Preparing Apheresis License Submissions

American Red Cross

Together, we can save a life

Stephen Kassapian

August 15, 2007

How do you begin? Step 1

The first thing to do:

call the FDA!

Call Early !

Why Call Early?

*Early involvement within your own organization is CRITICAL!

- Guidance on:
  - validation/QC data
  - product sample submission (if required)
  - SOP and label submissions
- Key information:
  - what information
  - what data

How do you begin? Step 2

The second thing to do:

call the FDA!

Call Often!

How do you begin? Step 3

The third thing to do:

Listen!

Follow FDA's directions!

What will be the result?

Appropriate content + expected format =

FAST APPROVALS!!

Preparing the BLA Supplement

APHERESIS LICENSURE SUBMISSION PURPOSE:

- To demonstrate to FDA that your facility manufactures an apheresis biologic product in a controlled manner that consistently meets pre-determined requirements and recommendations.

What should a BLA contain?

Apheresis BLA submissions should contain:

- Cover Letter
- Form FDA 356h
- Chemistry/manufacturing/controls:
  - SOPs and labeling
  - Data

Submissions may also contain:

- Comparability Protocol information

Cover Letter

Cover letters should include:

- Name of products to be licensed
- Facility/location information:
  - where collection/manufacturing is performed,
  - where donor screening testing is performed
  - where component QC testing is performed
- Table of contents of enclosures:
  - Listing or summarization of supporting information

Sample Cover Letter

Jesse Goodman, MD, MPH, Director
Center for Biologics Evaluation and Research
Food and Drug Administration HFM-375
Division of Blood Applications
Attn: John Doe
1401 Rockville Pike
Rockville, MD 20852-1448

RE: STN: BL 101727--Changes Being Effected in 30 Days (CBE-30) / 100 N. Main, Anywhere, US, 22222 (CNF No. 8888888).

Dear Dr. Goodman:

This letter is a request to supplement American Red Cross' (ARC) Biologics License Application to include the manufacture of the following products using the COBE Trima™ Accel cell separator:

- AS-3 Red Blood Cells (ACDA anticoagulant) (by pheresis) (both single and double products)
- AS-3 Red Blood Cells Leukocytes Reduced (ACDA anticoagulant) (by pheresis) (both single and double products)
- Platelets Pheresis Leukocytes Reduced (both single and double products)
- Fresh Frozen Plasma (by pheresis) collected every 28 days

Each of these products may either be collected as a standalone product or in combination with each other as consistent with the Accel's Package Insert. Fresh Frozen Plasma will be collected no more frequently than once in 28 days. Plasma volumes from concurrently collected units are consistent with FDA recommendations.

These products are collected in the donor center of the ARC Region (main facility) located at 200 N. Main, Somewhere, USA, 33333 (CNF No. 7777777). Testing of donor samples is performed by the NTL – Over There, (CFN No.3333333). Quality Control (QC) testing is also performed at the main facility of the Somewhere Region.

In accordance with advice from CBER staff Trima Accel 5.1 is being filed as a CBE-30 under approved Comparability Protocol STN No. 101727/0000 approved on July 19, 2006.

Sample Cover Letter

The following documents are enclosed as part of this supplement request:

- Biologics License Application Form FDA 356h
- Validation summary and Discrepancy Reports
- Two months of QC data for single and double Platelets, Pheresis (September & October 2006)
- 1% platelet QC (September & October 2006) and summaries (19.4.frm223, 19.4.frm221)
- WB/RB Leukoreduction Summary for Monthly QC (19.4.frm220), and
- Two months of Red Blood Cells, Pheresis QC Data (September & October 2006),

All Accel cell separators used at this facility were successfully validated in accordance with the device operator's manual (Initial Qualification, Operational Qualification and Performance Qualification). Documentation of the validation and phase one QC is available for review at the main facility of the Somewhere, USA (CFN No.193314).

Collection and manufacture of these products is performed in accordance with the manufacturer's instructions/package inserts for the Trima cell separator and one or more of the Standard Operating Procedures listed below (you then list the SOPs affecting the products collected).

