

MAYO
CLINIC



The Role of the Graft Processing Laboratory in Stem Cell Transplantation

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Stem Cell Product Life Cycle

- Procurement
- Transport to laboratory
- Processing and testing
- Storage
- Transport to patient bedside
- Administration to patient

Procurement

- Physician request(s) for procurement and processing
 - Scheduling with lab ensures proper staffing
 - Product type and target dose
 - Date of collection
 - Donor and recipient identifiers
 - Allows laboratory to confirm product identity at receipt
 - Donor identified before procurement
 - Product labeled immediately post procurement
 - Unique identifier needed

* Complete Donor Information for Allogeneic Collections Only		
Recipient Mayo Clinic Number	Donor Mayo Clinic Number *	
Recipient Name	Donor Name *	
Recipient Weight _____ kg	Start Date (Month DD, YYYY)	Location <input type="checkbox"/> Gonda 10 <input type="checkbox"/> SMH <input type="checkbox"/>
Diagnosis	Consented to Cell and Serum Bank - IRB 1087-01 <input type="checkbox"/> Yes <input type="checkbox"/> No	
On Protocol for BMT <input type="checkbox"/> Yes <input type="checkbox"/> No - IRB Number: _____	Informed Consent Obtained for Collection <input type="checkbox"/> Yes <input type="checkbox"/> No	
Product to be Collected	Target Dose	
<input type="checkbox"/> HPC-A (PBPC)	→ _____ x 10 ⁶ CD34/kg Intended Number of Transplants _____	
<input type="checkbox"/> TC-T (DU)	→ _____ x 10 ⁶ CD3/kg	
<input type="checkbox"/> HPC-M (BM)	→ _____ x 10 ⁶ Nucleated Cells/kg	
<input type="checkbox"/> Cellular Therapy Product - IRB Number _____ - Protocol Name _____		
<input type="checkbox"/> Other (Describe) _____		
Processing Requested		
<input type="checkbox"/> Cryopreserve		
<input type="checkbox"/> Give Fresh	→ RBC Reduction Needed <input type="checkbox"/> Yes <input type="checkbox"/> No	
<input type="checkbox"/> Both (Describe) _____		
Special Processing Request		
<input type="checkbox"/> Cellular Therapy Product - IRB Number _____ - Protocol Name _____		
<input type="checkbox"/> Other (Describe) _____		
I authorize Transfusion Medicine personnel to order and collect infectious disease testing as needed per procedure.		
Physician Signature	Pager Number	Date (Month DD, YYYY)

Sample Product Request

Transportation Within the Hospital

- Product labeled after procurement
- Carried by hand in a cooler or closed container
- No ice or cold packs necessary
- Processing usually begins shortly after product receipt in laboratory

Long Distance Transportation (non-frozen product)

- Usually from unrelated donor
 - Not processed before transport
- Insulated cooler required
 - Ice or Ice packs can be included
- Hand carried by courier instead of shipping company
- Should arrive <48 hours after collection
 - prolonged transport = worse outcomes

Long Distance Transportation (frozen product)

- Usually from cord blood bank
- Shipped in “dry shipper”
 - Liquid nitrogen in absorbent material
- Holds temperature for several days
 - Usually shipped without courier
- Monitor temperature during shipment



Receipt

- Assign or record unique laboratory identifier
- Document date/time of receipt
- Inspect for proper appearance
- Compare label to physician request
- Process per request

Collection Time

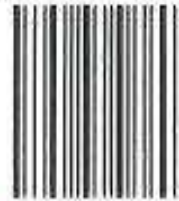
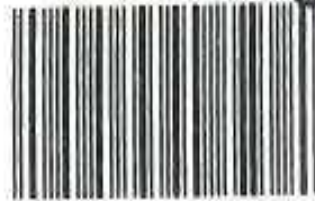
Donation Number

EXPIRES

00:40

Q 26829-3

23:59 HRS
06 OCT 31



TC-T CELLS
CRYOPRESERVED

FOR USE BY INTENDED RECIPIENT ONLY

Approx mL in ACD-A 73600
30% Normosol-R, 10% DMSO
10% Plasma, 5u/mL Heparin
Store at $\leq -120C$



A

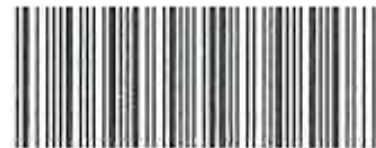
Rh POSITIVE

See circular of information for indications, contraindications, cautions and methods of infusion.

