Graft Processing
Staff, Procedures, Materials and Equipment

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Staff Qualifications, Training, Competency

- How to find qualified staff
- Steps in training
- How to keep staff competent

Staffing The Laboratory

- Establish detailed job descriptions
  - Key expectations and duties (processing & testing, data management, SOP revisions, etc)
  - Work hours, on call requirements, etc
- Screen & hire candidates
  - Educational background (lab, biology)
  - Previous experience (sterile technique, blood banking)
- Training (initial & ongoing)
- Competency assessment (initial & ongoing)

Initial Training

- Orientation
  - Generally by Institution
- Identify specific training needs
  - List all job functions
  - Establish uniform training plan for each function
- Define requirements for trainers
  - Must be trained and competent for function
  - Should have experience (1 year?)
- Document training- Use checklists
  - Observation and sign off by trainer and trainee
  - Written test to ensure comprehension

Initial Training

- Consists of
  - Reading
  - Observing
  - Practicing
  - Performing with supervision
  - Performing independently

Training Plan

- Define training content (using approved SOPs), timelines
- Orientation, Facility Quality Management Program
- Laboratory safety program, environmental control program to prevent product contamination
- Stringent aseptic technique to prevent cross contamination
- Biohazards, chemical hazards, radiation hazards
- Facility computer program
- Stringent training related to each job specific function performed, including when new process, test or service are introduced, before performing the task independently
- Emergency and disaster training

Appendix 9-4. Sample Cellular Therapy Facility Training Checklist

Employee: _____

#	Items Reviewed	Trainee Initials	Trainer Initials	Date of Satisfactory Performance
1	**Media Preparation**			
	Marrow Harvest			
	Cryopreservation Media			
	Handling Dimethyl Sulfoxide			
	Overnight Storage			
	Operation of Cell Selection Device			
2	**Product Manipulation—Bone Marrow**			
	Concentration or Buffy Coat			
	RBC Reduction			
	Plasma Depletion and Washing			
	Unrelated Donor Registry Products			
	Preparation for Transport			
	Database Use and Documentation			
3	**Product Manipulation—Peripheral Blood**			
	Concentration			
	Peripheral Blood Cell Selection			
	Allogeneic Donor Leukocytes (CD3) by apheresis and whole blood			
	Database Use and Documentation			
4	**Cryopreservation**			
	Sample Aliquots			
	Bone Marrow			
	Peripheral Blood Progenitor Cells			
	Donor Leukocytes (CD3)			
	CD34+ Selected Cells			
	Database Use and Documentation			
5	**Thawing, Infusion, and Transport**			
	Identification of HPCs for Infusion			
	Issue of HPCs			
	Thawing of HPCs			
	Thawing of Cord Blood			
	Thawing of CD34+ Selected Cells			
	Infusion of HPCs			
	Transportation of HPCs within the Facility			
	Transportation of HPCs to Other Facilities			
	Transportation of Registry Products			
	Return of HPCs			
	Database Use and Documentation			

Lab Supervisor or Designee Review:_____Date:_____

Training Challenges & Approach

- Rarely have dedicated trainers
  - Trainee observes trainer process clinical products
  - Trainer closely supervises trainee after skill assessment
- Many of most complex procedures rarely done
  - Initially train key skills that apply to simple & complex procedures (sterile technique, plasma removal)
  - Limit complex procedures to core staff
- Cellular source material for training not readily available
  - Mock products from expired blood or by-products (buffy coat)
- Reagents and supplies for training runs may be expensive
  - Use expired materials (companies will often supply)

Importance for Cellular Therapy Product Quality

- LOV= Lack of Variation = Controlled Process
- Personnel are the Major variable in any process
- To remove variation– TRAIN THEM APPROPRIATELY & EFFECTIVELY
- Training using Critical Control Points is widely used in WHO Quality Management Training Program for blood safety in the Blood Transfusion Services
- Critical Control Points – a factor, practice, process, procedure that can be controlled in order to prevent , control, eliminate Poor Quality Outcome

