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	≥ 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

competency assessment and proficiency testing. In addition, we recommend that you develop and document appropriate training on component preparation and/or machine maintenance as updated information becomes available (Ref. 12).

F. Quality Monitoring

You should assess the following:

- total component volume and equal distribution of volume in double and triple component collection containers. This assessment should include checking the performance of the scale; the use of the tare weight of the empty containers/tubing; and the weight/volume conversion.
- component bacterial contamination testing: Rates of bacterial contamination of plateletpheresis should be monitored, and bacterial contamination rates that exceed 1:3000 (Refs. 10 and 12) should be investigated.

VIII. PROCESSING AND TESTING

A. Processing

Platelets, Pheresis must be processed as described in 21 CFR 640, Subpart C – Platelets (21 CFR 640.20-640.27).

B. Communicable Disease Testing

Donations of Platelets, Pheresis must be tested for communicable diseases (21 CFR 610.40, 640.5(a) through (c), 640.23). Platelets, Pheresis may be released or shipped prior to completion of communicable disease testing in accordance with 21 CFR 610.40(g).

You must test donations of human blood and blood components from a donor whose donations are dedicated to and used solely by a single identified recipient except that, if the donor makes multiple donations for a single identified recipient, you may perform such testing only on the first donation in each 30-day period (21 CFR 610.40(c)(1)(i)).

C. Expiration Date

The dating period for Platelets, Pheresis collected using an FDA cleared or approved collection container under a closed or functionally closed system will be specified by the collection container manufacturer.

In accordance with such instructions and our recommendation, Platelets, Pheresis collected in an open system expire 24 hours from the termination of the procedure if the integrity of the hermetic seal is broken during processing.

If the integrity of the hermetic seal is broken after collection, the Platelets, Pheresis expire 4 hours from the time of the integrity violation, or at the original expiration date, whichever is earlier (21 CFR 606.122(l)(2)).

IX. LABELING

An instruction circular must be available for distribution if the product is intended for transfusion (21 CFR 606.122).

Your container labels must comply with 21 CFR 606.121 and 610.60.

In addition:

- The label should include the estimated amount of anticoagulant in the component container.
- Platelets, Pheresis components for transfusion, containing less than 3.0×10^{11} platelets per storage container, should be labeled with the actual platelet content.
- A component from a double or triple Platelets, Pheresis may accurately be labeled as Leukocytes Reduced when the residual WBC count of the collection is $\geq 8.0 \times 10^{6}$ (double) or $\geq 1.2 \times 10^{7}$ (triple) **IF** the transfusable component is tested and found to have a residual WBC count $< 5.0 \times 10^{6}$.
- Platelets, Pheresis may be labeled (i.e., tie-tag) with the residual WBC count if counted and found to contain $< 1.0 \times 10^{6}$.

X. REPORTING CHANGES TO AN APPROVED BIOLOGICS LICENSE APPLICATION (BLA)

Licensed establishments must report changes to their approved application(s) in accordance with 21 CFR 601.12. For assistance in reporting your changes see FDA's "Guidance for Industry: Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or for Further Manufacture." The information below is intended to assist you in determining which reporting mechanism is appropriate for a change to your approved BLA, as it applies to the manufacture of Platelets, Pheresis. You should prominently label each submission with the reporting category under which you are reporting your change, e.g., "Prior Approval Supplement;" "Supplement - Changes Being Effected in 30 Days;" "Supplement - Changes Being Effected;" or "Annual Report."

A. Prior Approval Supplement (PAS): Changes Requiring Supplement Submission and Approval Prior to Distribution of the Product Made Using the Change (Major Changes) (21 CFR 601.12(b))

Under 21 CFR 601.12(b), changes that have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product must be reported to FDA in a Prior Approval Supplement (PAS).

Under this standard, the following kinds of manufacturing changes would fall within this category, warranting submission of your request to implement the following changes to your approved BLA as a PAS:

- if you currently hold an unsuspended, unrevoked BLA to manufacture blood components other than Platelets, Pheresis, and you intend to manufacture and distribute Platelets, Pheresis under that license.
- if you are currently approved to manufacture Platelets, Pheresis at a specific facility, and you intend to manufacture Platelets, Pheresis at a different facility, not under an approved Comparability Protocol. To submit a request for a Comparability Protocol see below.
- if you are approved to manufacture Platelets, Pheresis, but intend to change your manufacturing process in a manner that presents a substantial potential for an adverse effect on the product. FDA believes that such manufacturing changes include: change in storage conditions; change in anticoagulant; leukocyte reduction; and collection of an additional or different product.
- if you intend to collect Platelets, Pheresis using an automated blood cell separator device new to the market or new to your establishment.
- if you are requesting approval for a Comparability Protocol. The Comparability Protocol described in 21 CFR 601.12(e) is a supplement that describes the specific tests and validation studies and acceptable limits to be achieved to demonstrate the lack of adverse effect for specified types of manufacturing changes on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. A new Comparability Protocol, or a change to an existing one, requires approval from FDA prior to distribution of the product which, if approved, may justify a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect (21 CFR 601.12(e)).

