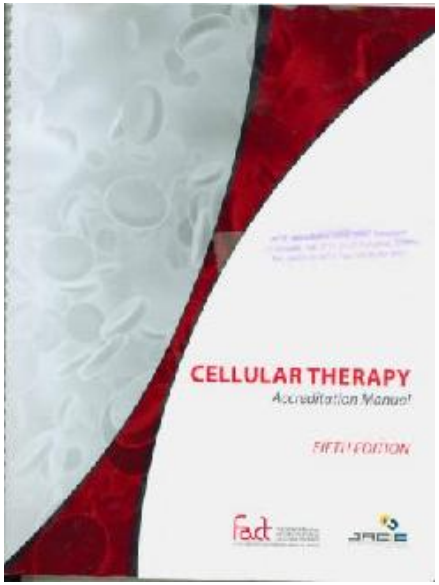
FACT-JACIE Standards

Processing

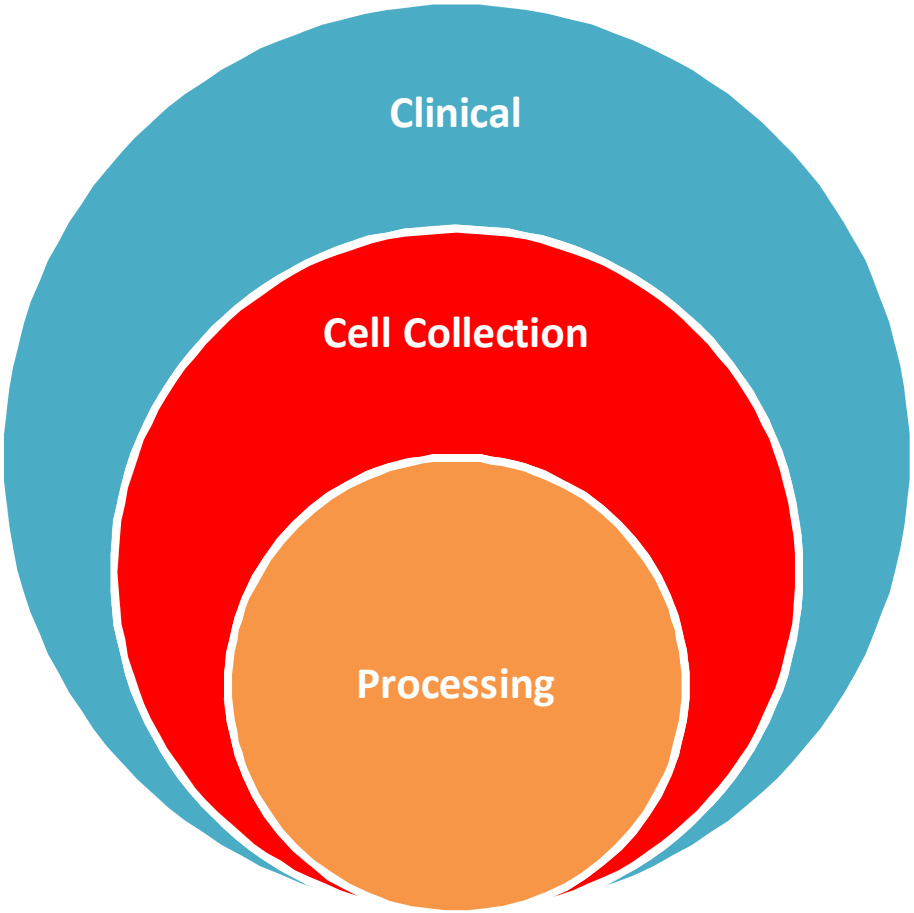


FACT-JACIE Standards

- Part A • Definitions
- Part B • Clinical
- Part CM • Bone Marrow Collection
- Part C • Apheresis
- Part D • Processing

