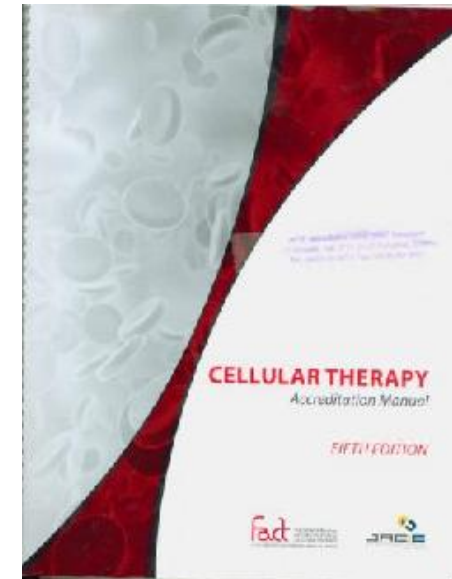




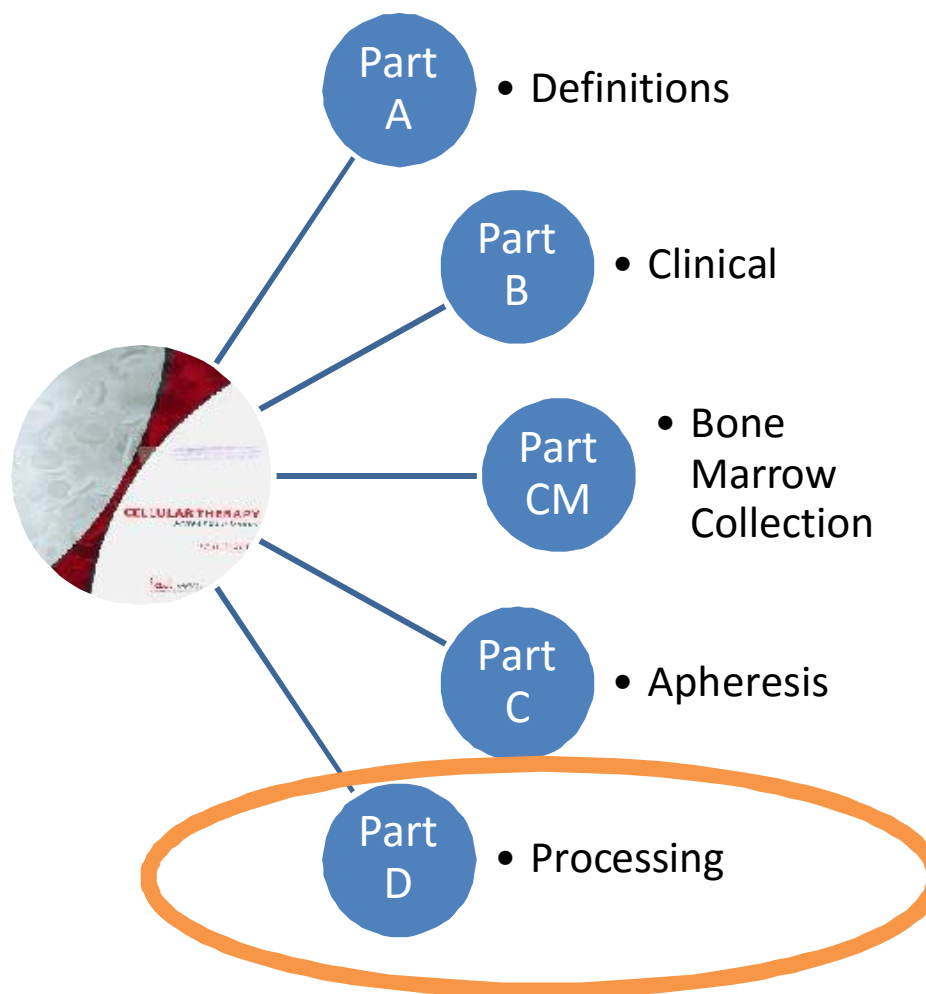
FACT-JACIE Standards

Processing





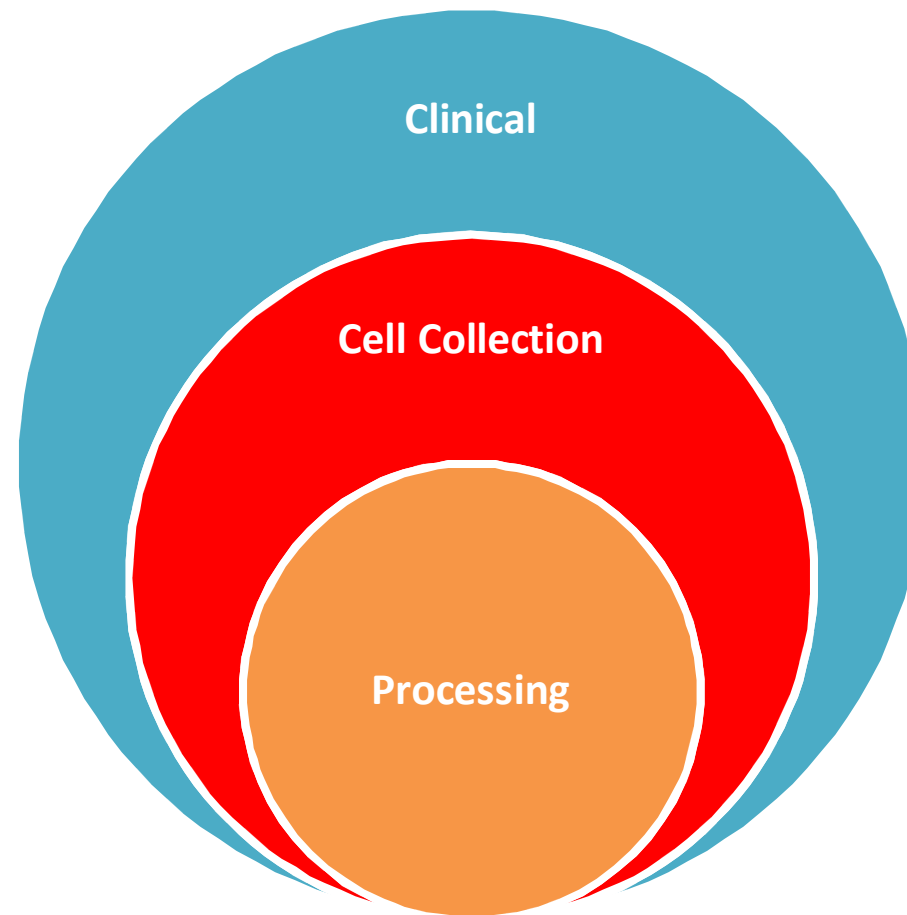
FACT-JACIE Standards





Transplant Programme

Use cell processing facilities that meet FACT-JACIE Standards with respect to