Sample Cover Letter

Document Number	Title/Version	Date Submitted to FDA	FDA Reference No.	Date of FDA Approval
XXXX	Donor Registration and Qualification, Version 1.1	Reported in 2006 Annual Report (AR)	NA	NA[1]
XXXX	Apheresis Component Collection, Version 1.1	To be reported in 2007 Annual Report (AR)	NA	01/06/yyyy
XXXX	Finished Product Quality Control, Version 1.1	08/11/yyyy	101XXX/xxxx	pending
XXXX	Operating the Sterile Tubing Welder, Version 1.1	Reported in 2003 Annual Report	NA	NA

Sample Cover Letter

The following labels, previously submitted for review, will be used for pheresis products collected on the Trima:

Product Name	Product Code	Form Number	FDA Reference Number
AS-3 Red Blood Cells (ACDA anticoagulant) (by pheresis) (for single or first bag of double Red Blood Cell pheresis)	04271	n/n	101###/#####
AS-3 Red Blood Cells Leukocytes Reduced (ACDA anticoagulant) (by pheresis) (for single or first bag of double Red Blood Cell pheresis)	04771	n/n	101###/#####
Platelets Pheresis (for single or first bag from a multiple plateletpheresis)	12010	n/n	101###/#####
Platelets Pheresis (second bag from a multiple plateletpheresis)	12050	n/n	101###/#####
Platelets Pheresis Leukocytes Reduced (for single or first bag from a multiple plateletpheresis)	12710	n/n	101###/#####
Platelets Pheresis Leukocytes Reduced (second bag from a multiple plateletpheresis)	12750	n/n	101###/#####
Fresh Frozen Plasma (by pheresis)	18211	n/n	101###/#####
Source Plasma	19711	n/n	101###/#####

Please address any correspondence regarding this application to The American Red Cross Biomedical Services, Regulatory Affairs, 2025 E Street, NW, Washington, DC 20006. Any questions regarding this application should be directed to Mickey Mouse at 888-555-1212.

Sincerely,

Donald Duck
Director, Regulatory Affairs
Blood Services

Sample Form FDA 356h – Page 1

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE
(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2006
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
BL 101###

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
American National Red Cross (The)	March 23, 2007
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
202-303-5829	202-303-0190
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 2025 E Street NW, Washington, DC 20006, U.S. License Number 190	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE: N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)*: 190

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY	
See Cover Letter	N/A	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*		**CODE NAME** *(If any)*
See Cover Letter		N/A
DOSAGE FORM	**STRENGTHS**	**ROUTE OF ADMINISTRATION**
N/A	N/A	N/A

(PROPOSED) INDICATION(S) FOR USE
Refer to Circular of Information (COI)

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)*: ☐ NEW DRUG APPLICATION (NDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) ☒ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE: ☐ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION:
Name of Drug: N/A Holder of Approved Application: N/A

TYPE OF SUBMISSION *(check one)*: ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO APPENDING APPLICATION ☐ RESUBMISSION ☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☒ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY: ☐ CBE ☒ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION:
CBE-30 for products collected on the COBE Trima™ Accel

PROPOSED MARKETING STATUS *(check one)*: ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED: 1 THIS APPLICATION IS: ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and CMFs referenced in the current application)

STN 101###/####, Comparability Protocol for the manufacture of blood components using the GAMBRO BCT Trima version 4.0, approved 06/13/yyyy.
STN 101###/####, Comparability Protocol for the manufacture of blood components using the GAMBRO BCT Trima Accel version 5.1 approved on 07/1/yyyy
STN 101###/####, Submission to manufacture blood components using the GAMBRO BCT Trima version 4.0 at this facility, approved 06/13/yyyy

Sample Form FDA 356h – Page 2

This application contains the following items: *(Check all that apply)*

☐	1. Index
☐	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☒	4. Chemistry section
☒	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Non-clinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☒	20. OTHER *(Specify)* Cover Letter/CBE-30