Use of Critical Control Points

- During interactive learning e.g. demonstrations, emphasize these steps must be followed strictly and explain the rationale
- **Do the RIGHT Thing RIGHT the First Time, Every Time and All The Time**
- Good practice to comprehend **WHY I am doing WHAT I am doing**
- Training must be documented concurrently and records maintained in personnel file as per National or International regulation, accreditation / certification requirements
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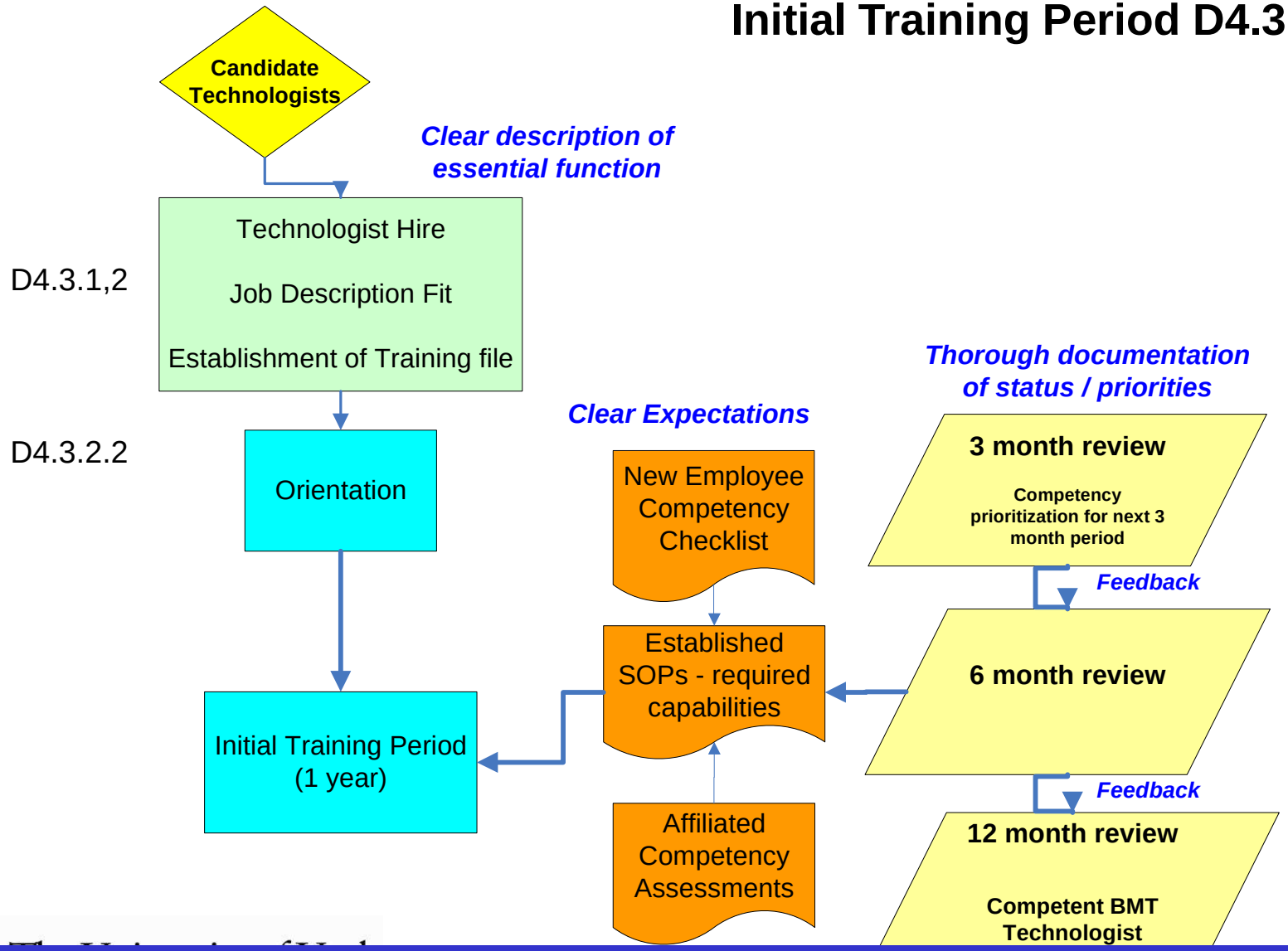
Overview of Initial Training



