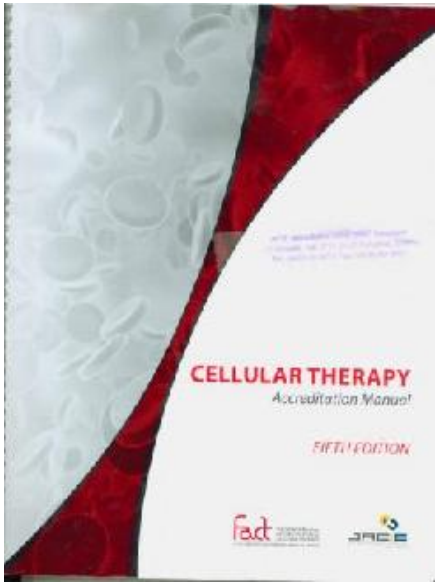
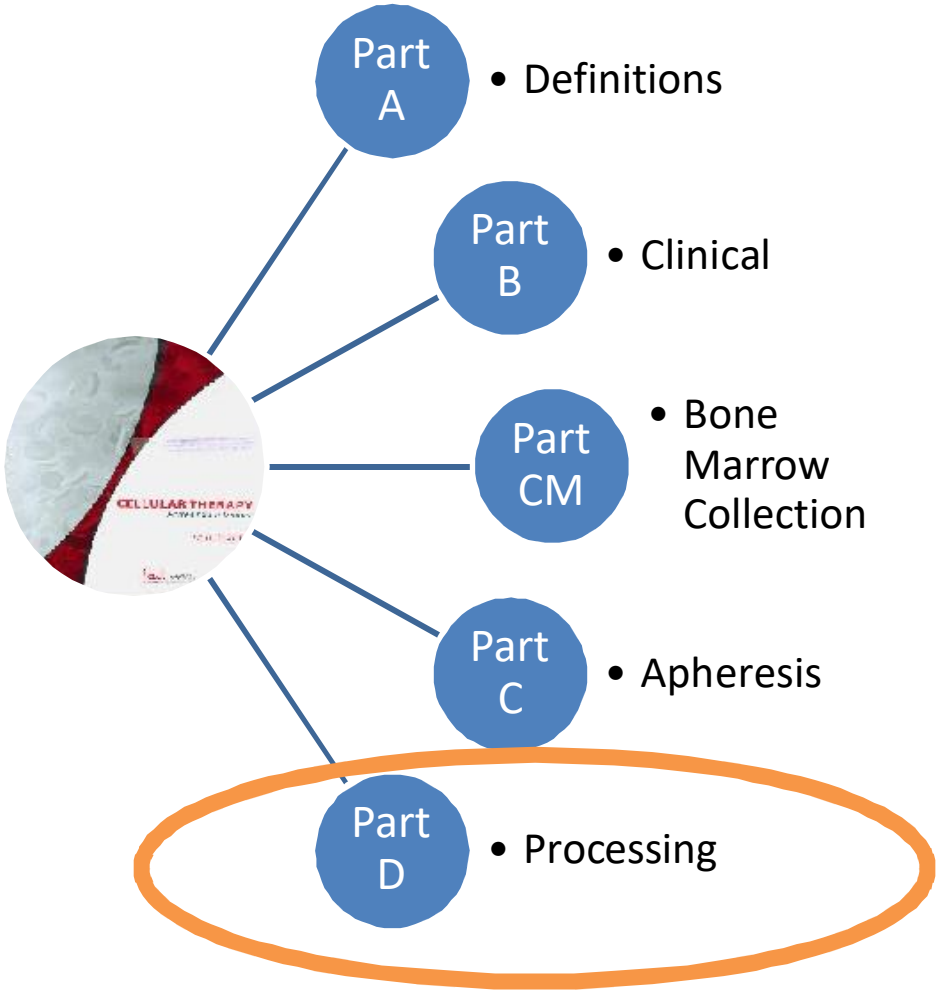
# FACT-JACIE Standards