their interactions with the Apheresis Collection Facility.





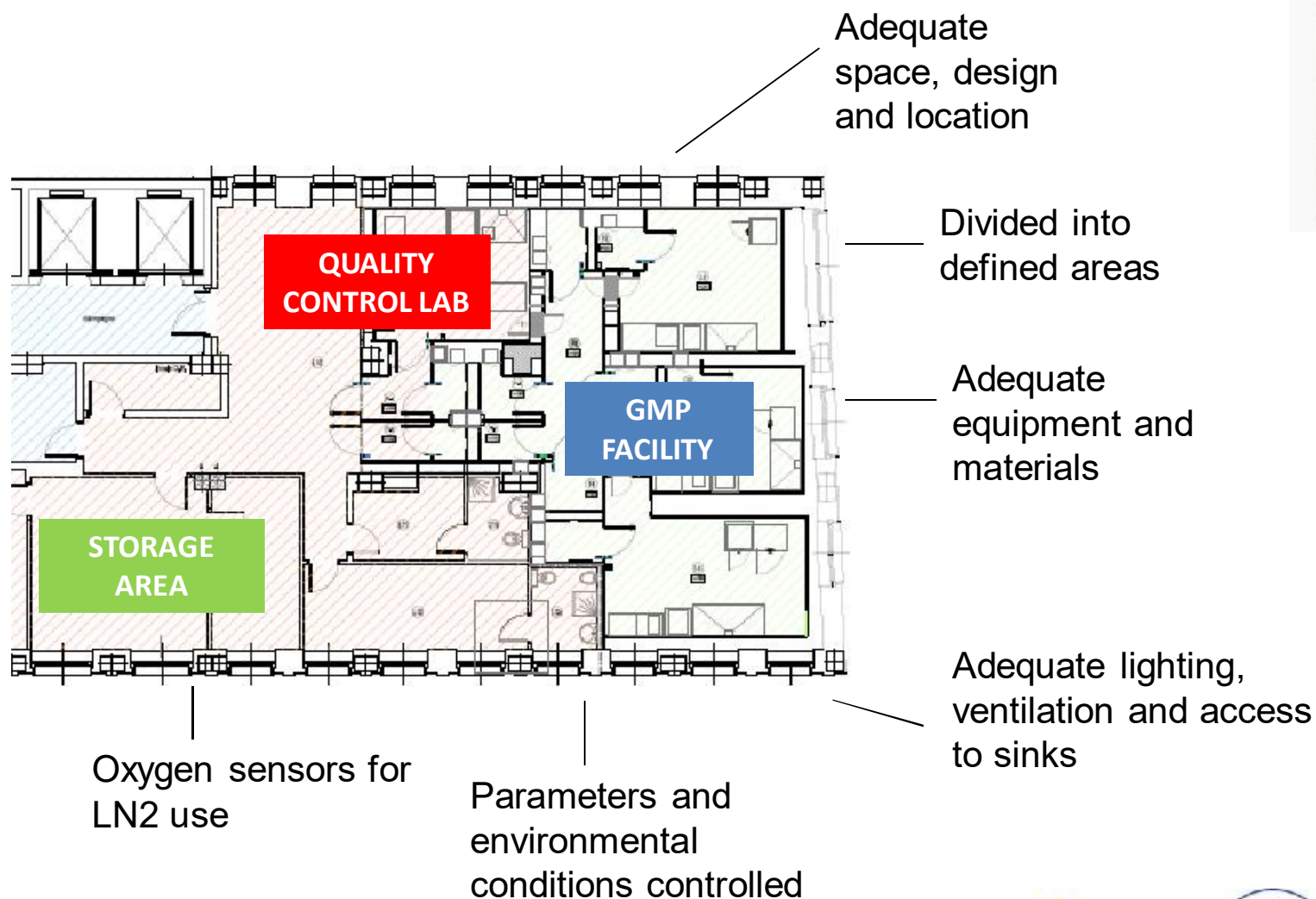
D1 General Requirements

- Comply with applicable laws and regulations
- Compliance with JACIE does not guarantee compliance with all applicable laws and regulations and vice versa