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Stephen Kassapian, Director, Regulatory Affairs Blood Services	March 23,2007

ADDRESS (Street, City, State, and ZIP Code)	Telephone Number
2025 E Street NW, Washington, DC 20006	(202)303-5829

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services

Food and Drug Administration
CDER, HFD-99
1451 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Supporting information – enclosures, attachments

- **Data:**
  - **Two consecutive months of QC**
    - Daily log sheets & monthly summary forms
      - Platelets
      - RBC
      - Leukoreduction

QC Data

Two Months of QC data:

- Pass or fail evaluation for each data point
  - Platelets - pH, color, yield, and volume
  - RBCs - hemoglobin and volume
  - leukoreduced WBC counts
    - linked to QC WBNs, or
    - statistical sampling
- Monthly summaries of platelet, RBC and LR data
- Number of samples tested/number of samples passed
- Pass or fail decision with QA review

Sample Form - Platelet QC Log

(Proprietary – Not for Direct Copy)

Collection Site: ______________________________ Month/Year: ______________________________

Product Type: Single ☐ Double ☐ Triple ☐ Equipment Type: Amicus ☐ TRIMA ☐ SPECTRA ☐

pH Meter ID# ______________________ Scale ID#: ______________________ Hematology Analyzer ID#: ______________________

Whole Blood Number	Product Code	pH (≥ 6.2)	Color (Light Straw to Light Pink)	Weight (g) ÷ 1.027	=	Volume (mL)	X	Platelet Count (X $10^3/\mu L$)	x 1,000	=	Platelet Yield (x 10^{11}) (≥ 3.0×10^{11})	Pass /Fail	Performed By Initials /Date	Reviewed By Initials /Date	Distribution Verified By Initials/Date
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐
				( ) ____ 1.027	=		X		x 1,000	=		PASS ☐ FAIL ☐			Y ☐ N ☐

Comments: ____

Sample Form - Platelet QC Summary

(Proprietary – Not for Direct Copy)

Collection Site: _____ Date Range or Month/Year: _____

Equipment Types	Trima ☐	Spectra ☐	Amicus ☐
Acceptance Criteria			
pH must be ≥ 6.0	100%	100%	100%
pH must be ≥ 6.2	90%	90%	90%
Platelet Yield is ≥ $3.0 X 10^{11}$	90%	90%	90%
Sampling Criteria	4 singles (4), 4 doubles (8), 4 triples (12) for each equipment type		

Calculations and Results			
Percent of Products with pH of ≥ 6.2			
Number of Products with pH ≥ 6.2 / Number of Products Tested	( ) / ( )	( ) / ( )	( ) / ( )
X 100 = Percent of Products Acceptable			
Pass/Fail Criteria	Pass ☐ Fail ☐	Pass ☐ Fail ☐	Pass ☐ Fail ☐
Was there any failure of pH < 6.0? (If yes = failed monthly QC)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

Percent of Products with Platelet Yield ≥ $3.0 X10^{11}$			
Number of Products with ≥ $3.0 X10^{11}$ Platelet Yield / Number of Products Tested	( ) / ( )	( ) / ( )	( ) / ( )
X 100 = Percent of Products Acceptable			
Pass/Fail Criteria	Pass ☐ Fail ☐	Pass ☐ Fail ☐	Pass ☐ Fail ☐

Sampling Criteria – As applicable for each equipment type: 4 Singles (4), 4 Doubles (8), 4 Triples (12)			
Was sampling criteria met?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

Comments: _____

Actions Taken: ☐ Problem initiated (specify #_____)

Performed By: _____ Date: _____ Reviewed By: _____ Date: _____

Sample Form - RBC QC Log

(Proprietary – Not for Direct Copy)

Collection Site: ______________________________ Scale ID #: ______________________________

Collection Date: ______________________________ Hematology Analyzer ID #: ______________________________