Competency Assessment

- SOP for initial and ongoing competency
- Assess through
  - Direct observation during processing
  - Use of mock samples
  - Not feasible to assess all competencies yearly, choose key
- Written tests to focus on: theory, technical procedures, interpretation of results, trouble shooting
- Review of processing records, product tests results, event management reports, etc
- Document competency (checklists) and file in personnel records
- Retrain if defined criteria not met or if warranted by deviations from established procedures

Appendix 9-6. Sample Cellular Therapy Facility Competency Assessment Checklist

Peripheral Blood Stem Cell Concentration

Employee:_____ Date:_____

#	Items Reviewed	Performed Correctly? Check Appropriate Box	
		Yes	No
1	Ensures stem cell evaluation packet is completed properly?		
2	Determines when the collection process for hematopoietic progenitor cells from apheresis (HPC-A) will conclude?		
3	Assigns stem cell collection number correctly?		
4	Generates labels correctly?		
5	Orders blood cultures, blood type, flow analysis, or other testing correctly?		
6	Obtains correct blood type accession label from the laboratory?		
7	Labels all samples correctly?		
8	Cleans the biological safety cabinet correctly?		
9	Records lot numbers of supplies used?		
10	Primes COBE 2991 correctly?		
11	Installs tubing set correctly?		
12	Verifies information on HPC-A collection label attached to the product?		
13	Collects samples for cell counts correctly?		
14	Uses and discards needles and sharps correctly?		
15	Operates COBE 2991 correctly to concentrate HPC-A?		
16	Performs calculations correctly?		
17	Maintains aseptic technique correctly?		
18	Completes HPC-A worksheet correctly?		
19	Is competent to perform HPC-A concentration?		