D2 Facilities



Secure Access



Critical facility parameters

Temperature

Humidity

Air quality

Surface
contaminates

Monitoring for
microorganisms

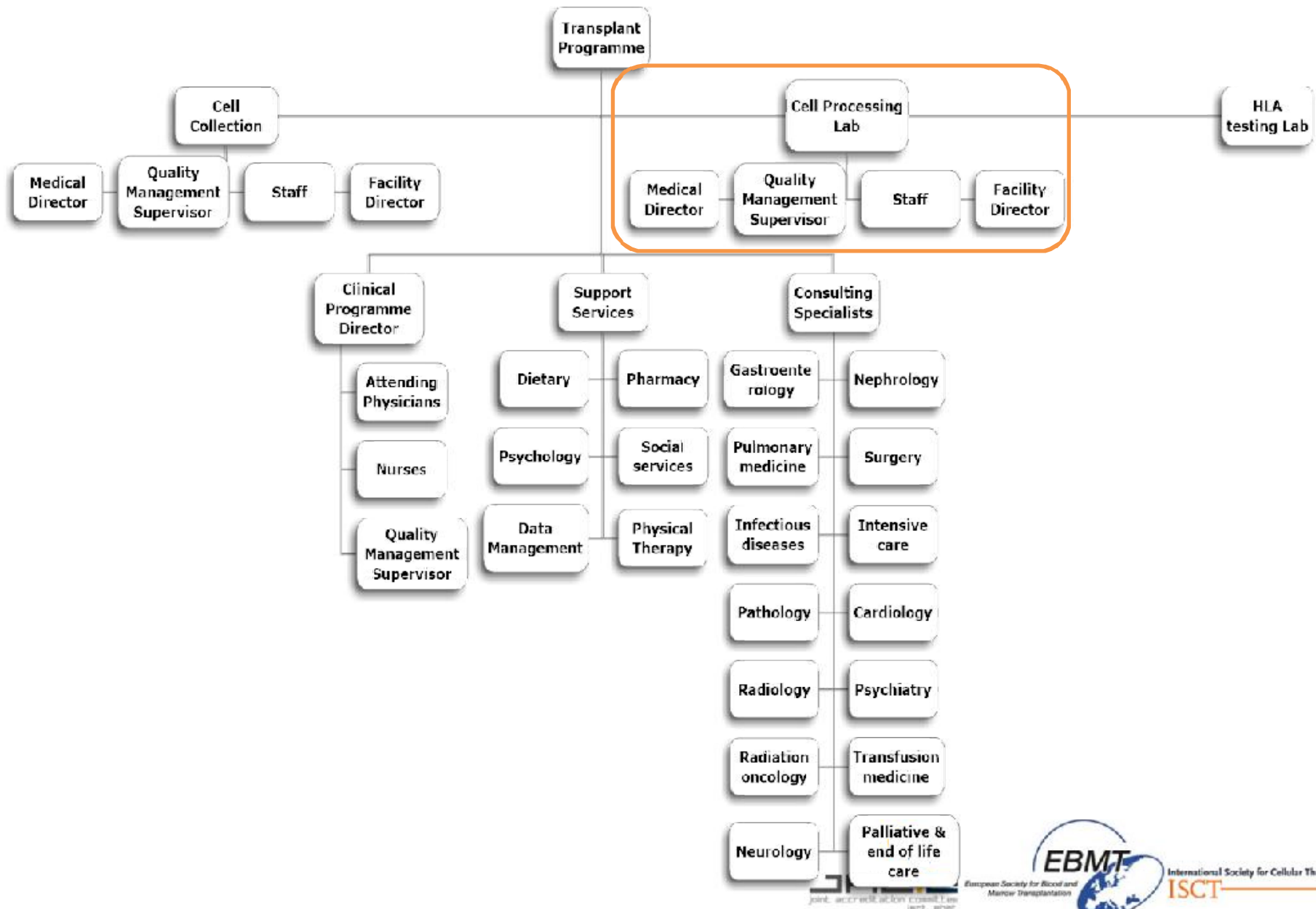
Parameters identified to be a risk
must be controlled, monitored and
recorded



Cleaning

- Documented facility cleaning and sanitation to ensure adequate conditions for proper operations
- Qualify environmental control systems and validate cleaning and sanitation procedures appropriate for the environmental classification and degree of manipulation performed

D3 Personnel





**Processing Facility
Director**

Medical, doctoral or
equivalent degree
2 years training and
experience

Medical Director

Licensed or certified
physician, 2 years post
graduate training and
practical experience

**Quality
Manager**





Staff

- The Facility shall have an **adequate** number of trained staff.
- Shall include a minimum of one designated trained individual with an identified trained backup to maintain sufficient coverage.

HOW MANY IS “ADEQUATE”?



D4 Quality Management

D4.2 The Processing Facility shall establish and maintain a written Quality Management Plan.

QM activities shall be reported at a minimum, quarterly review the performance of the QM plan



D4.7 The Quality Management Plan shall include, or summarize and reference, policies and procedures for review of outcome analysis and cellular therapy product efficacy to verify that the procedures in use consistently provide a safe and effective product.