Performed at the Collection Site						Performed at the Lab								
Trima Equipment ID #	Whole Blood Number	AL, M, or QNS	R2, P3, P4, or P5	Product Code	Initials /ID Date	Weighing Performed By (initials /date)	Weight (g) ÷ 1.06 sp. gr.	=	❶ Volume (mL)	❷ Hgb (g/dL)	Total Component Hgb (g) $\frac{(❶ \times ❷)}{100}$ (mL/dL)	Volume (315-385mL)	Total Component Hgb (>50g)	Initials /Date
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	
							( ) / 1.06	=				PASS ☐ FAIL ☐	PASS ☐ FAIL ☐	

Comments: ____

Reviewed By: ____________________ Date: ____________________

Sample Form - RBC QC Summary

(Proprietary – Not for Direct Copy)

Collection Site:_____ Date Range or Month/Year:_____

Equipment Type	Trima ☐	Haemonetics 832F ☐	ALYX ☐
Acceptance Criteria			
Mean total hemoglobin	≥ 60 g	≥ 51 g	≥ 51 g
Product Volume (In ≥ 95% of products tested)	< 10% difference of display to actual product volume	NA	Absolute Red Cell Volume 400 ± 10% (360 – 440mL)
Total component hemoglobin (In ≥ 95% of products tested)	> 50 g	> 42.5 g	> 42.5 g

Calculations and Results

Mean Total Component Hemoglobin of Products (Do not round up calculated result)			
Sum of Total Component Hgb of Products ÷ Number of Products Tested	( ) / ( )	( ) / ( )	( ) / ( )
= Mean Total Hgb of Products			
Acceptance Criteria	≥ 60 g	≥ 51 g	≥ 51 g
Pass/Fail	Pass ☐ Fail ☐	Pass ☐ Fail ☐	Pass ☐ Fail ☐

Percent of Acceptable Total Component Hemoglobin			
Number of Products with Acceptable Total Component Hgb x 100 ÷ Number of Products Tested	( ) / ( ) X 100	( ) / ( ) X 100	( ) / ( ) X 100
= Percent Acceptable Total Component Hgb			
Acceptance Criteria	≥ 95 %	≥ 95 %	≥ 95 %
Pass/Fail	Pass ☐ Fail ☐	Pass ☐ Fail ☐	Pass ☐ Fail ☐

Percent of Products Tested That Meet Product Volume Acceptance Criteria (Trima and ALYX Only)			
Number of Products That Passed Volume Criteria x 100 ÷ Number of Products Tested	( ) / ( ) X 100	N/A	( ) / ( ) X 100
= Percent of Products Tested That Pass Volume Acceptance Criteria			
Acceptance Criteria	≥ 95%		≥ 95%
Pass/Fail	Pass ☐ Fail ☐		Pass ☐ Fail ☐

Comments:_____

Form Completed By: _____ Date: _____ Reviewed By:_____Date: _____

Sample Form - Counting Log for Leukoreduced Platelet Pheresis

(Proprietary – Not for Direct Copy)

Collection System Name: Amicus ☐ TRIMA ☐ SPECTRA ☐ Timer ID #:_____

Microscope ID #_____ Pipette ID #'s:_____

Turk's Reagent Lot #:_____ Turk's Reagent Expiration Date: _____

Collection Date	Whole Blood Number	Number of Rectangles Scanned	❶ Product Volume (mL)	X	❷ Number of WBCs Counted	X 100	=	❸ Total Residual WBCs Per Unit X 10^6	Residual WBC Count < 6 x 10^6?	Performed By (Initials /date)
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	
				X		X 100	=		PASS ☐ FAIL ☐	

If performing counts for submission for licensure, all 40 Rectangles must be counted. Otherwise....

