that allows tracking of cumulative RBC loss over time.

- **Bacterial contamination testing**: You must maintain written SOPs and include all steps to be followed in the testing of blood and blood components (21 CFR 606.100(b)). Bacterial contamination testing should be performed using a culture based methodology, and using your established procedures.

- **QC failures**: You must thoroughly investigate any unexplained discrepancy or the failure of a batch to meet any of its specifications (21 CFR 211.192). You should define appropriate criteria for retesting of components, testing of additional components, final labeling, and disposition of components that fail to meet specifications.

- **Failure investigations**: (see 21 CFR 211.192; 606.100(c)) The criteria to assess in the performance of a thorough failure investigation (including the conclusions and followup) should include, but not be limited to: donor characteristics or specifications; operation and or performance of the collection device; adherence to SOPs; lot numbers of reagents or supplies; sample collection, handling, storage or shipping; operator performance, training or competency; and cell counting instrument performance including shifts or trends in controls.

- **Manufacturer's performance specifications**: You should state the acceptable tolerance specifications for the volumes, platelet concentration, and/or actual platelet yield for each storage container as described by the manufacturer. You should have a procedure addressing the handling of components that do not meet the manufacturer's performance specifications (e.g., use in research or further manufacture).

- **Labeling**:
  - The final component volume stated on the label should be determined after removal of samples for platelet count determination, QC, and/or bacterial contamination testing.
  - Platelets, Pheresis for transfusion should routinely contain $\geq 3.0 \times 10^{11}$ platelets. When special circumstances warrant their use, Platelets, Pheresis components containing less than 3.0×10^{11} platelets should be labeled with the actual platelet content.

- **Component Storage**:
  - If Platelets, Pheresis are stored at 20 to 24 °C, you must maintain a continuous gentle agitation throughout the storage period (21 CFR 640.25(a)). You should describe how temperature and agitation will be monitored, and the disposition of platelet components that are not stored properly.
  - You must follow the automated blood cell separator device manufacturer's directions for use (21 CFR 606.60(a)). If sterile connecting an additional container(s) is necessary, use a container(s)

designed to achieve and protect a sterile conduit. Because of differences in container specifications, you should use containers from the same manufacturer.

3. Recordkeeping

All recordkeeping requirements of 21 CFR Part 606, Current Good Manufacturing Practice for Blood and Blood Components, Subpart I (Records and Reports); Part 211, Current Good Manufacturing Practice for Finished Pharmaceuticals, Subpart J (Records and Reports); and applicable provisions of 21 CFR 640.20 through 640.27, must be met.

B. Donor Monitoring

1. Platelet Counts

If the platelet count is known, you should notify your Medical Director when a donor has a post collection platelet count less than 100,000/uL, and you should defer the donor until his/her platelet count has returned to at least 150,000/uL.

Transient decreases in platelet counts have been reported in donors undergoing multiple collections of Platelets, Pheresis (Ref. 16). You should periodically review a donor's records to monitor platelet counts.

2. Adverse Reactions in Donors

Records must be maintained of any reports of complaints of adverse reactions regarding each unit of blood or blood product arising as a result of blood collection or transfusion and a thorough investigation of each reported adverse reaction must be made (21 CFR 606.170(a)).

3. Red Blood Cell Loss

- **Per collection**:
  - If the collection procedure needs to be discontinued for any reason before completion, and if the Operator's Manual allows, you should attempt to return RBCs to the donor.
  - Donor eligibility based on RBC loss (with or without RBC rinseback, and including all other types of donation) is described in Table 2.

Table 2: Recommendations for donor eligibility based on RBC loss per collection

Donor's Initial packed RBC loss	**Donor's Second packed RBC loss within 8 weeks**	**Eligibility**
Less than 200 mL	No donation or total from initial and second loss less than 200 mL	No deferral of donor for packed RBC loss; frequency of donation of Platelets, Pheresis as discussed in section III.B.2
Less than 200 mL	More than 200 mL but less than 300 mL total	Donor is not eligible to donate for 8 weeks from 2nd loss
More than 200 mL but less than 300 mL	NA	Donor is not eligible to donate for 8 weeks from initial loss
Less than 200 mL	Total loss from initial and second loss of more than 300 mL	Donor is not eligible to donate for 16 weeks from the 2nd loss
300 mL or more	NA	Donor is not eligible to donate for 16 weeks from initial loss.

- **Per 12 months**:
  Under 21 CFR 640.3(b), a person may not serve as a source of Whole Blood more than once in 8 weeks. In any such assessment, and in assessing a donor's RBC loss during the past rolling 12-month period, the RBC loss associated with the collection of Platelets, Pheresis, and including any other donation type (i.e., Whole Blood, RBC by apheresis), should also be considered.
- **Total plasma volume loss per 12 months**:
  The maximum volume (excluding anticoagulant) collected from a donor during a rolling 12-month period, and including any other donation type (i.e. Whole Blood, plasmapheresis) should not exceed:
  - 12 liters (12,000 mL) for donors weighing 110 – 175 lbs
  - 14.4 liters (14,400 mL) for donors weighing more than 175 lbs

  (Ref. 2).