Processing

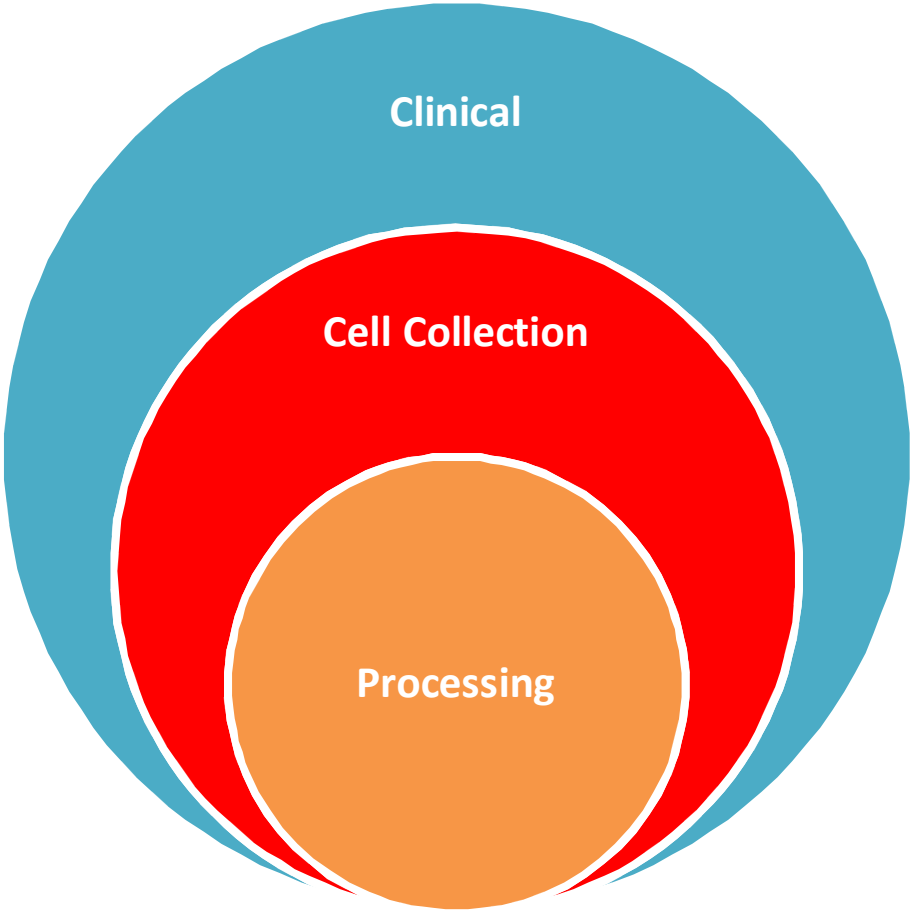


# FACT-JACIE Standards



# Transplant Programme

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

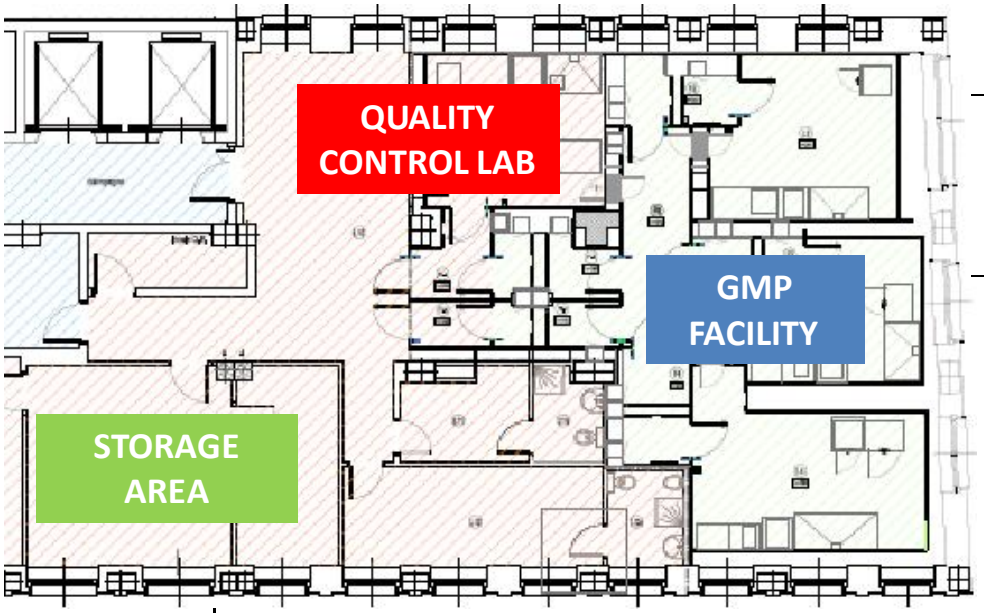


# D1 General Requirements

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

# D2 Facilities

Adequate space, design and location




Divided into defined areas

Adequate equipment and materials

Secure Access

Adequate lighting, ventilation and access to sinks

Oxygen sensors for LN2 use