Patient outcome data including adverse events and engraftment, Evidence of analysis.



Audit Management

D4.8 The Quality Management Plan shall include, or summarize and reference, policies, procedures, and a schedule for conducting, reviewing, and reporting audits of the Processing Facility's activities to verify compliance with elements of the Quality Management Program and operational policies and procedures.

D4.8.2 The results of audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions when necessary, and follow-up on the effectiveness of these actions in a timely manner.

- ✓ ***Audit plan***
- ✓ ***Audit report***
- ✓ ***External audit***
- ✓ ***Follow-up and actions to take after audit***



Errors, accidents, deviations, serious adverse events and complaints





- Investigation – root cause
- Documentation
- Reporting
- Corrective and Preventative action





D4.11 Product tracking and tracing

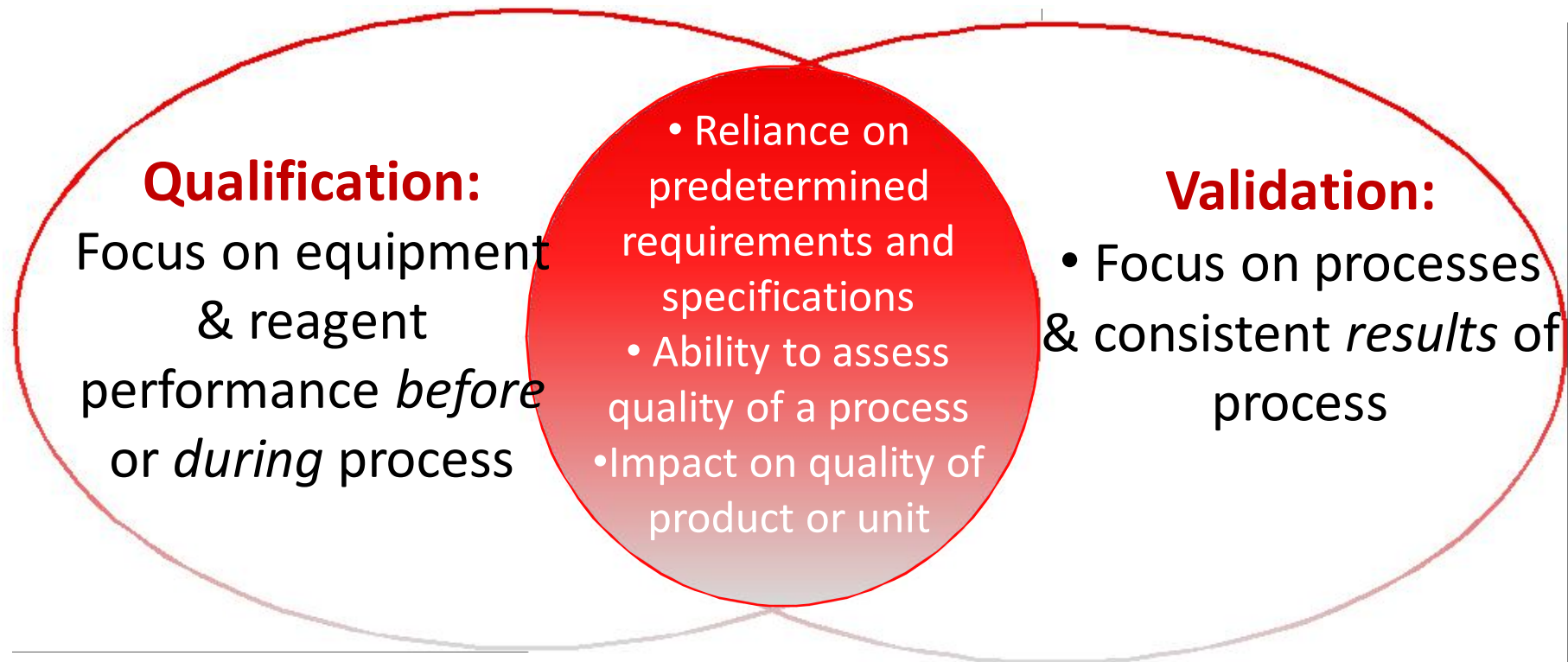
- Policies and procedures for cellular therapy product tracking and tracing that allows tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

 W1234 12 123456 B [w] University Medical Center Anytown, 99010	  RHD POSITIVE
Collection Date and Time 012300010 2012-02-05 09:15 Do Not Irradiate Do Not Use Leukocyte Reduction Filter	FOR AUTOLOGOUS USE ONLY
 61142 LL CRYOPRESERVED HPC, APHERESIS 6% HES + 5% DMSO Apexx _____ nil with approx _____ nil Cells are _____ in Heparin (_____) Bx 10 ⁶ ± 15% G or code	 12/1/13 200 2022-02-05 22:59 Copy Date and Time
	Donor/Recipient PATIENT, JOHN Q MRN: 123456789 Date of Birth: 31 Dec 1984  Processing Laboratory E sawtara, Worldwide