  A Comparability Protocol is appropriate, but not required, if you wish to add multiple collection facilities under your direction and control, using the same process to manufacture Platelets, Pheresis. If you request approval for a Comparability Protocol, you should describe the procedures and processes that each new collection facility will implement to ensure conformance with the Comparability Protocol. You may identify one or more collection facilities for the purpose of validation and submission of the Comparability Protocol and supporting data to CBER for review. Approval of such a Comparability Protocol for future collection facilities justifies a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect.

  If you are using an approved Comparability Protocol, you should routinely review the procedures and specifications in the Comparability Protocol to assure that they remain current and consistent with the applicable application and current guidance. If modifications are required, you should contact FDA to discuss the change and to determine the appropriate reporting category.

- We consider the recommendations in this guidance document to provide appropriate criteria for a biologics license application or supplement for Platelets, Pheresis. You may use an alternative approach if such approach satisfies the requirements of the applicable statutes and regulations. Your alternative procedure(s) may be acceptable if you demonstrate that the resulting Platelets, Pheresis components meet applicable standards. We have determined that it may be adequate to determine the actual platelet yield at collection, and that re-determination of the actual platelet yield at issue or outdate is unlikely to provide additional relevant information. If you choose to discontinue determining the platelet count for QC testing as described under 21 CFR 640.25(b)(1), you must submit a request for an alternative procedure under 21 CFR 640.120.

You must not distribute in interstate commerce blood components made using a changed manufacturing process requiring a PAS until you have received our approval of your PAS (21 CFR 601.12(b)(3)).

B. Changes Being Effected in 30 Days (CBE-30) Supplement: Changes Requiring Supplement Submission at Least 30 Days Prior to Distribution of the Product Made Using the Change (21 CFR 601.12(c))

Under 21 CFR 601.12(c), changes that have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product must be reported to FDA in a Changes Being Effected in 30 days (CBE-30) supplement.

You must submit your request to implement manufacturing changes with a moderate potential for an adverse effect to your approved BLA as a CBE-30 supplement under 21 CFR 601.12(c). The manufacturing changes described below are examples of changes that we believe fall within this category:

- certain software and hardware upgrades provided by the manufacturer to your cleared or approved automated blood cell separator device
- addition of concurrent plasma collection
- implementation of a new collection facility under an approved Comparability Protocol

You may distribute your blood components made using the change requested in your CBE-30 supplement in interstate commerce 30 days after we receive your supplement, unless we notify you otherwise (21 CFR 601.12(c)(4)).

C. Submission Inclusion Documents

1. PAS: To comply with the requirements in 21 CFR 601.12(b)(3), the following must be included in the supplement:

- identification of the components involved (e.g., single plateletpheresis component, double plateletpheresis components, and/or triple plateletpheresis components) and manufacturing site(s) or area(s) affected, and a detailed description of the manufacturing change (including device collection technology and the collection protocol(s)) (21 CFR 601.12(b)(3)(i) through (iii)). We recommend that this information be documented in a cover letter and FDA Form 356h. To permit assessment of the manufacturing change we recommend including copies of the following SOPs:
  - collection
  - informed consent
  - labeling including labels
  - donor qualification, deferral and adverse event follow-up
  - a description of training (or an example of training documents)
  - component manufacturing
  - monitoring donor RBC and plasma loss
  - failure investigation
  - quality control including sampling scheme, sample handling, tracking and trending
  - equipment standardization/calibration
  - quarantine and disposition of unsuitable products

Additionally, we recommend that the following SOPs, if already approved for other blood collection activities and unrevised, would not need to be submitted:

- sample preparation
- component storage and shipping
- donor arm preparation

- product labeling for each component, if changed (21 CFR 601.12(f)). We recommend submitting a Form FDA 2567 including Circular (unless already on file at FDA)
- a reference list of relevant SOPs (21 CFR 601.12(b)(3)(vii))
- relevant validation protocols and data (21 CFR 601.12(b)(3)(vi)). We recommend a summary of the validation protocol, including failure investigations.
- a description of the methods used and studies performed to evaluate the effect of the change and the data derived from such studies (21 CFR 601.12(b)(3)(iv) through (v)). We recommend submitting the following information and data:
  - the device manufacturer
  - the device type
  - blood unit number
  - component description (i.e., leukocytes reduced)
  - date of collection
  - date of testing
  - result interpretation(s)
  - the identity of the person performing the testing

- the identity of the collection facility
- evidence of QA oversight, and
- expected component specifications.