Parameters and environmental conditions controlled

# Critical facility parameters

Temperature

Humidity

Air quality

Surface contaminates

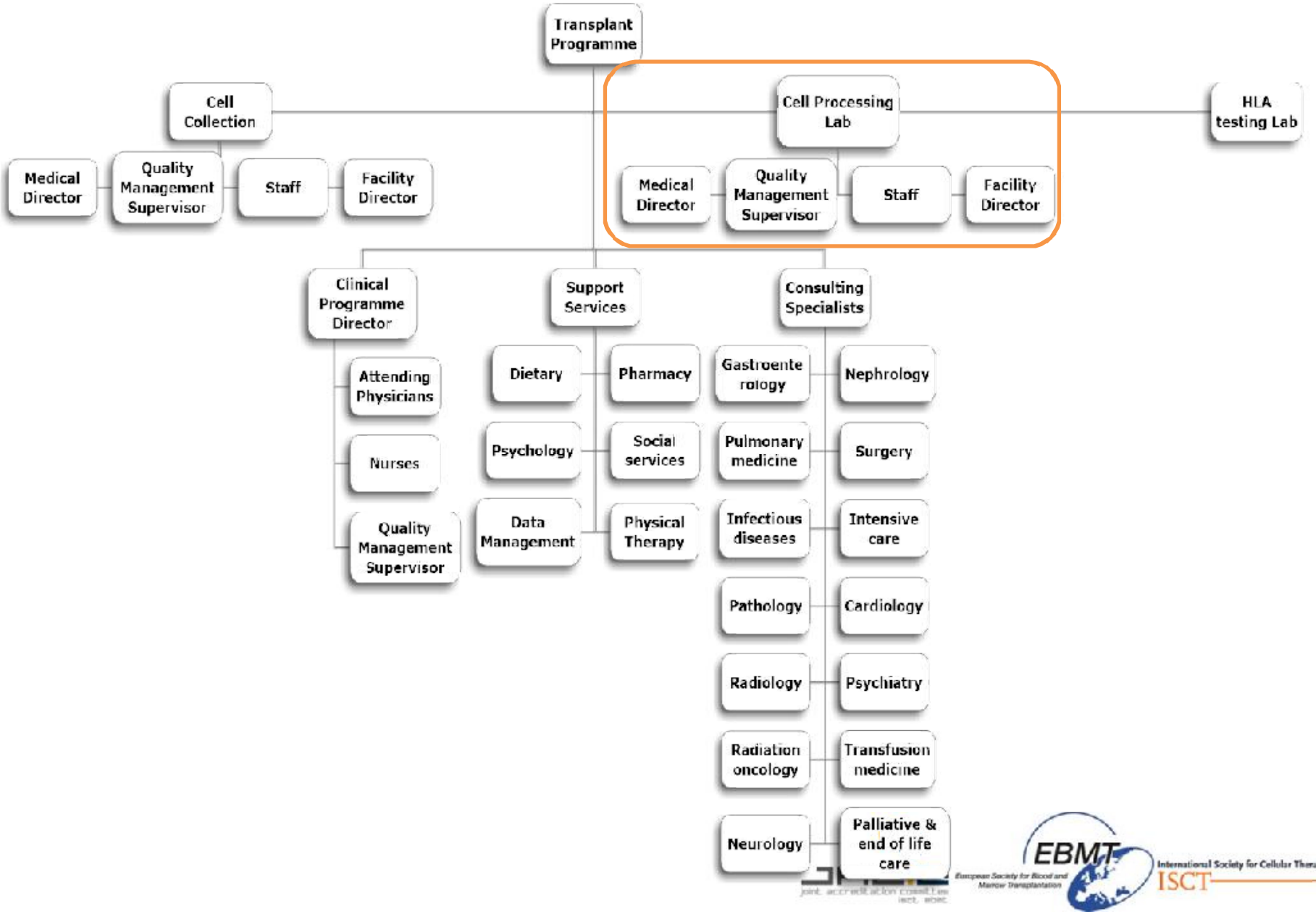
Monitoring for microorganisms

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, quarterley 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.

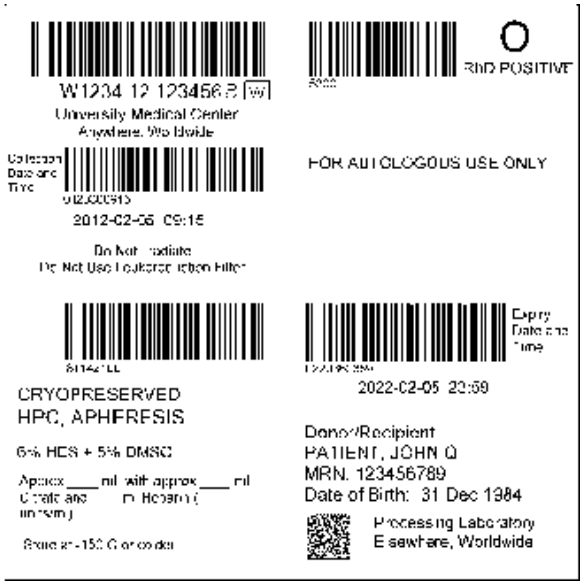

- ✓***Audit plan***
- ✓***Audit report***
- ✓***External audit***
- ✓***Follow-up and actions to take after audit***