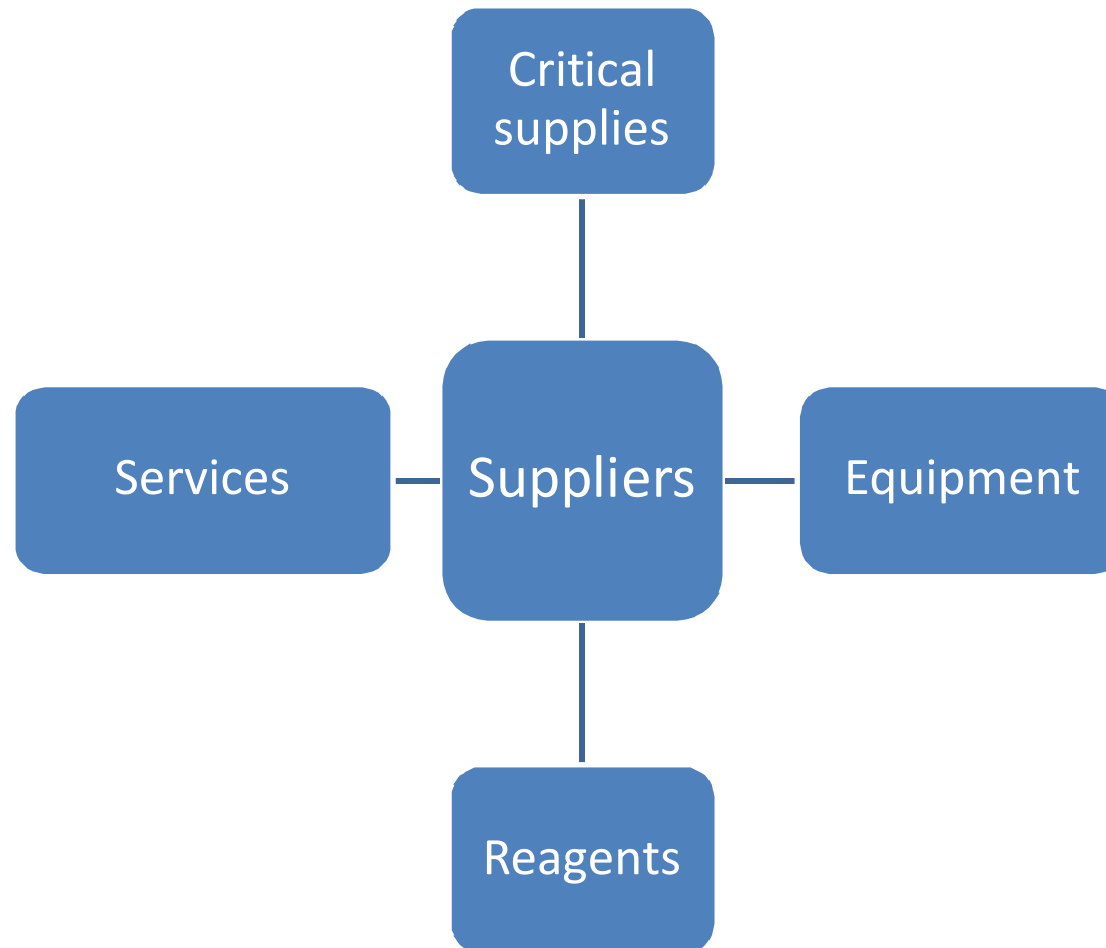
Qualification & Validation: What is the difference?

(or, more importantly, what is the same?)





Qualification - processing





Validation

- Policies and procedures for validation and/or verification of critical procedures to achieve the expected end points
- There shall be documentation of review and acceptance of validation
- Each validation shall include:
 - An approved validation plan, including conditions to be validated.
 - Acceptance criteria.
 - Data collection.
 - Evaluation of data.
 - Summary of results.
- There shall be documentation of review and acceptance of validation studies by the appropriate individual from Quality Management