C. Component Testing

1. Component Specification Check

- Actual platelet yield (volume x platelet count) must be determined after each collection (21 CFR 211.103).
- Weight/volume conversion is necessary to determine the volume of each collection. To convert weight to volume, divide the weight of the collection (the total weight minus the weight of the bag) by the specific gravity (1.03).

- Bacterial contamination testing: You should perform bacterial testing as specified by the storage container manufacturer (i.e., 7-day storage of Platelets, Pheresis, Leukocytes Reduced).

2. QC Monitoring

Under 21 CFR 211.160(b), laboratory controls must include the establishment of scientifically sound and appropriate specifications, standards, sampling plans and test procedures to assure that components and products conform to appropriate standards. One example of a scientifically sound statistical sampling and analytic plan is based on a binomial approach (see Table 1: Product Performance Qualification Criteria for the Platelet Component Collection Process). The sampling sizes described in Table 1 will confirm with 95% confidence a < 5% non-conformance rate for pH and residual WBC count, and < 25% non-conformance rate for actual platelet yield.

However, other statistical plans may also be appropriate, such as the use of scan statistics.

As part of your QC protocol you should:

- define a plan for non-selectively identifying collections to be tested. This should ensure testing of components collected on each individual automated blood cell separator device, each collection type, and each location.
- define sampling schemes for actual platelet yield (including volume determination) and pH, and residual WBC. We recognize that these sampling schemes may be mutually exclusive. However, the platelet yield of the collection (and designation of single, double or triple) should be made prior to performing the residual WBC count QC.
- test actual platelet yield (platelet count times the volume) and pH at the maximum allowable storage time for the container system used (or representing the dating period). Title 21 CFR 640.25(b) specifies that QC testing, including platelet count and measurement of actual plasma volume, be performed at the end of the storage period. We believe that such testing may be conducted "at issue" or within 12 hours after expiration. In addition, actual platelet yield and pH testing may be conducted on one storage container of a double or triple collection.
- include the residual WBC count (Ref. 1) for Leukocytes Reduced collections, if manufacturing leukocytes reduced products.
    - Perform the residual WBC count on the collection. For the purpose of labeling as Leukocytes Reduced (see 21 CFR 606.121(c)(1)), you may also perform a residual WBC count on the transfusable units for double and triple collections that fail the collection acceptance criteria listed (see below in this section).

  - Test for the residual WBC count within 48 hours after collection (Ref. 15), or per the manufacturer's directions for the cell counting methodology, to reduce aberrant results due to cellular deterioration and clumping.
  - Test for percent platelet retention, if leukocytes reduced by filtration.
- describe the criteria for investigation of failures during QC, including the factors to consider in categorizing a failure as process or non-process.
- have a method to document all calculations and test results.

We recommend that you consider the following QC results to be acceptable:

- pH $\geq$ 6.2. If one component from a double or triple collection is found to have a pH < 6.2, the corresponding component(s) from the collection should be retrieved and/or quarantined until they are tested and found to be acceptable.
- transfusable Platelets, Pheresis components $\geq 3.0 \times 10^{11}$ platelets.
- residual WBC count:
  - Single collection: $< 5.0 \times 10^{6}$ WBC
  - Double collection: $< 8.0 \times 10^{6}$ WBC
    Note: If $\geq 8.0 \times 10^{6}$, **but** each transfusable component is $< 5.0 \times 10^{6}$, this is not considered a collection failure.
  - Triple collection: $< 1.2 \times 10^{7}$
    Note: If $\geq 1.2 \times 10^{7}$, **but** each transfusable component is $< 5.0 \times 10^{6}$, this is not considered a collection failure.
- percent platelet retention should be $\geq$ 85% or per the manufacturer's specifications. Components with < 85% platelet retention may be distributed, but a failure investigation should be performed.
- negative for bacterial contamination testing, when performed.

D. Equipment/Supplies

Equipment must be observed, standardized, and calibrated on a regularly scheduled basis as prescribed in the Standard Operating Procedures Manual (21 CFR 606.60(a)). Such equipment includes, but may not be limited to, the automated blood cell separator device, cell counting instrument(s), pH meter, scales and sterile connector.

All supplies (including containers) and reagents must meet all of the requirements described in 21 CFR 606.65.

E. Operator Training

Operators must have adequate training, education and experience, or combination thereof, to assure competent performance of their assigned functions (21 CFR 606.20(b)). We recommend that assessment of operators include scheduled