# Errors, accidents, deviations, serious adverse events and complaints

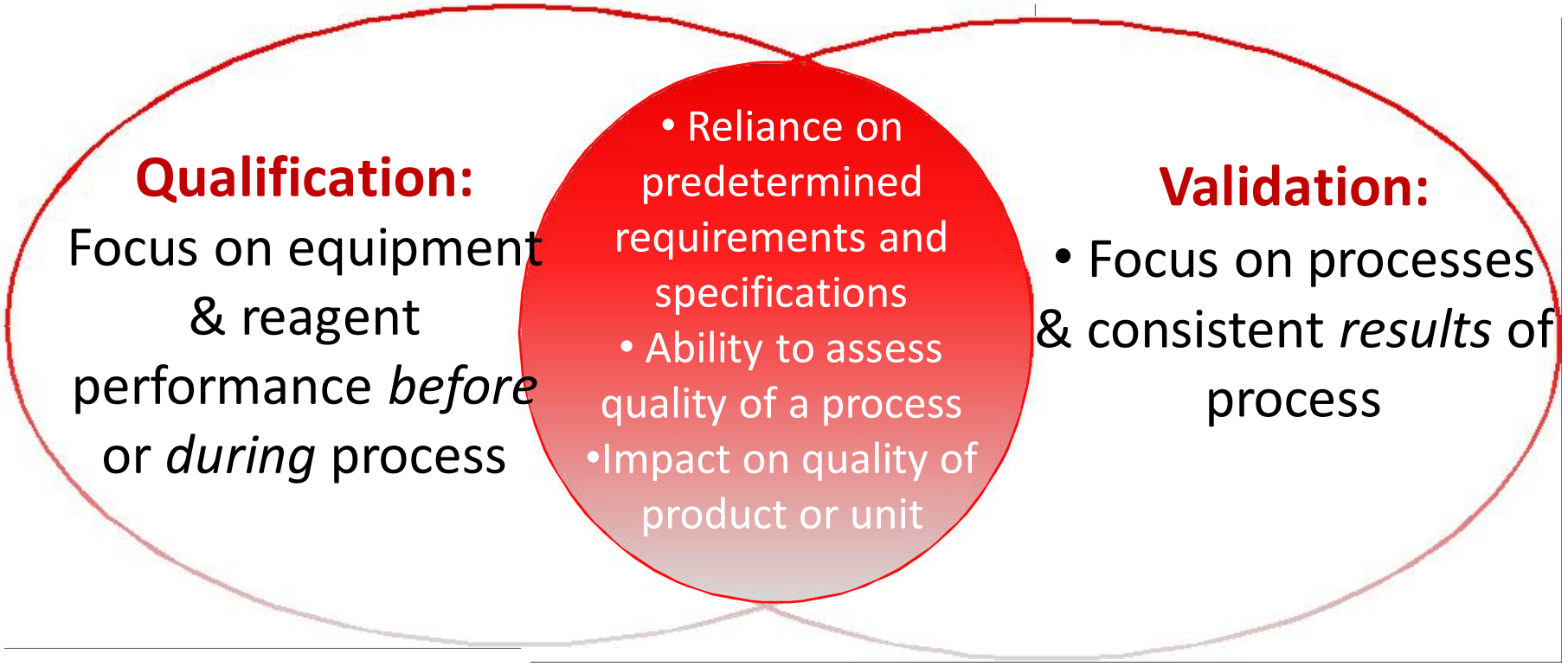
- Investigation – root cause
- Documentation
- Reporting
- Corrective and Preventative action

# D4.11 Product tracking and tracing

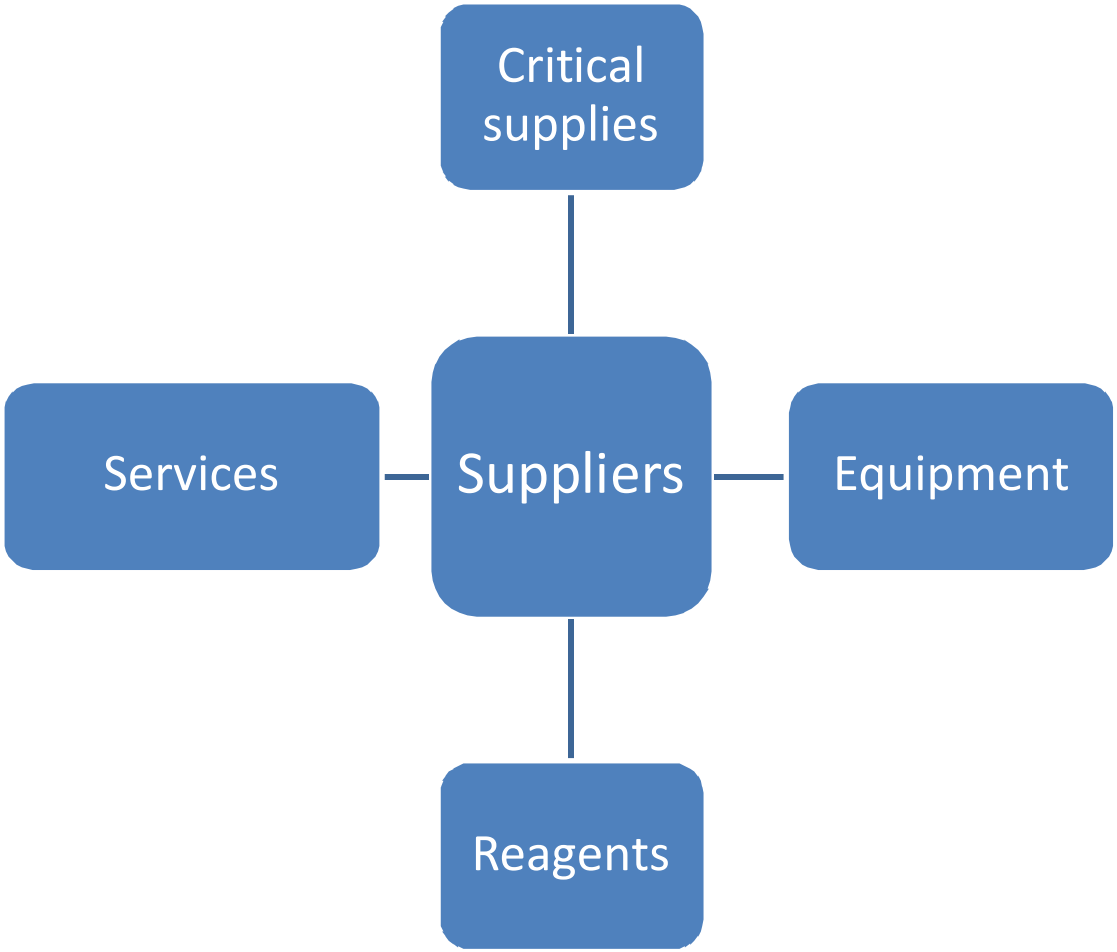
- Policies and procedures for cellular therapy product tracking and tracing that allows tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.