Did, you count . . . < 25 WBCs in the **First Rectangle?**

YES → **Then,** Continue counting the number of leukocytes in the next **Nine Rectangles.** → **Was** your count and component volume in the first **10 Rectangles?**

0 WBCs	and	Any Volume
1 to ≤ 15 WBCs	and	≥ 400 mL
≤ 20 WBCs	and	300 to 399 mL
≤ 25 WBCs	and	175 to 299 mL
≤ 45 WBCs	and	< 175 mL

NO ← **Then,**

1. Discontinue counting WBCs
2. **Record** "≥ 25" in the "❷ Number of WBCs Counted" column.
3. Count the sample on the automated hematology analyzer (AHA) **or** discard the product and record "> 5" in the ❸ Total Residual WBCs per Unit x10^6 column.
4. Calculate to see if Total WBCs per Unit is < 1.0 x10^6/product.

[AHA Result x 10^3] x 1000 x [Volume] = Total WBCs per Unit x10^6

Then **Record** this [result x10^6] in the "❸ Total Residual WBCs per Unit x10^6 column and evaluate the result.

If < 1x10^6/product, Then the product may be labeled as non-leukoreduced.
If ≥ 1x10^6/product, Then the product must be discarded.

YES → **Then,** Discontinue counting WBCs: this product contains < 5x10^6 WBCs.

If "0" WBCs are counted, **Record** "< 3.5 x 10^{6}" otherwise, **Record** "< 5" in the "❸ Total Residual WBCs per Unit x10^6 column.

NO → **Was** your count and component volume in the first **10 Rectangles?**

> 15 WBCs	and	≥ 400 mL
> 20 WBCs	and	300 to 399 mL
> 25 WBCs	and	175 to 299 mL
> 45 WBCs	and	< 175 mL

Then, Continue counting WBCs in the remaining **30 Rectangles**, and Calculate and **Record** the result in the "❸ Total Residual WBCs per Unit x10^6 column If the sample contains ≥ 5x10^6 WBCs, the product may Not be labeled as leukoreduced.

Comments:_____

Reviewed By: _____ Date: _____

Sample Form - Leukoreduction Summary

(Proprietary – Not for Direct Copy)

Manufacturing Site: _____ Date Range or Month/Year: _____

Acceptance Criteria

Leukoreduction System	Amicus ☐	Spectra ☐	Trima ☐
Residual WBC count	< $5.0X10^6$	< $5.0X10^6$	< $5.0X10^6$
Process Control Sampling Criteria	60 consecutive units	60 consecutive units	60 consecutive units
Monthly QC Sampling Criteria	≥1% of production	≥1% of production	≥1% of production

Calculations & Results – Sampling Criteria

Total # of Products Tested	( )	( )	( )
÷			
Number of Products Manufactured	( )	( )	( )
x100 = % of Products Tested			
Was sampling criteria met?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

Calculations & Results – Leukoreduction (Residual WBC) Criteria

Total # of Products Acceptable	( )	( )	( )
÷			
Number of Products Tested	( )	( )	( )
x100 = % of Products Acceptable			
Was 100% Pass Criteria Met?	Pass ☐ Fail ☐	Pass ☐ Fail ☐	Pass ☐ Fail ☐

Comments: _____

Actions Taken: ☐ Problem Initiated (Specify #_____)

Performed By: _____ Date: _____ Reviewed By: _____ Date: _____

Validation

Provide Validation Summary:

- Describe pass/fail criteria
- Summarize results
  - Number of machines validated
  - number procedures/number passed
  - Discrepancies
    - description of failures
    - investigation
    - corrective actions taken (if any)

Based upon an evaluation of the validation, a decision is made to accept the device or to take corrective action and repeat the validation process.

Validation Discrepancies

Investigation:

- Complete and thorough
- Resolution required!

Evaluate for impact:

- Is data point a failure or excluded from the PQ?
- If failure, is PQ acceptable or must PQ be repeated?