Transplant Programme

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



C/D1 General Requirements

- Comply with applicable laws and regulations

Competent Authorities for tissues, HPC and ART

http://www.eurocet.org/

Last update:: ***March 24, 2014***

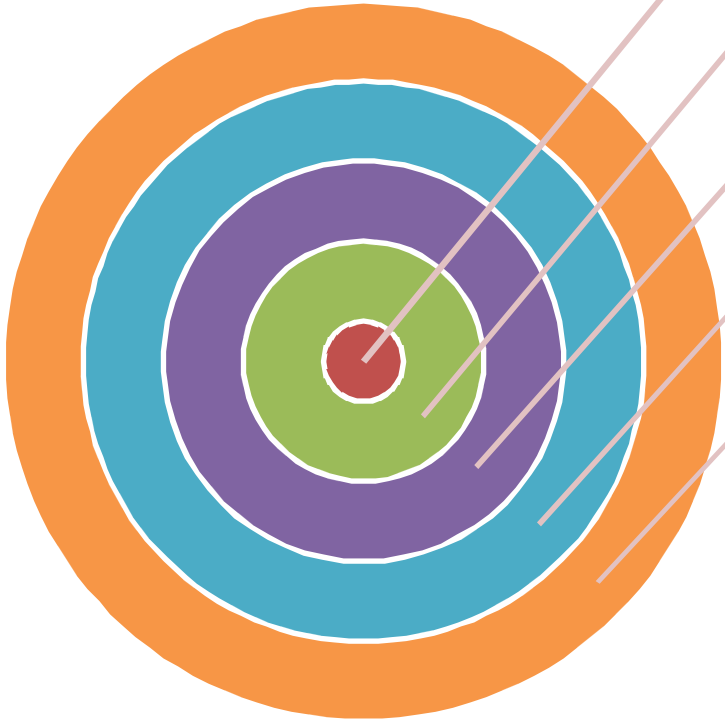
Choose a Country:

AT BE BG CH CY CZ DE DK EE ES FI FR GR HR HU IE IS IT LV LT LU MD ME MK MT NL NO PL PT RO SK SI SE TR UK

- **AT - Austria/**

Competent authority for Tissues , HPC and ART:
Bundesministerium fur Gesundheit, Familie und Jugend (Federal Ministry of Health, Family and Youth)
2 Radetzkystrasse
1031 Wien
Phone: + 43 1 711000
Fax: + 43 1 7110014300
E-mail contact: buergerservice@bmg.gv.at