# 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.

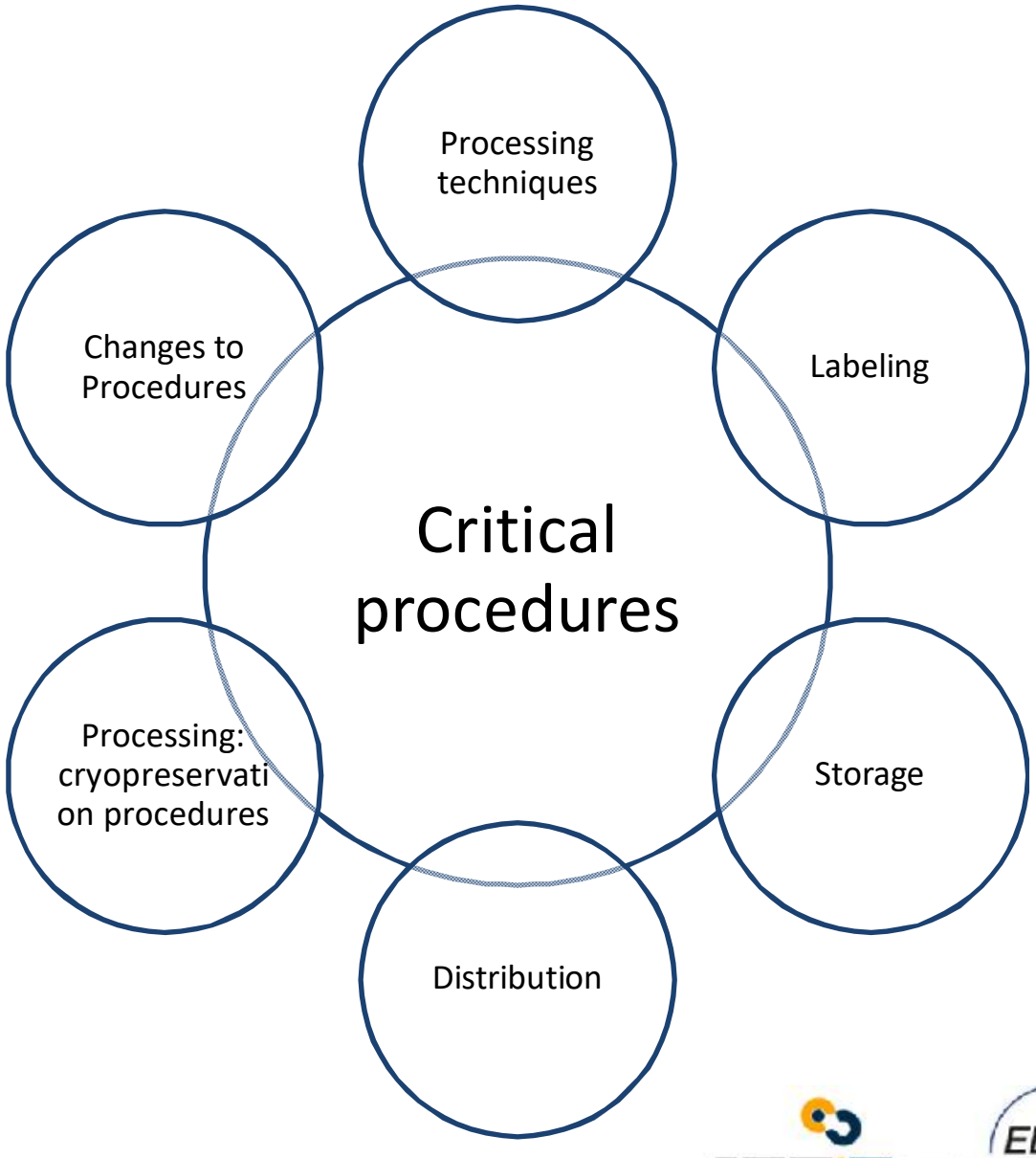
- There shall be documentation of review and acceptance of validation studies by the appropriate individual from Quality Management

# 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<br>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


Processing techniques
Changes to Procedures
Labeling
Critical procedures
Processing: cryopreservation procedures
Storage
Distribution