/ /

Trainer signature Employee signature Date

If not competent, correction plan recommended: _____

Correction plan completed: / /

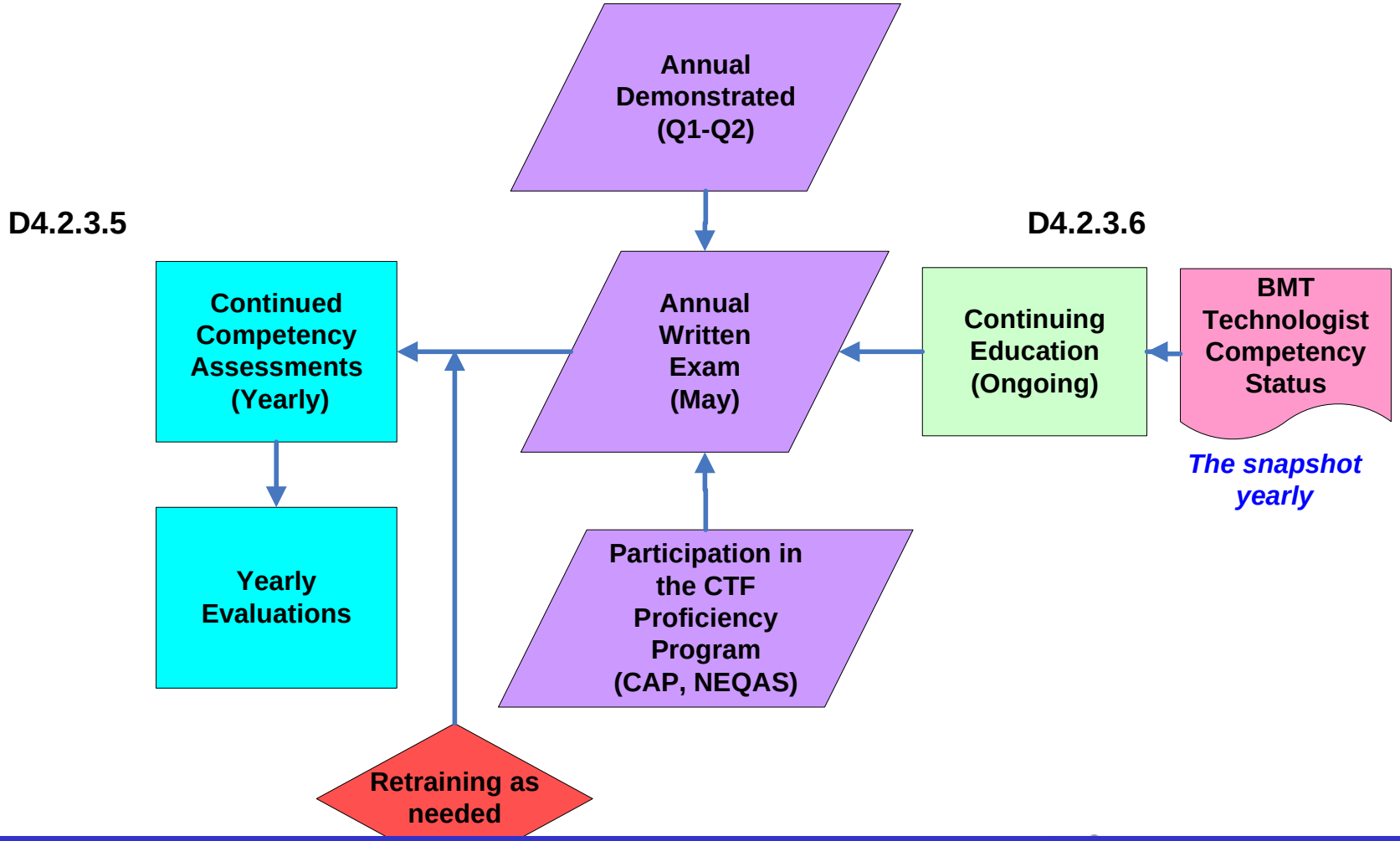
Trainer signature Employee signature Date

Comments: _____

Proficiency Testing (PT)

- Measures adequacy of analytical methods, procedures, equipment and personnel competency
  - External (supplied by outside vendor, not all required analytes available due to limited use outside of cell processing)
  - Internal (produced and tested exclusively within a facility)
- For external PT some vendors provide PT samples and programs that appear like hematopoietic progenitor cell products and integrate testing into daily graft processing facility e.g. nucleated cell counting, cellular viability test and colony-forming unit identification
- Internal PT can provide documentation of reproducibility among staff when personnel subjectivity is involved in determining results
- Process control e.g. SOPs should be adopted to handle PT and corrective action for meeting expected results. All testing, review and corrective action must be documented