Facilities



Adequate space, design, and location

Divided into defined areas

Adequate equipment and materials

Adequate lighting, ventilation, and access to sinks

Oxygen sensors for LN2 use

Secure access

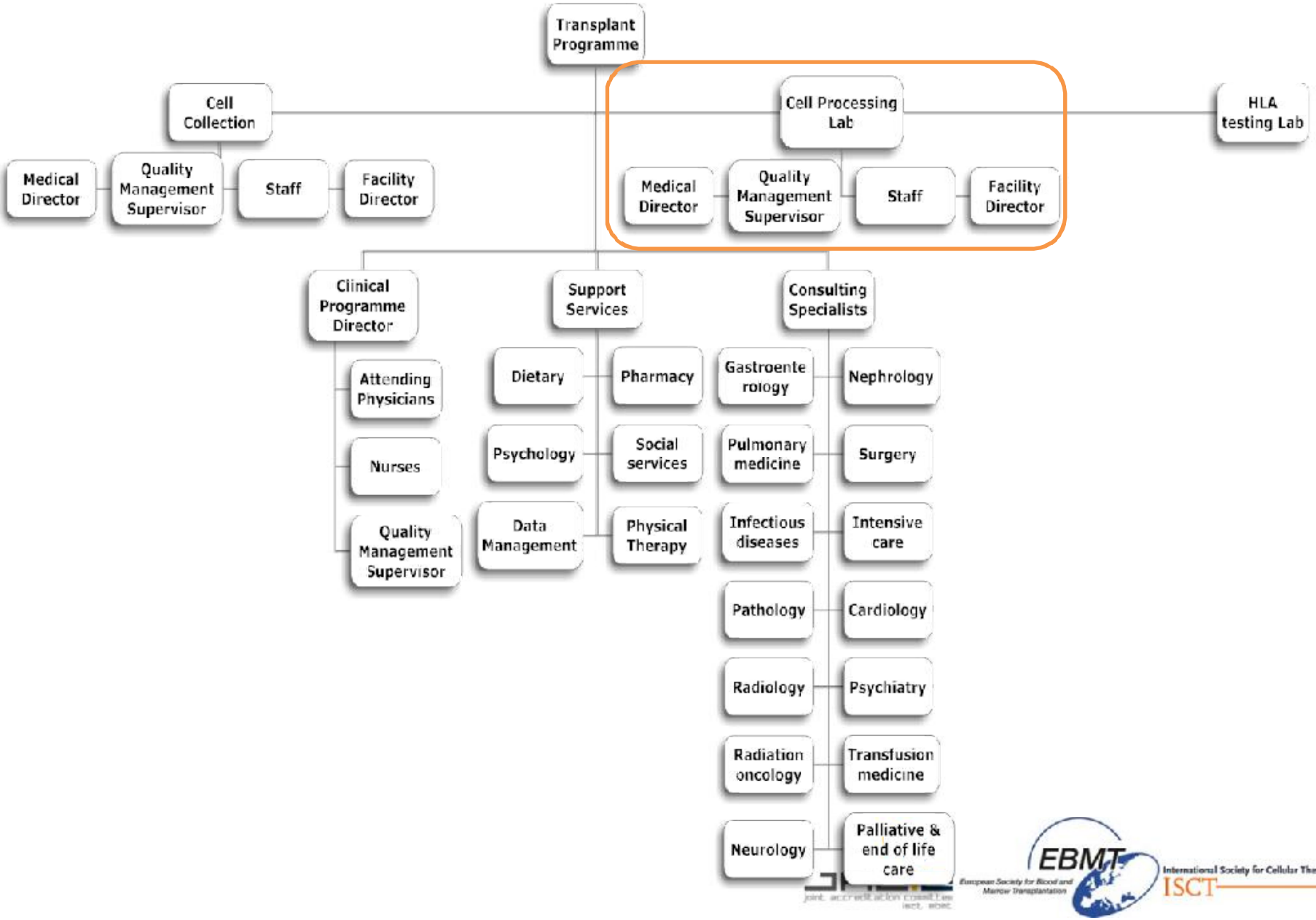
Critical facility parameters

- Temperature
- Humidity
- Air quality
- Surface contaminates
- Monitoring for microorganisms

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 lassification and degree of manipulation performed

C/D3 Personnel



Facility Directors

Licensed - Processing	Education	Experience - Collection
• Medical degree, doctoral degree, or equivalent degree in a relevant science	• Participate in ten (10) hours of educational activities related to cellular therapy annually at a minimum.	• Minimum of two (2) years training and experience for the scope of activities carried out in the Processing Facility

Facility director – Processing - responsibilities

All procedures

Administrative operations

Quality Management Program of the Facility

Compliance with Standards and laws and regulations

Facility Medical Director

Licensed	Education	Experience
• Licensed or certified physician with postgraduate training • Postgraduate training	• Participate in ten (10) hours of educational activities related to cellular therapy annually at a minimum.	• Minimum of two (2) years postgraduate training and practical and relevant in the preparation and clinical use of cellular therapy products

Facility medical director - responsibilities

Processing

- All medical aspects related to the Facility

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”?