# 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

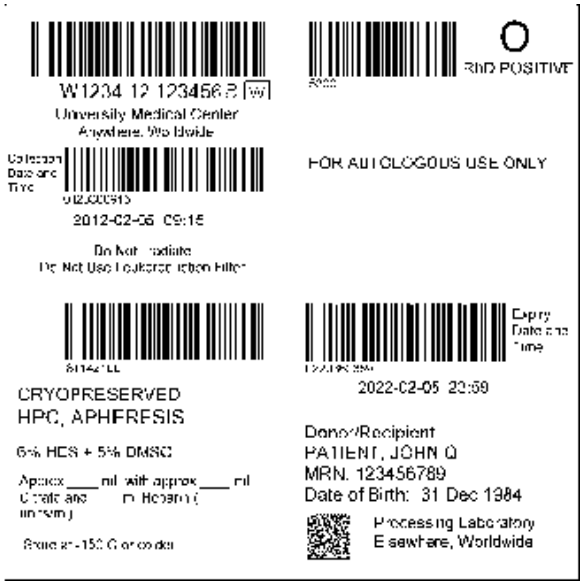
Records of receipt

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.




ISBT 128
More than Identification

JACIE
EBMT
European Society for Blood and Marrow Transplantation
International Society for Cellular Therapy
ISCT

# 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.

ISBT 128
More than Identification

JACIE joint accreditation committee
EBMT European Society for Blood and Marrow Transplantation
ISCT International Society for Cellular Therapy

# 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

Process for controlling and monitoring the manufacturing of cellular therapy products to ensure products meet predetermined release specifications.

# D8 Process controls: Processing

Documented system for the identification and handling of test samples so that they are accurately related to the corresponding cellular therapy product, donor, or recipient, as applicable.

# D8 Process controls: Processing

Mechanism to identify the individual obtaining the sample, the date, the time (if appropriate), and the sample source.

# 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 ncluding
  - 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

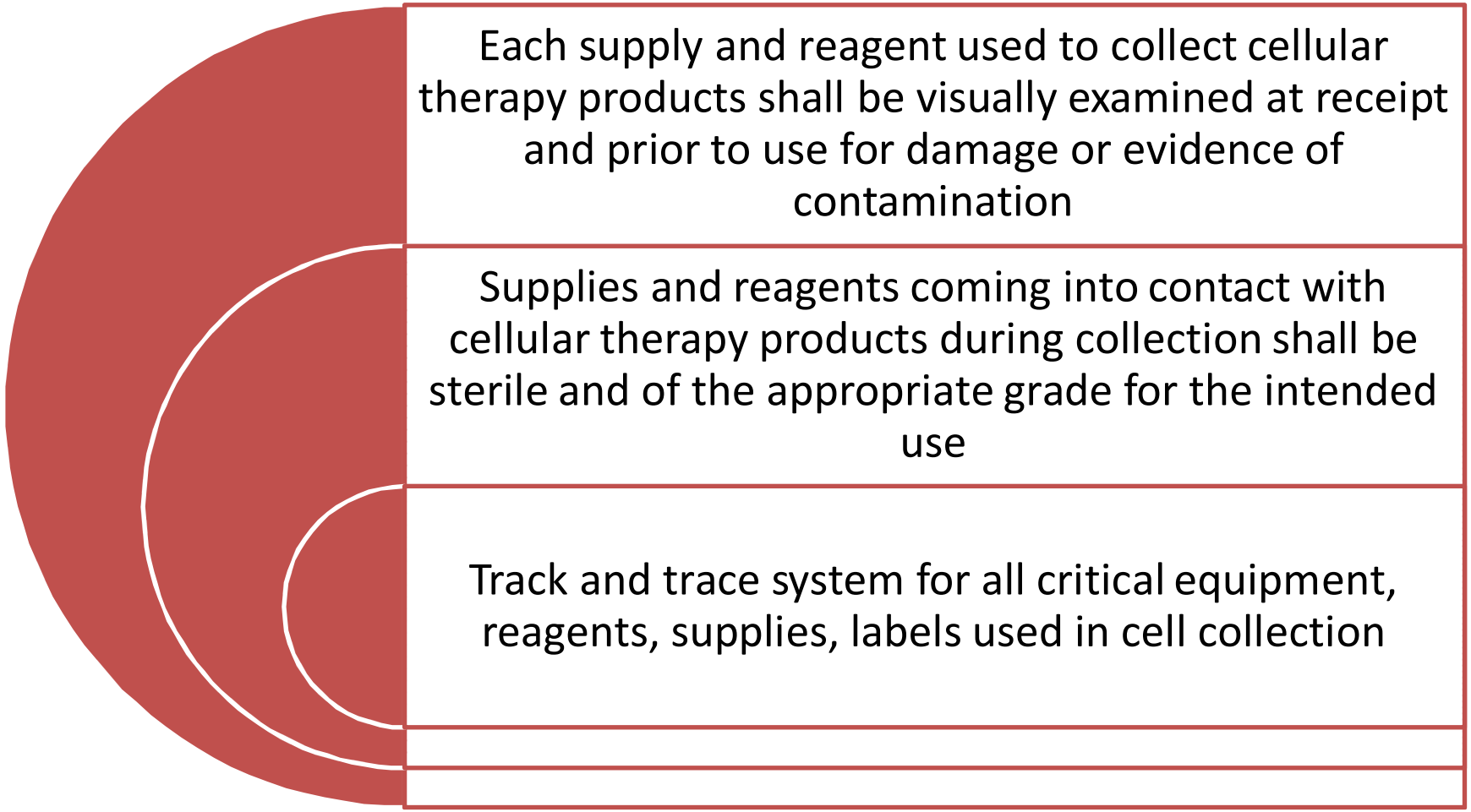
# Proficiency Testing (D8.1.4.5)