DO NOT USE LEUKOREDUCTION FILTERS and DO NOT IRRADIATE
Collected and processed by
MAYO CLINIC ROCHESTER
Transfusion Medicine
Rochester, Minnesota 55905

VOLUNTEER DONOR

Warning: This product may transmit infectious agents.
Rx only



- Collection Time
- Unique identifier
- Expiry date
- Blood Type
- Product Type
- Additives
- Blood Type
- Collection site
- Other required phrases and warnings

ISBT 128

- International Labeling Standard for Cellular Therapies
 - Standardized terminology and numbering system
 - Standardized label format
- Easier international exchange of products
- Being phased in over the next several years
 - Not widely used yet

Cellular Therapy Laboratory Documentation - Product Manufacturing

- Manufacturing record for each product
 - All details of product manufacturing
 - Receipt
 - Testing- tests and results
 - Details of processing
 - Staff involved
 - Materials and reagents used
 - Lot numbers, expiry date
 - Cell counts, volumes, process performed
 - Equipment used for testing and storage
 - Storage conditions
 - Deviations or events
 - Disposition of product
 - Administered, shipped, or discarded

Processing for Fresh Administration

- No processing
 - Perform required testing only
 - Label and distribute for administration
- Red Blood Cell Reduction
- Volume Reduction

Red Blood Cell Reduction

- To remove incompatible red cells
 - Type A, B or AB donor to type O recipient
 - ABO mismatched transplants are not unusual
 - Hemolytic reaction without removing RBC
 - Bone marrow > 300 mL RBC
 - PBSC 10-30 mL
 - Red cells removed by centrifugation or sedimentation in blood bags
 - HES improves process
 - Predictable loss of stem cells (~15-25%)

Volume Reduction

- For pediatric patients
- To remove plasma containing antibodies against recipient rbc's
- Centrifugation in blood bags
- High recovery of stem cells



Cryopreservation

- Autologous transplants
- Some allogeneic transplants
 - Usually for logistic reasons
 - Donor and recipient are not available at the same time or in the same location
- Long term storage of stem cells