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

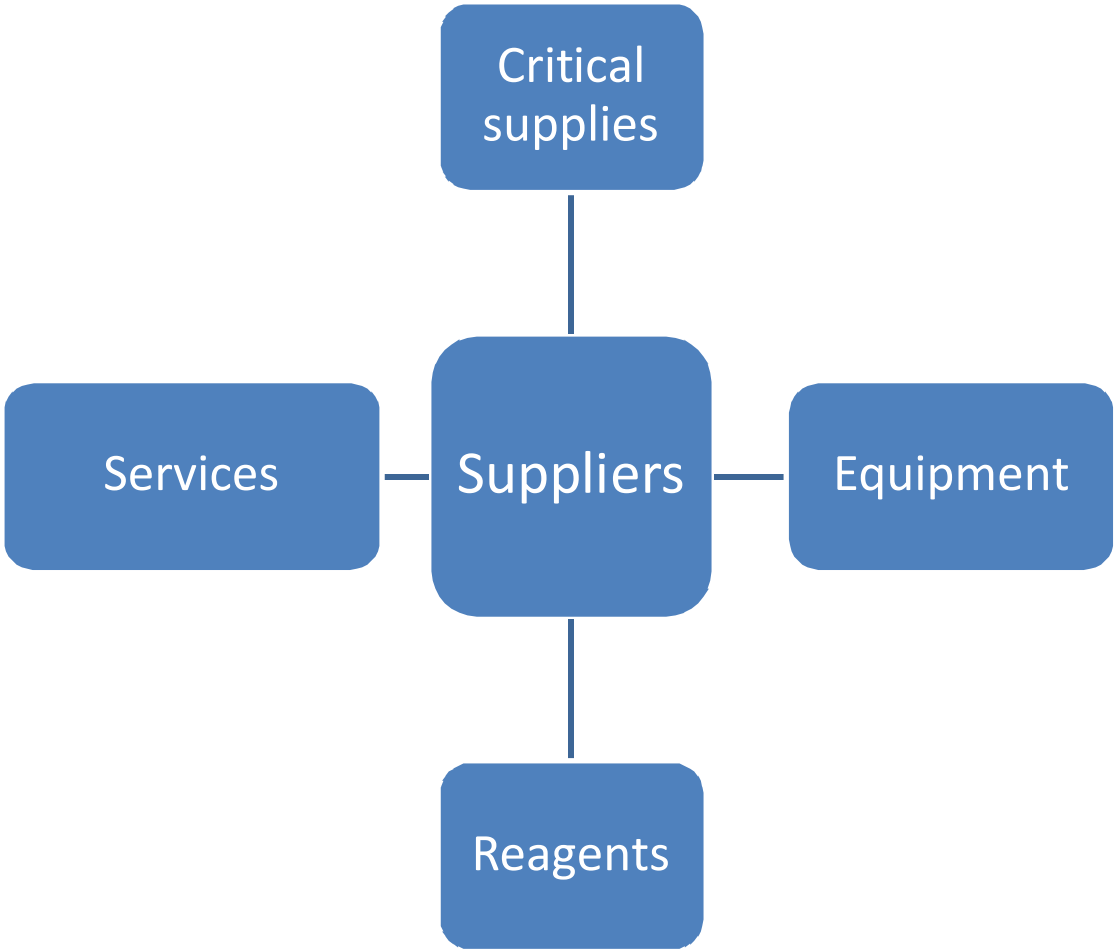
Qualification & Validation: What is the difference?
(or, more importantly, what is the same?)

Qualification:
Focus on equipment & reagent performance *before* or *during* process

- Reliance on predetermined requirements and specifications
- Ability to assess quality of a process
- Impact on quality of product or unit