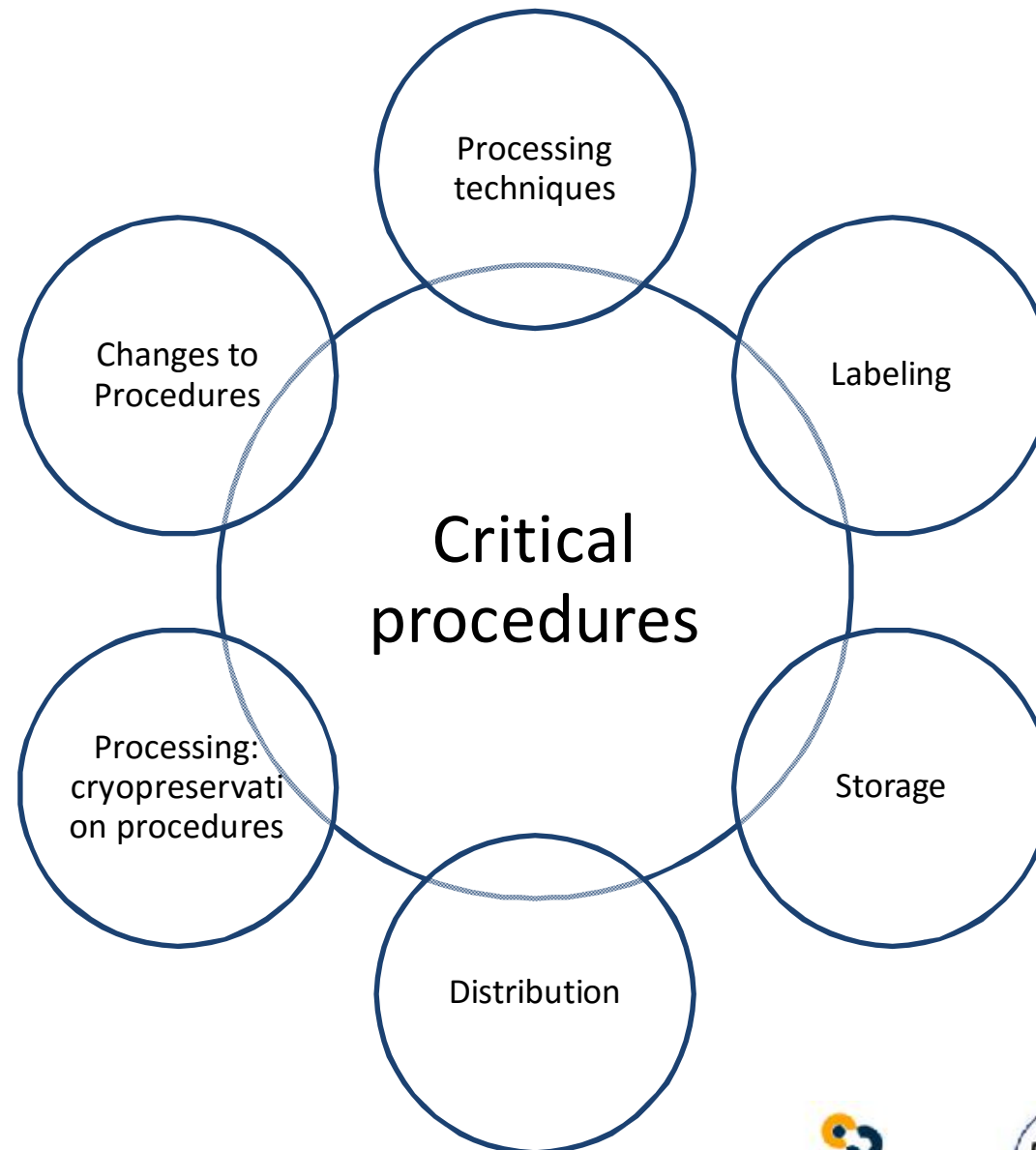
Validation

Changes to a process shall include evaluation of risk to confirm that they do not create an adverse impact anywhere in the operation and shall be validated or verified as appropriate.

Risk Consequence x Probability		Probability			
		Unlikely	Not very likely	Possible	Probable
Consequence	Very Serious	Hazardous	Hazardous	Very Hazardous	Very Hazardous
	Serious	Moderately Hazardous	Hazardous	Hazardous	Very Hazardous
	Mild	Moderately Hazardous	Hazardous	Hazardous	Hazardous
	Insignificant	Not Hazardous	Not Hazardous	Moderately Hazardous	Hazardous



Validation





JACIE Requirements for Validation

- ✓ Include in Quality Management Plan (QMP)
 - All details in QMP or a summary in QMP with reference(s) to the details
- ✓ Oversight
 - QA Review and acceptance of validation plan before starting
 - QA Review and approval of results and conclusions





D5 Policies and Procedures

D5.2 The Processing Facility shall maintain a detailed Standard Operating Procedures Manual that includes a listing of all current Standard Operating Procedures, including title, identifier, and version.



D5.5 Staff training and, if appropriate, competency shall be documented before performing a new or revised procedure.



D6 Equipment Supplies and Reagents

- Stock control/inventory control
- Supplies and reagents used according to manufacturers instructions
- Track equipment/critical reagents used
- Cleaning/calibration/maintenance
- Equipment failure
- Procedure to link reagents/supplies/equipment used in processing of each cellular therapy product



D6.2 Materials Management System for Consumables and Reagents

- Records include :
 - consumable or reagent type,
 - quantity
 - manufacturer
 - lot number
 - date of receipt, acceptability,
 - if applicable, expiration date.





Materials management system

Visual examination

Records of receipt






Appropriate
environmental
conditions

Sterile supplies and
reagents that are of
the appropriate grade
for the intended use.



D7 Coding and Labeling of Cellular Therapy Products

- If coding and labeling technologies have not yet been implemented, the Processing Facility shall be actively implementing ISBT 128.

 W1234 12 123456 B [w] University Medical Center Anytown, NY 10001	  RhD POSITIVE
Collection Date and Time 012300010 2012-02-05 09:15 Do Not Irradiate Do Not Use Leukoreduction Filter	FOR AUTOLOGOUS USE ONLY
 61142 LL	 123456789 2022-02-05 20:59
CRYOPRESERVED HPC, Apheresis 6% HES + 5% DMSO Apexx _____ nil with approx _____ nil Cells and _____ in Heparin (_____) Store at -150 C or colder	Donor/Recipient PATIENT, JOHN Q MRN: 123456789 Date of Birth: 31 Dec 1984  Processing Laboratory E sawtara, Worldwide





ISBT 128

Evidence:

- Organizations must, minimally, demonstrate a clearly documented infrastructure including:
 1. Registration with ICCBBA.
 2. Identification or creation of appropriate product codes.
 3. Label designs according to the requirements of ICCBBA for Cellular Therapy Products.
 4. Label validation.
 5. Use of scanned information at the time products are released from collection, received into the laboratory, and at distribution from the processing facility.
- It is understood that some organizations may have difficulty with active implementation early after the effective date of these standards. Organizations may be requested to provide updates throughout the accreditation cycle via interim reporting.