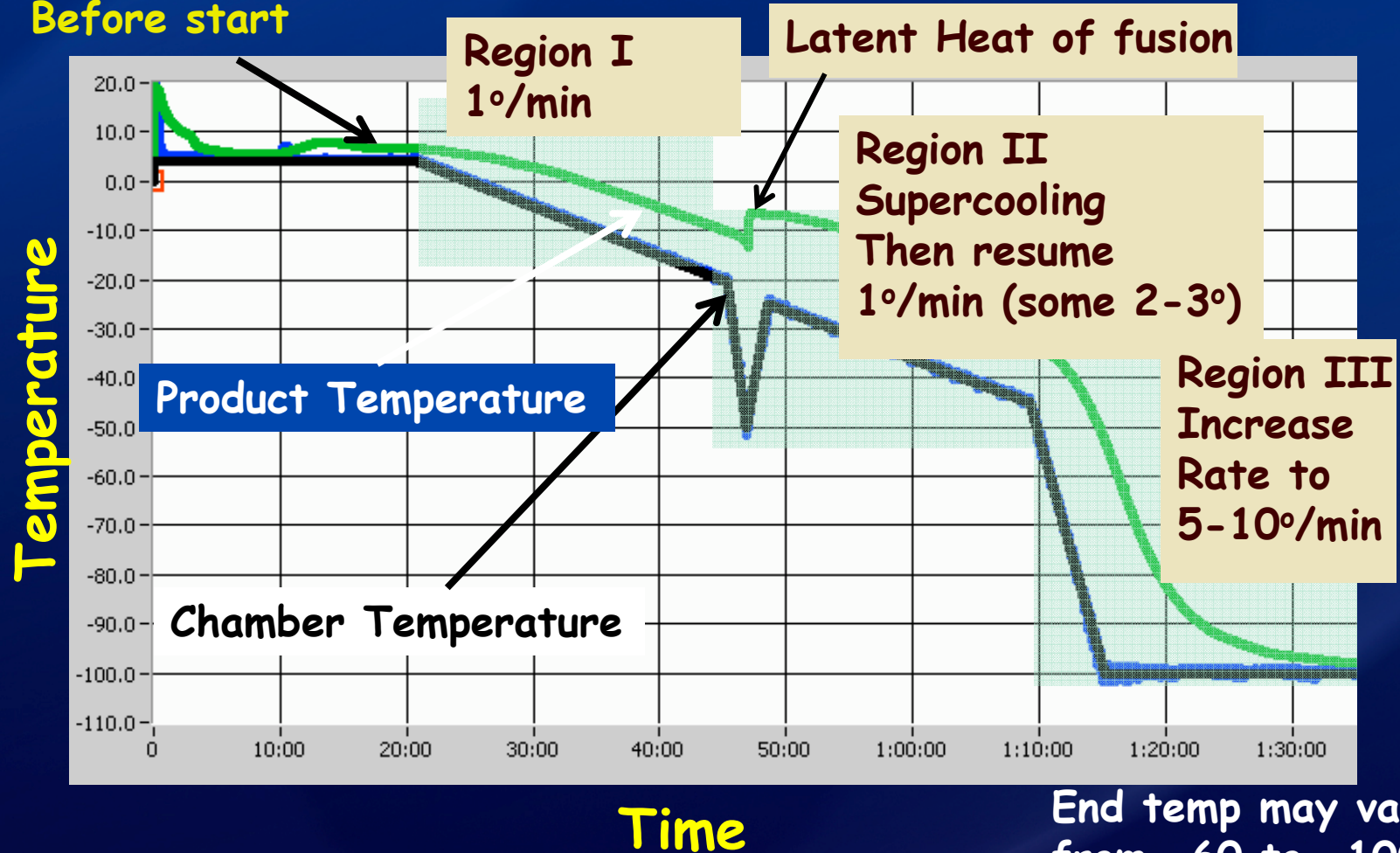
Steps of Cryopreservation

- Cell count
- Concentration/volume reduction
- Addition of Cryoprotectant
 - 10% DMSO, Electrolyte solution, plasma
- Freezing
 - Controlled rate or mechanical freezer
 - Controlled rate more expensive + LN2 source
 - Mechanical – shorter term storage

Computer Controlled Freezing

Let product = Chamber
Before start

Need to determine during validation





Storage of Products

- Liquid/Vapor nitrogen tanks
 - -196 C Best for long term storage
 - Less susceptible to power interruptions
- Mechanical Freezer
 - - 80 C to -150 C
 - Need back up power supply
- Both methods need back up plan with alternate storage location

Storage of Products

- Temperature monitoring of storage location
 - Continuous recording or regular frequency
- Alarm system to notify of abnormal temperature
- Inventory system to track/locate products

Product Certificate of Analysis

- Document summarizing product details
 - Donor identifier, if applicable
 - Processing
 - Additives
 - Test results all meet specifications
 - Biohazard warnings, if applicable
 - Reviewed by laboratory director prior to administration

Preparation for Administration (frozen products -1)

- Physician request to administer cells
- Locate product in freezer
- Confirm identity of product with physician request
- Ensure proper labeling
- Ensure all required tests are completed
 - Infectious diseases
 - Cell dose
 - Sterility culture of product

Preparation for Administration (frozen products -2)

- Compare product label with recipient identity
- Prepare waterbath
- Thaw product
- Administer product
 - IV infusion
 - No Leukoreduction Filter

Post Administration

- Monitor for adverse events
- Track patient outcome as quality monitor

Process Control and Traceability/Trackability

- A well documented, controlled, reproducible, manufacturing process is the best way to ensure high quality products
- It is critical to document all steps of product manufacturing from procurement to administration
 - To facilitate recalls and lookbacks (Biovigilance)
 - To allow for thorough investigations of adverse events or other outcomes
- Process control and traceability/trackability equals cGMPs
- This is accomplished via Quality Systems

Elements of a Quality System

- Organization, Leadership, and Customer Focus
- Facilities, Work Environment, and Safety
- Human Resources
- Suppliers and Supply Management
- Equipment Management
- Process Management
- Documents, Records, and Information Management
- Nonconforming Events
- Monitoring and Assessment
- Continual Improvement

The laboratory and BMT program should have processes, policies, and procedures addressing each of these topics.