- Additionally, we recommend two months of QC data for actual platelet yield and volume, pH, and residual WBC count (if requesting approval for Leukocytes Reduced platelets).

We further recommend that you provide an agreement to summarize bacterial contamination testing results for the first two hundred and fifty (250) Platelets, Pheresis collections in your Annual Report.

2. Comparability Protocol: If you are an establishment with multiple manufacturing sites and wish to submit a comparability protocol to justify a reduced reporting category for a manufacturing change at multiple sites (see Section X.C.4 below), you must submit that protocol as a PAS (21 CFR 601.12(e)). In addition to the information listed in Section X.C.1 above , we recommend that you include the following:

- implementation plan
- proposed reporting category for changes made under proposed Comparability Protocol

3. CBE-30 submissions (excluding new facilities under an approved Comparability Protocol): Under 21 CFR 601.12(c)(3) and 601.12(b)(3)(i) through (vii), the following information must be included in your CBE-30 submission:

- identification of the Platelets, Pheresis components involved (e.g., single plateletpheresis component, double plateletpheresis components, and/or triple plateletpheresis components) and manufacturing site(s) or area(s) affected, and a detailed description of the proposed manufacturing change (including device collection technology and the collection protocol(s)). We recommend that you document this information in a cover letter and FDA Form 356h. To permit assessment of the documented manufacturing change, we recommend that you include copies of any new or revised SOPs.

- relevant validation protocols and data. We recommend that you submit a summary of the validation protocol, including failure investigation.

- the data derived from such studies. We recommend two months of QC data for actual platelet yield and volume, pH, and residual WBC count (if requesting approval for Leukocytes Reduced platelets).

4. CBE-30 submissions for new facilities under an approved Comparability Protocol: To comply with 21 CFR 601.12(c)(3) and 601.12(b)(3)(i) through (vii), the following information must be included:

- identification of the components involved (e.g., single plateletpheresis component, double plateletpheresis components, and/or triple plateletpheresis components) and new manufacturing site(s) or areas(s) affected, and a detailed description of the proposed implementation plan (manufacturing change including device collection technology and the collection protocol(s)). Additionally, we recommend that this information be documented in a cover letter and FDA Form 356h.

- relevant validation protocols and data. We recommend a summary of the validation protocol, including failure investigations to meet the requirement.

- the data derived from studies. We recommend two months of QC data for actual platelet yield and volume, pH, and residual WBC count (if requesting approval for Leukocytes Reduced platelets).

In addition, you should include the submission tracking number (STN) of the approved Comparability Protocol, or the STN(s) of changes to the SOPs associated with an approved Comparability Protocol.

D. Submission of Platelets, Pheresis Sample(s) to CBER

To obtain a biologics license under Section 351 of the Public Health Service Act for any biological product, the manufacturer must submit an application to CBER, and sample(s) representative of the product must be listed in the application (21 CFR 601.2(a)).

We recommend that:

- applicants with no prior experience in the collection of Platelets, Pheresis schedule submission of Platelets, Pheresis products to CBER.
- applicants who submit a CBE-30 for an additional facility under an approved Comparability Protocol generally would not need to submit Platelets, Pheresis products to CBER.

CBER may request the submission of product samples by other applicants, as necessary, during the review process or at any other time (21 CFR 610.2(a)).

E. Shipping Platelets, Pheresis Sample(s) to CBER

If CBER has requested you to submit a Platelets, Pheresis sample(s) to CBER, you should contact CBER Division of Hematology, Laboratory of Cellular Hematology at (301) 496-2577 to schedule delivery of the products to arrive prepaid. Platelets, Pheresis sample(s) should be shipped to the following address between 8:30 a.m. and 4:00 p.m. Monday through Friday, excluding Federal holidays:

Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration
8800 Rockville Pike
Building 29, Room 323
Bethesda, Maryland 20892

We recommend that you enclose a pre-paid, self-addressed shipping label to allow return of shipping boxes and coolants, if desired.

We recommend that you ensure that the Platelets, Pheresis sample(s) arrives at CBER prior to the expiration time. The Platelets, Pheresis sample(s) should not expire on Friday or Saturday at midnight, or at midnight on the day before a Federal holiday.

Labeling and processing, including required testing for evidence of infection due to communicable disease agents (21 CFR 610.40), should be complete prior to shipment.

When shipping to us, you should follow your SOPs for collection, processing, storage and distribution of blood components intended for transfusion.

XI. CONTACT INFORMATION

You may direct questions specific to Platelets, Pheresis application submissions to the Division of Blood Applications. You may also direct questions to the Office of Communications, Training, and Manufacturers Assistance (OCTMA) as an initial general point of contact. Submit all registration forms (Form FDA 2830) and licensure applications/supplements to the Director, CBER.