Validation:
- Focus on processes & consistent *results* of process

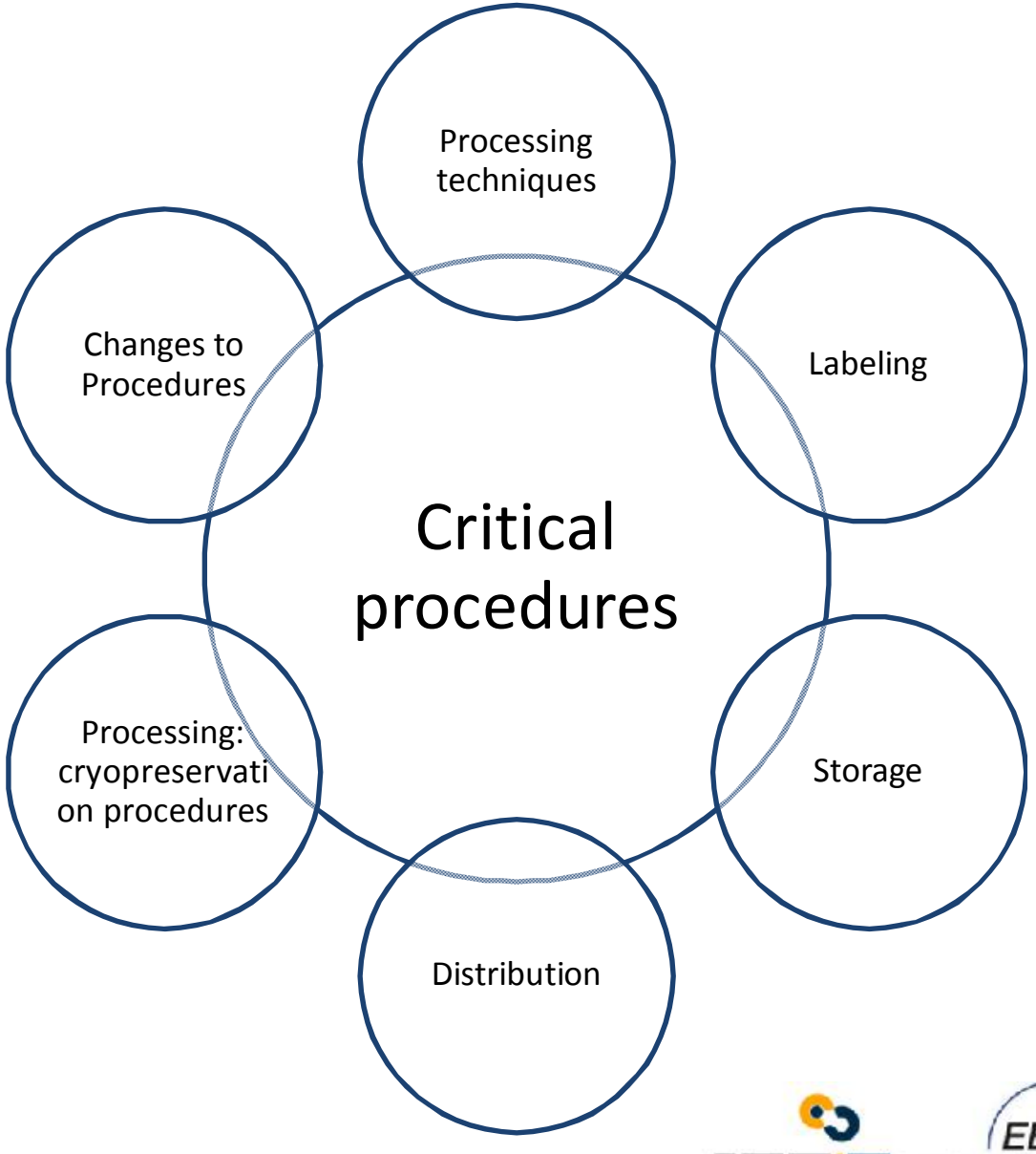
Qualification - processing



Validation

- Policies and procedures for validation and/or verification of critical procedures.
- There shall be documentation of review and acceptance of validation studies by the appropriate individual from Quality Management.
- Procedures for manufacturing reagents in-house shall be validated.