Validation Discrepancies

Discrepancies with no impact:

- donors become uncomfortable and the collection process must be stopped
- the needle infiltrates and staff discontinues the procedure
- staff accidentally performs a function with the machine that they should not have
- staff completes collecting the product and then realizes they failed to follow the procedure as written
- the instrument beeps and the WBC count is failed (this indicates the machine is working properly)
- staff collect more products than is required for the PQ

Sample Form - Discrepancy Resolution

(Proprietary – Not for Direct Copy)

Discrepancy Resolution Form

1. Description of Discrepancy	
Discrepancy #	
Protocol ID and Step #	
Equipment ID #	
Description of Discrepancy	
Clarify case #, if applicable	
APMS #, if applicable	
Name of Supervisor Notified	
Supervisor Notified by Initial/Date:	
Section 1 completed by Initial/Date:	
2. Vendor/BHQ/Testing Support	
Initial/Date if N/A	☐ N/A, Vendor/BHQ/Testing Support not needed Initial/Date:
Name of Vendor/BHQ/Testing Support personnel notified	
Contact by: Staff -Initial/Date/Time	
Comments:	
Section 2 completed by Initial/Date:	
3. Corrective Action	
Corrective Action	
Type of Discrepancy	☐ Execution ☐ Protocol/Relocation Job Plan ☐ Vendor
Section 3 completed by Initial/Date:	
4. Conclusion of Discrepancy	
Is Discrepancy Resolved?	☐ Yes ☐ No If no, describe in Follow Up/Comments below.
Follow Up/Comments	
Section 4 completed by Initial/Date:	
Operations Review/Approval Signature/Date:	
Quality Assurance Review/Approval Signature/Date:	

Sample Form - Validation Summary

Page 1 (Proprietary – Not for Direct Copy)

QUALIFICATION SUMMARY REPORT

Facility Name	
Equipment ID Number	
Protocol/Relocation Job Plan Title and Version	
Date(s) Qualification Protocol/Relocation Job Plan was executed	
Total number of discrepancies	

Section I: Protocol/Relocation Job Plan Execution Summary:

Yes	No	N/A	
☐	☐	☐	1.1 Has the execution of the protocol/relocation job plan been completed in accordance with the protocol/relocation job plan requirements?
☐	☐	☐	1.2 Have all discrepancies been documented, investigated and resolved appropriately?
☐	☐	☐	1.3 Have all unusual occurrences been documented and determined not to be discrepancies?

Pass: ☐ All protocol/relocation job plan requirements were successfully met.

Fail: ☐ Protocol/relocation job plan requirements were not met. Explain:

Comments :

_____

_____

_____

_____

_____

Section I: Protocol/Relocation Job Plan Execution Summary written by (signature/date):

_____

Sample Form - Validation Summary Page 2 (Proprietary – Not for Direct Copy)

Section II: Qualification Package Operational and Quality Assurance Reviews and Approvals

The Operational and Quality Assurance reviews and approvals ensure the following:

- All documentation generated in the execution of the protocol/relocation job plan was reviewed and approved.
- All actual results were reviewed and approved according to this protocol/relocation job plan and System 6, Validation documents.
- All unexpected results were fully investigated, documented and resolved.
- All unusual occurrences were documented appropriately and determined not to be discrepancies.

Operations Comments:

_____

_____

_____

_____

_____

Qualification Package Operational Approvals (signature/date)

_____

Quality Assurance Comments :

_____

_____

_____

_____

_____

_____

Qualification Package Quality Assurance Approval (signature/date)

Equipment may be placed into service before obtaining Laboratory or Medical Director's signature.

Section III: Signatures:

Laboratory/Medical Director , If applicable (signature/date) _____

(If facility license requires Laboratory or Medical Director signature, obtain the appropriate signature. Place "N/A" on the signature line, if not required by facility license.

Additional Supporting Information

- Results of sterility testing
- Submission of product samples for QC testing

- Comparability Protocol (CP)
  - May reduce reporting category

Comparability Protocol (CP)

Can be used to reduce the reporting category in cases of multiple facilities

- Include comparability protocol request in first submission
- Include following information:
  - Subsequent submissions will be identical
    - SOPs standardized
    - Labels standardized
  - How organization maintains control of manufacturing process
    - Standardized training
    - Internal audits
  - Specific request
    - For example: upon approval, subsequent submissions will be CBE-30

QUESTIONS ?