- 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

# Testing Performed by an External Laboratory (D8.1.5)

- Laboratory must be certified or accredited by appropriate laboratory regulatory agency (D8.1.5)
- Documentation must be available to inspector
  - However, actual certificates are not required to be on-site at Processing Facility


# Process controls: Processing



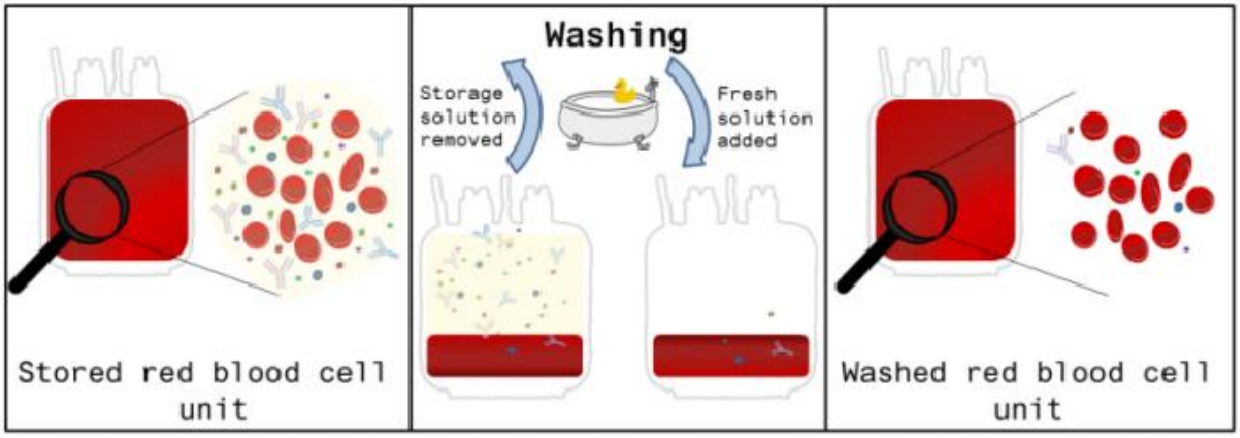
# D8.4 Validation of Processing Procedures

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

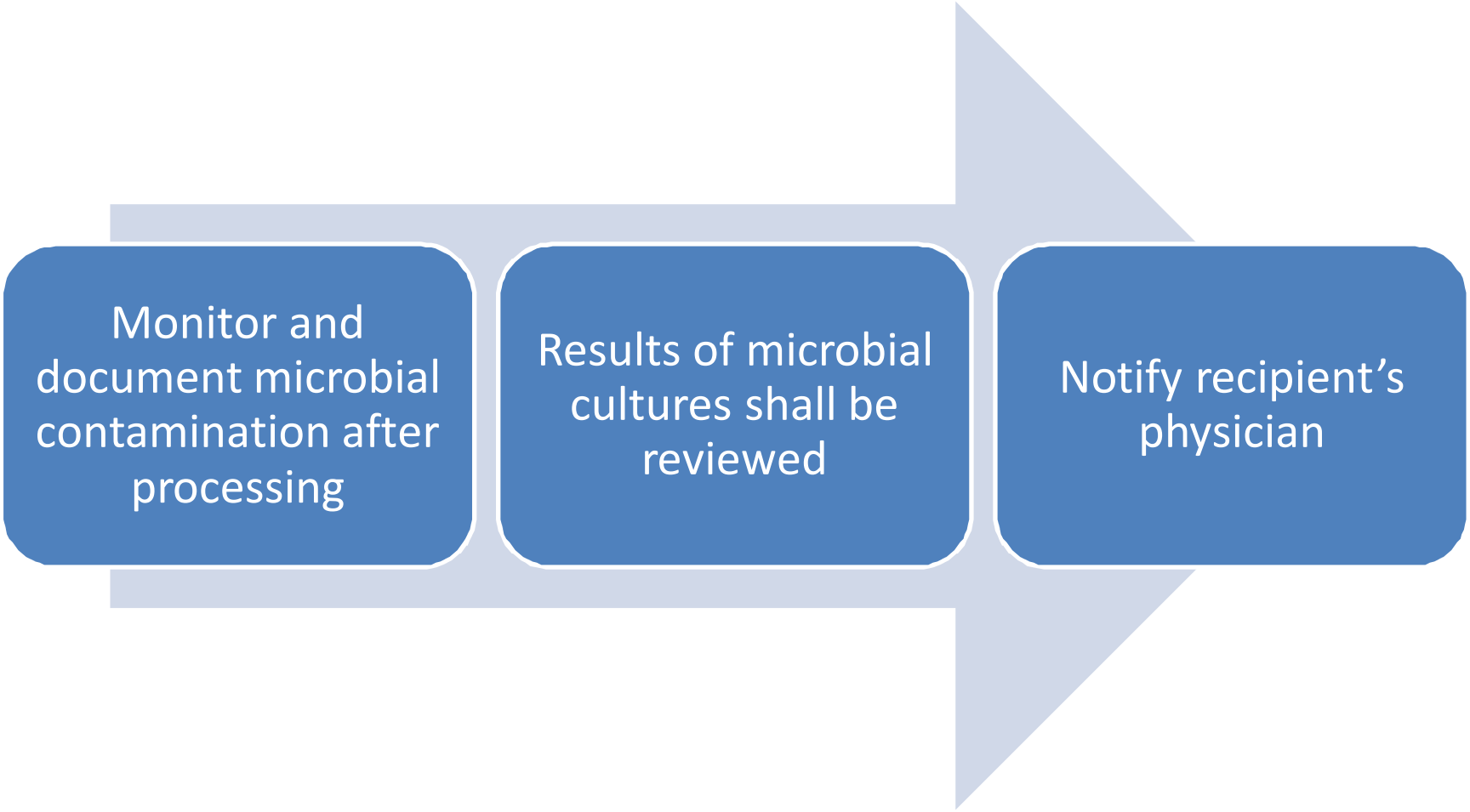
- D8.4.3 Cord blood units that <u>have not</u> been red cell reduced prior to cryopreservation <u>shall</u> be washed prior to administration.
- D8.4.4 Cord blood units that <u>have</u> been red cell reduced prior to cryopreservation <u>should</u> be diluted <u>or</u> washed prior to administration.