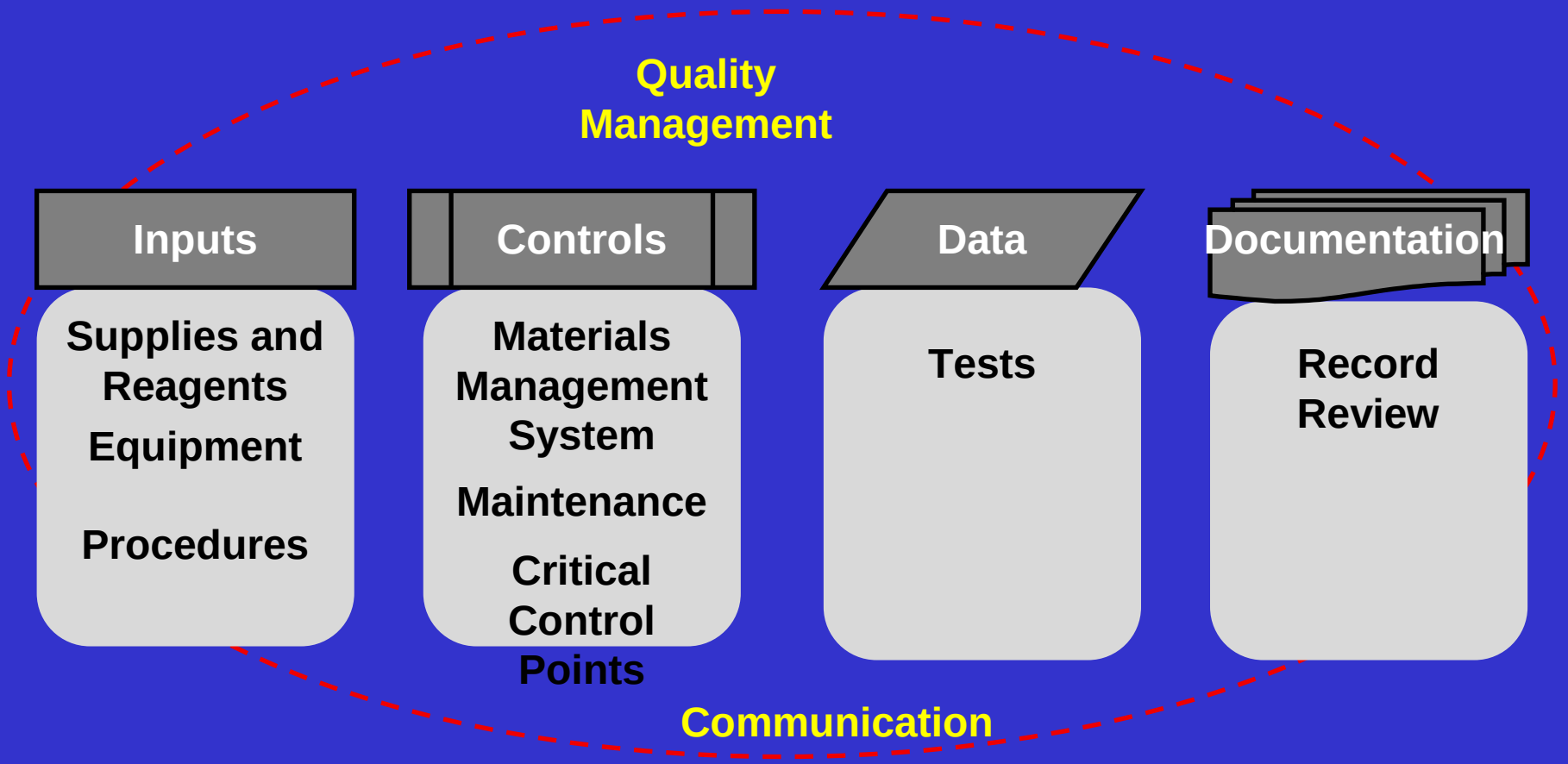
Overview of Competency



Process Control

- Inherent variations in biological products
  - Difficult to control these variations
- Procedures and tests can be tools to reduce variability
  - Combination of proactive and retrospective steps ensure only safe and effective products are administered to patients
- Includes staff training and competency

Process Control



Materials Management

- Integrated process to plan and control steps in the acquisition and use of materials used for the collection or processing of cellular therapy products, Includes:
  - Vendor qualification
  - Establishing acceptance criteria
  - Documenting receipt and acceptability
  - Ensuring proper and monitored storage
  - Approval of materials for use
  - Documentation of material use

Equipment Qualification & Maintenance

- Must ensure equipment is qualified for the intended function within the laboratory (cryopreservation, storage, processing, testing).
- Procedures to ensure equipment is clean and in compliance with preventative maintenance schedule prior to use
- Equipment must be standardized and calibrated on a regular schedule as per SOP and manufacturer's recommendation. Logs must be maintained.
- Defined process for actions to be taken when equipment is out of calibration or specification for products manufactured & need to revalidate

Requirements For Cryopresevation Storage Equipment

- Monitoring of temperatures continually with records every 4 hr
- Mechanism to ensure LN_2 levels sufficient to maintain HPC products within the specified temperature range
- Ensure continuously active alarm system for storage devices. System must:
  - Have audible signals or other effective notification methods, checked periodically
  - Alert responsible staff of alarm conditions on a 24-hr basis

Laboratory Equipment Annual Preventive & Calibration Schedule

Stem Cell Laboratory

Instructions:

1. Place a √, initial and date underneath the month that the service was performed.
2. Technical Specialist or designee will be notified of any equipment problems.