Validation


Processing techniques
Labeling
Storage
Distribution
Processing: cryopreservati on procedures
Changes to Procedures
Critical procedures

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

Validation Plan

- Written plan stating how validation will be conducted:
  - Test parameters
  - Product or unit characteristics
  - Production equipment
  - Acceptable results
  - Variables
  - Worst-case scenarios, upper and lower limits

- Include **several** cellular therapy products

Validation Summary

- Results attached (may be bulky with multiple graphs)
- Deviations from plan (almost nothing goes completely as planned)
- Summary of findings
- Assessment
  - Acceptable
  - Acceptable with limitations
  - Reject
- Comments
- Corrective actions if needed
- Review and Approvals

D8.1.4 Overview of Laboratory Controls Requirements

- Facilities performing in-house testing (e.g. Flow cytometry and automated cell counts) must meet the same general requirements as those for an external accredited testing facility.
- Including
  - Use of controls
  - Calibration and standardization of reagents and equipment
  - Staff training and proficiency testing
- Requirements would not be applicable to testing such as CFU assays

Testing Reagent Lots (D8.1.4.2)

New lots must be verified before use to:

- Ensure comparable results to current lots
- Produce results in agreement with suitable reference material
  - e.g. Change of CD34 Monoclonal Antibody / Stem Cell Enumeration Kit

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

Function Checks (D8.1.4.4)