# 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



# 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 asessments
- 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

| | | | | | | |
|---|---|---|---|---|---|---|
| 237 | D-07 | CODING AND LABELING OF CELLULAR THERAPY PRODUCTS | | | | |
| 238 | D-07.01 | ISBT 128 CODING AND LABELING | | | | |
| 239 | D-07.01.01 | Cellular therapy products shall be identified according to the proper name of the product, including appropriate modifiers and attributes, as defined in ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions. | Compliant | | Partially compliant | TC-T is an outdated term in the ISBT128 Standard terminology |
| 240 | D-07.01.02 | If the Processing Facility has not fully implemented ISBT 128 technology, an implementation plan for the usage of ISBT 128 coding and labeling shall be in place. | Compliant | implementatieplan | Compliant | |
| 241 | D-07.02 | LABELING OPERATIONS | | | | |
| 242 | D-07.02.01 | Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of cellular therapy products and product samples. | Compliant | TR-06LA3-016<br>TR-06LA3-020<br>TR-06LA3-024 | Compliant | |
| 243 | D-07.02.02 | The labeling operation for pre-printed labels shall include, at a minimum, the following controls | | | | |
| 244 | D-07.02.02.01 | Labels shall be held upon receipt from the manufacturer pending review and proofing against a copy or template approved by the Processing Facility Director or designee to ensure accuracy regarding identity, content, and conformity. | Not applicable | | Not applicable | Print on demand labels are used |
| 245 | D-07.02.02.02 | Stocks of unused labels for different cellular therapy products shall be stored in a controlled manner to prevent errors. | Compliant | | Not applicable | Print on demand labels are used |
| 246 | D-07.02.02.03 | Stocks of obsolete labels shall be destroyed. | Compliant | | Not applicable | Print on demand labels are used |
| 247 | D-07.02.03 | Print-on-demand label systems shall be validated to ensure accuracy regarding identity, content, and conformity of labels to templates approved by the Processing Facility Director or designee. | Compliant | | Compliant | |
| 248 | D-07.02.04 | A system for label version control shall be employed. | Compliant | muzlidoc | Compliant | |
| 249 | D-07.02.04.01 | Representative obsolete labels shall be archived minimally for ten (10) years with inclusive dates of use or as defined by applicable laws and regulations. | Not applicable | | Compliant | Previous versions of labels displayed in old versions of the relevant SOPs |
| 250 | D-07.02.05 | A system of checks in labeling procedures shall be used to prevent errors in transferring information to labels. | Compliant | | Compliant | |
| 251 | D-07.02.05.01 | Cellular therapy products that are subsequently re-packaged into new containers shall be labeled with new labels before they are detached from the original container. | Compliant | | Compliant | |
| | D-07.02.05.02 | A controlled labeling procedure consistent with applicable law shall be defined and followed if container label information is transmitted electronically during a labeling process. This procedure shall include a | Compliant | TR-06LA3-016<br>TR-06LA3-020<br>TR-06LA3-024 | Compliant | |

Instructions | Basic application details | Part B Clinical | Part B MED-A audit forms | B-CM-C 6 Donors | Part CM Marr

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# Remember

- The ACCREDITATION MANUAL includes examples of what to look for