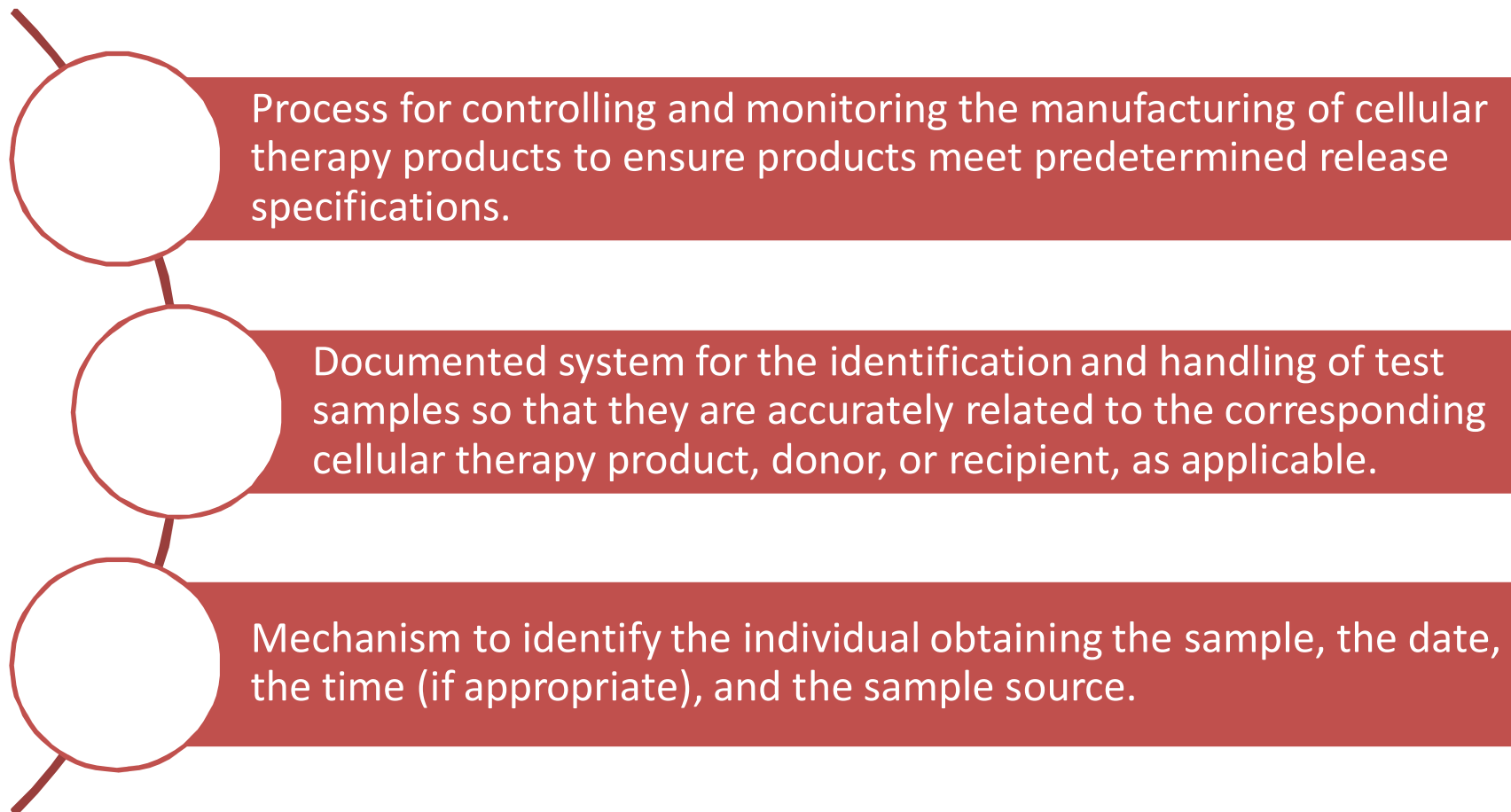


D7 Labeling

- Requirements include:
 - Labeling operations to prevent mislabeling or misidentification of cell products
 - Product identification to prevent mix-ups
 - Print on demand systems validated
 - Label version
 - Label validated for storage



D8 Process controls: Processing



D8.1.4 Overview of requirements for tests performed within the Processing Facility



- Process for monitoring the reliability, accuracy, precision and performance of laboratory test procedures and instruments
- Including
 - Use of controls
 - Calibration and standardization of reagents and equipment
 - Staff training and proficiency testing



New lots must be verified before use to:

- Ensure comparable results to current lots
- Produce results in agreement with suitable reference material



Controls (D8.1.4.3)

- Must be used each day of testing
- Must give results within the defined range established for that material
- Only required if reference material is available
 - Control cells must be appropriate for the instrument in use



Proficiency Testing (D8.1.4.5)

- Must have documentation of ongoing proficiency testing
 - Processing Facility Director responsible for determining schedule
- Results must be reviewed by the Director and outcomes reviewed with the staff
- Availability of proficiency testing:
 - Administered by external organizations
 - Established internally if no external test is available