Perform prior to testing donor, recipient, or cellular therapy product samples

(e.g. Flow cytometry startup procedures)

Processing reagents:
Lot-to-Lot Qualification

Reagents that are not the appropriate grade must undergo qualification for intended use

- Includes DMSO **not** approved for human use
  - *Critical reagent that performs a function (protects cells)*
  - *Failure to function as intended would have dire consequences to recipient*

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

Proficiency Testing (D8.1.4.5)

- College of American Pathologists (CAP)
- Stem Cell Technologies
- Center for Communicable Diseases
- National Institute for Allergies and Infectious Disease
- United Kingdom National External Quality Assessment Schemes (NEQAS)
- Internal if external proficiency test is unavailable.

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

D8 PROCESS CONTROLS

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

Process controls: Processing

- Process for controlling and monitoring the manufacturing of cellular therapy products to ensure products meet predetermined release specifications.
- 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.
- Mechanism to identify the individual obtaining the sample, the date, the time (if appropriate), and the sample source.

Process controls: Information required by the Processing Facility prior to processing

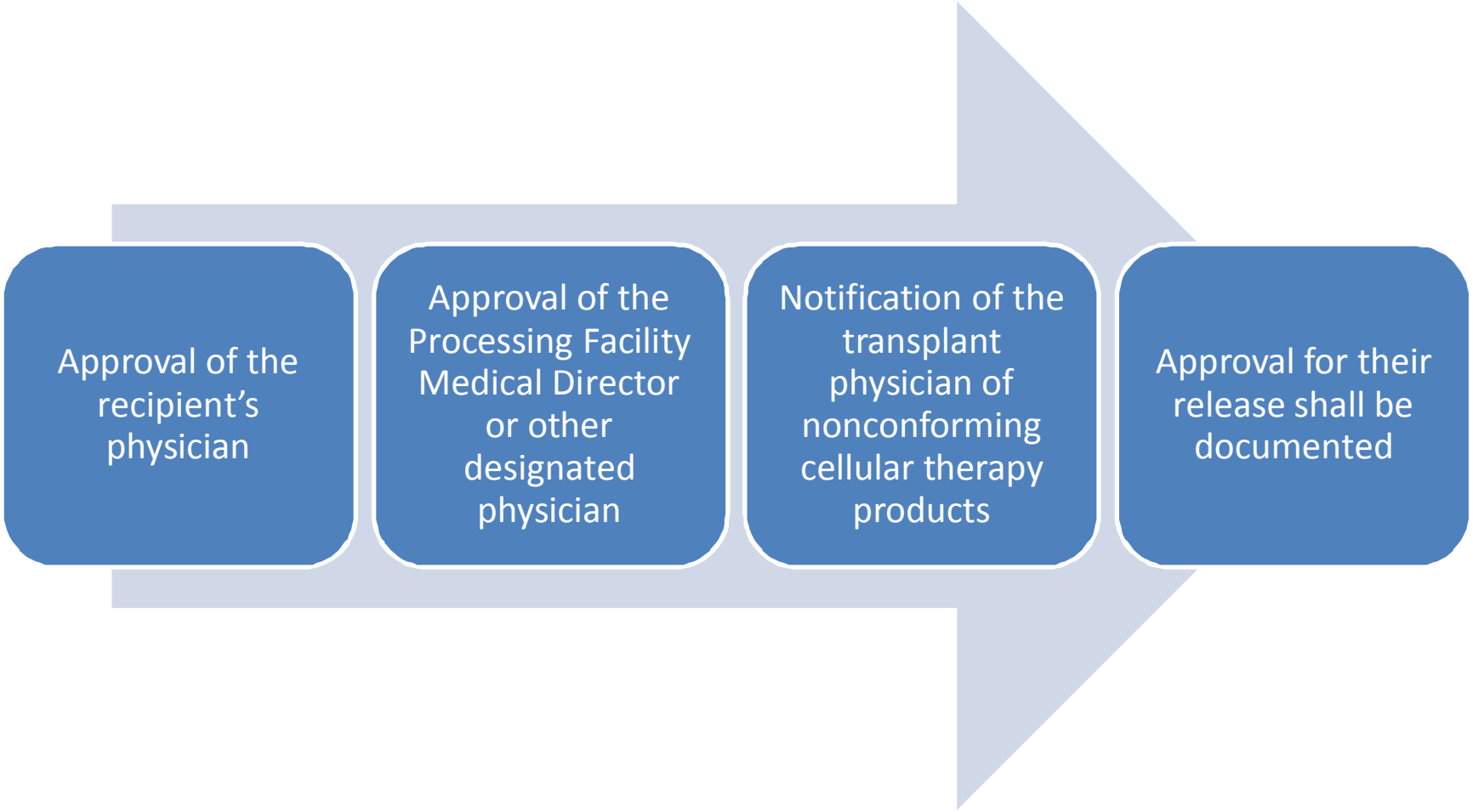
- The cellular therapy product type
- Recipient and donor identifiers
- The type of processing that is to be performed
- The anticipated date of processing