Year :_____

Preventive Maintenance	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
Biohazard Safety Cabinet - Annual												
CliniMACS Instrument - Annual												
Sorval Legend Centrifuge – Annual												
Control Rate Freezer - Annual												
Refrigerator & Thermo Freezer - Biannual												
Liquid Nitrogen Freezer - Biannual												
Calibration/ Verification												
Sorval Legend Centrifuge - Annual												
Informer Thermometer - Annual												
Isotemp Waterbath - Annual												
Scale - Annual												
Standard Thermometers - Annual												
Reference Thermocouple - Annual												
Timer - Annual												
Performance Assessments												
Biological Safety Cabinet Viable Particle Air Assessment - Quarterly												
Biological Safety Cabinet Contact Surface Cultures - Quarterly												
Biological Safety Cabinet UV Light Replacement - Biannual												
Planer Kryo Control Rate Freezer Validation - Biannual												
Scale – surface cleaning, power cord & display check - Quarterly												
Other Maintenance - *Annually, ** Biannually or as needed												
Change Reference bag for cryopreservation of Cellular Therapy Product**												
Change Reference vial for cryopreservation of CD34 enriched product**												
Denco Total Containment Device (TCD) – Clean surface**												
Hand Held Vertrod Heat sealer – clean electrodes**												
Portable Pipet Aid – replace filter*												

Reviewed By: _____ Date: _____

Biohazard Safety Cabinet and Equipment Maintenance Log

Stem Cell Laboratory

Month: _____ **Year:** _____

Cabinet: _____ Serial #: _____

Disinfect cabinet each day of use (before and after each product)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Initial																															
Initial																															
Initial																															

Cabinet: _____ Serial #: _____

Disinfect cabinet each day of use (before and after each product)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Initial																															
Initial																															
Initial																															

Disinfect bench with 70% ethanol each day of use (before and after each product)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Initial																															

Disinfect Ventrod heat sealer #2 with 70% ethanol each day of use (beginning and end of each day)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Initial																															

Disinfect Vertrod heat sealer #1 by wiping with a sterile towel soaked with 70% ethanol each day of use (beginning and end of each day)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Initial																															

Clean Waterbath before each use. Temperature:38±2°C

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Digital readout																															
Thermometer temperature																															
Initial																															

Clean Sorval Legend Centrifuge with 70% ethanol before each use or as required

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Mistral- Initial																															
Beckman-Initial																															

Reviewed by: _____ Review Date: _____

Standard Operating Procedures

- Crucial to Training, Competency & Process Control
- Includes:
  - Purpose and description
  - Sample or product requirements
  - Reagents, Supplies, Equipment
  - Step wise description of procedure
  - Calculations and expected results
  - List of other needed SOPs
  - References
  - Approvals
  - Example worksheets, forms, labels
- All processing SOPs must be validated to ensure products meet predetermined specifications

Standard Operating Procedures

- SOPs Typically include
  - Aseptic Technique
  - Product Labeling
  - Equipment use
  - Laboratory Processing Records
  - Technical Processing (cryopreservation, thawing, RBC removal, plasma removal, subset enrichment or depletion)
  - Testing methods (cell counts, viability, CD34 assay, etc)
  - Transport methods (fresh and frozen products)
  - Quality Management (quality plan, equipment maintenance, environment monitoring, cleaning, reagent performance testing, validation, qualification, and verification, personnel training and competency, proficiency testing, SOP preparation, etc)

Thank you