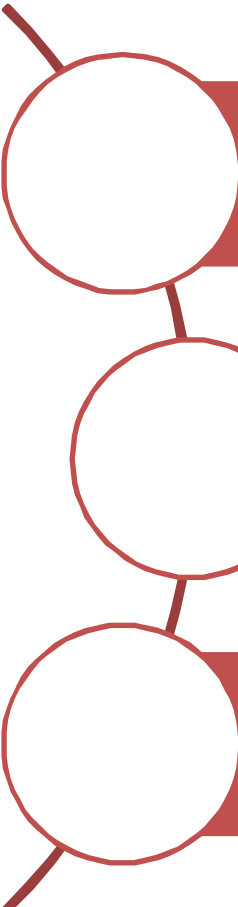


- [illegible]





Process controls: Processing



Each supply and reagent used to collect cellular therapy products shall be visually examined at receipt and prior to use for damage or evidence of contamination

Supplies and reagents coming into contact with cellular therapy products during collection shall be sterile and of the appropriate grade for the intended use

Track and trace system for all

- critical equipment, reagents, supplies, labels used in cell collection



D8.4 Validation of Processing Procedures

Processing procedures shall be validated in the processing facility and documented to result in acceptable target cell viability and recovery

- ✓ Retrospective, concurrent or prospective
- ✓ Ongoing evaluation of processing results, data analysis
- ✓ Expected ranges



Cord blood units

- D8.4.3 Cord blood units that have not been red cell reduced prior to cryopreservation shall be washed prior to administration.
- D8.4.4 Cord blood units that have been red cell reduced prior to cryopreservation should be diluted or washed prior to administration.

D8.6 Aseptic Technique / Minimise Risk of Cross Contamination

- Eliminate possibility of product mix-ups and/or cross contamination.
 - Physical separation of records / and products during processing
 - Labelling
- Specify cleaning and disinfection pre and post-processing
- Use of disposable closed systems



D8.7 Microbial contamination

Monitor and document microbial contamination after processing

Results of microbial cultures shall be reviewed

Notify recipient's physician

D8.9 Review of Processing Records



The Processing Facility Director or designee shall review the processing record for each cellular therapy product prior to release or distribution

- Notification of the recipient's physician and the Processing Facility Medical Director when the clinically relevant processing end-points are not met.
- Documentation of notification and any remedial actions in processing record.





D8.12 ABO Group & Rh Type

- Standards require testing on 2 independently collected specimens
 - Donor work up (PB)
 - Donor PB at time of collection
 - Specimen from HPC
- Policy for Management of products that are ABO and/or Rh incompatible
- Policy should indicate how many incompatible red cells are acceptable for infusion and instructions for other positive antibody screens





D9 Cellular Product Storage

- Duration and temperature of storage must maintain viability and function and inhibit infectious agents
- Products must not be stored with other materials that may adversely affect the products
- Quarantined products must be stored in a manner that minimizes cross-contamination
- Storage units must be monitored and have alarm systems
- An inventory control system must be used to manage supplies, reagents, and cell products



Storage Area Tour



- Temperature
- Quarantine system
- Alarm systems
- Back-up storage plan
- Inventory control system





- D9.2.2 There shall be a written stability program that evaluates the viability and potency of cryopreserved cellular therapy products, minimally annually

E.g. retrospective, could use products scheduled for discard, samples stored



- Alarm systems shall have audible and visible signals or other effective notification methods.



Quarantine (D9.4.3.3)

- Many methods for quarantine are acceptable
 - Physical (separate storage, overwrap, etc.)
 - Electronic (flags and warnings in the processing record)
 - Tie tags
- Must be effective for minimizing risks of cross-contamination and inappropriate distribution



D10 Transportation and Shipping

- Procedures in place, risk assessments
- Container validation
- Courier qualifications
- Time limits
- Records kept of transport times and temperature



D10.5.2.1 The temperature of the shipping container shall be continuously monitored during shipment of cellular therapy products.



D10.5.3 The outer container shall be secured.

D10.5.6 The outer container shall be labeled in accordance with applicable laws and regulations regarding the cryogenic material used and the transport or shipment of biological materials.

- ✓ time at the start of transportation or shipping
- ✓ specification of the conditions of transportation or shipping relevant such as “Keep Cool,” “DO NOT FREEZE”



D11 Distribution and Receipt

- Records for each product must allow tracking and tracing between the donor and the recipient
- Pre-determined release criteria must be met before distribution, unless Director provides authorization
- Each cellular therapy product issued for administration shall be visually inspected by 2 trained personnel
- Handling instructions/indications/side effects
- Processing records include written record of distribution



Receipt of each cellular therapy product shall include inspection of:

- Container integrity
- Appearance
- Labelling
- Appropriately transported
- Temperature of outer container



D12 Disposal

Procedure/policy for discard and method of disposal

D12.1.1 A pre-collection written agreement between the storage facility and the designated recipient or the donor defining the length of storage and the circumstances for disposal of cellular therapy products.

D12.1.2 The option to transfer the cellular therapy product to another facility if the designated recipient is still alive after the agreed upon storage interval.

D12.2 Records shall indicate the product was discarded or transferred, date of discard, method of disposal

D12.1.6 Processing facilities shall establish policies for the duration and conditions of storage and indications for disposal



D13 Records

- Records Management
- Tracking product
- Assignment of unique identifiers
- Development/installation/validation
- Maintenance
- Staff training
- Monitoring of data integrity



Remember

- The ACCREDITATION MANUAL includes examples of what to look for