Process controls: Information required by the Processing Facility prior to processing

- A statement of donor eligibility.
- For ineligible donors, the reason for their ineligibility.
- Documentation of urgent medical need and physician approval for use, if applicable

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

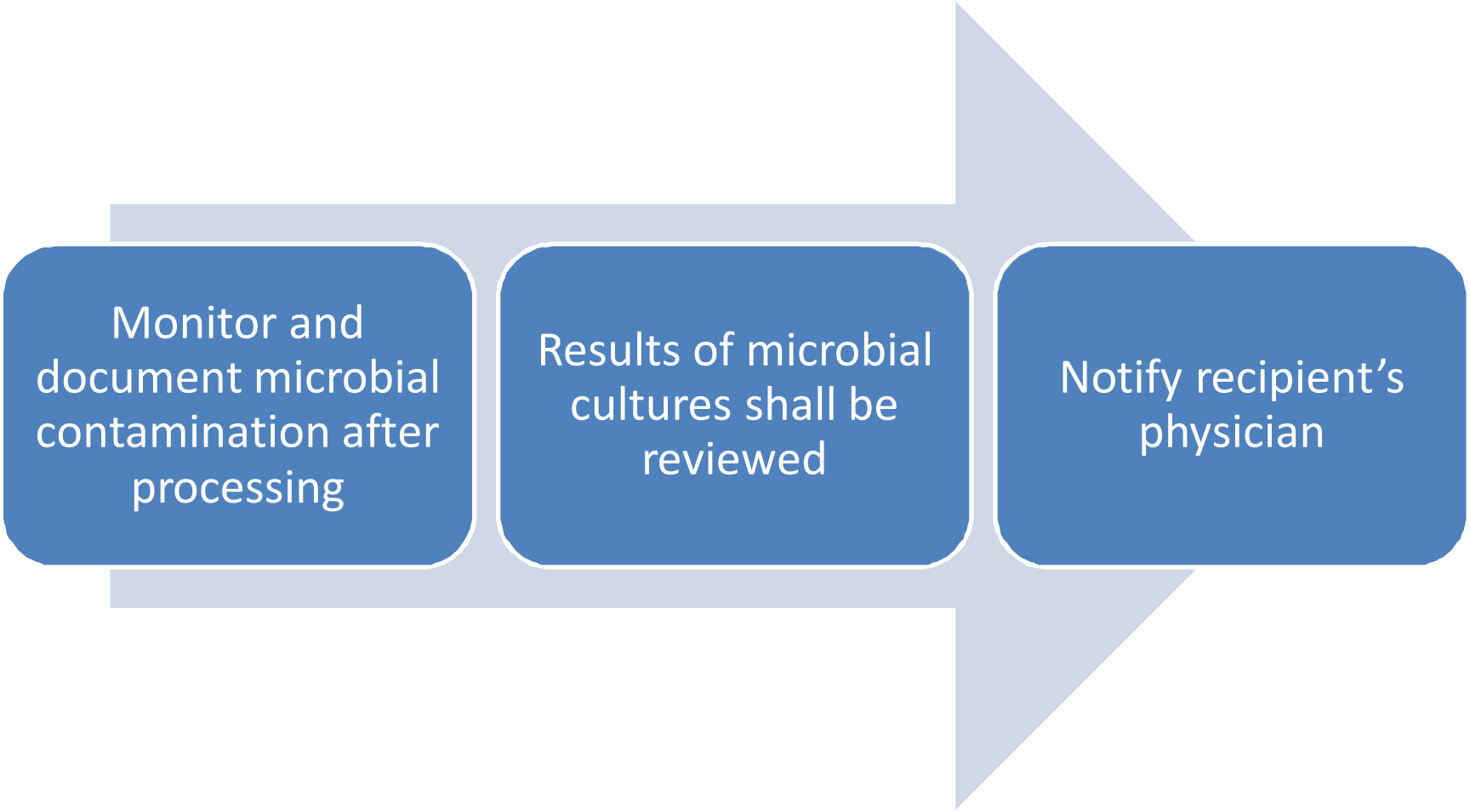
D8.1.7 Urgent medical need



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



D6.2 Materials Management System for Disposables and Reagents

- Records include :
  - disposable 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.

D6.4 Cleaning, Disinfection, Calibration & Maintenance

- Equipment used for product processing or testing must be located to allow access for maintenance and calibration at pre-determined intervals.

- A schedule for equipment cleaning, sanitation, disinfection, calibration & maintenance is required

D6.6 and D6.8 Equipment

Standardised and calibrated according to manufacturer's specifications on a regular basis including after a critical repair or move

- Use of traceable standards

Conforms to applicable laws and regulations

- CE Marking
- Electrical safety testing

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.

D8.11 More-than-Minimal Manipulation

- Requires Institutional Review Board or Ethics Committee approval.
- Processing requires written informed consent of consent of the donor, if applicable, and the recipient.
- If the approved study forbids something FACT-JACIE requires, the study requirements prevail
- If the approved study does not include a FACT-JACIE standard, but does not forbid it, the standard prevails

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
- SOPs for
  - Processing HPC products when ABO major or minor mismatch
  - Management of CT products in case of infusion reaction

Cord blood units – New standards

- 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.

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 joint accreditation committee isct. ebmt
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.

D7 Labeling

- Requirements include:
  - Labeling operations to prevent mislabeling or misidentification of cell products
  - Product identification to prevent mix-ups
  - Label content
- In 6th edition, active implementation of ISBT 128 coding and labeling technologies required
  - Demonstrated by a budget with secured funds and active interaction with a selected vendor

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
- Distribution records must provide certain details, for example, date, time, and product identifier

D9 Cellular Therapy 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

- For cryopreserved products received from another facility, the Processing Facility shall ensure availability of adequate storage space at the appropriate temperature.

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

- Alarm systems shall have audible <u>and visible</u> 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

Remember

- The ACCREDITATION MANUAL includes examples of what to look for