XVII Corso Nazionale di Aggiornamento SIdEM

Parallela SIdEM-GITMO

Aggiornamento in tema di raccolta e conservazione di cellule emopoietiche

# Recepimento dello Standard JACIE nel Laboratorio di Manipolazione

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# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Part D: Processing Facility Standards*

***Activities***

Processing
Storage
Distribution

***CTP*** (from living donors)

BM, PB, CB cells
TC-T, TC-MSC, TC-NK, TC-Tregs cells

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

FACT-JACIE Standards: professional standards designed to provide minimum guidelines for quality care and laboratory practice

EUD 2004/23/EC: “Setting standards on quality and safety fo the donation, procurement, testing, processing preservation, storage and distribution of tissue and cells”.
EUD 2006/17/EC and EUD 2006/86/EC

EUD 2001/83/EC and ATMP for cellular therapy products used in clinical trials (GMP manufacturing license)

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Processing Facility*

…. Adequate space, design and location….to minimize the risk of errors (ie cross-contamination, mix-ups, improper labeling)….

→ ***SAFETY OF CTP AND PERSONNEL, PATIENTS, DONORS***

- **Defined areas** for receipt, processing, storage , research activities (***defined workflow***)
- Process to **control storage areas** (individual freezers, unequivocal labeling, quarantine etc)
- **Access** to facility limited to authorized personnel
- **Prevention** of introduction, transmission or spread of communicable disease

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

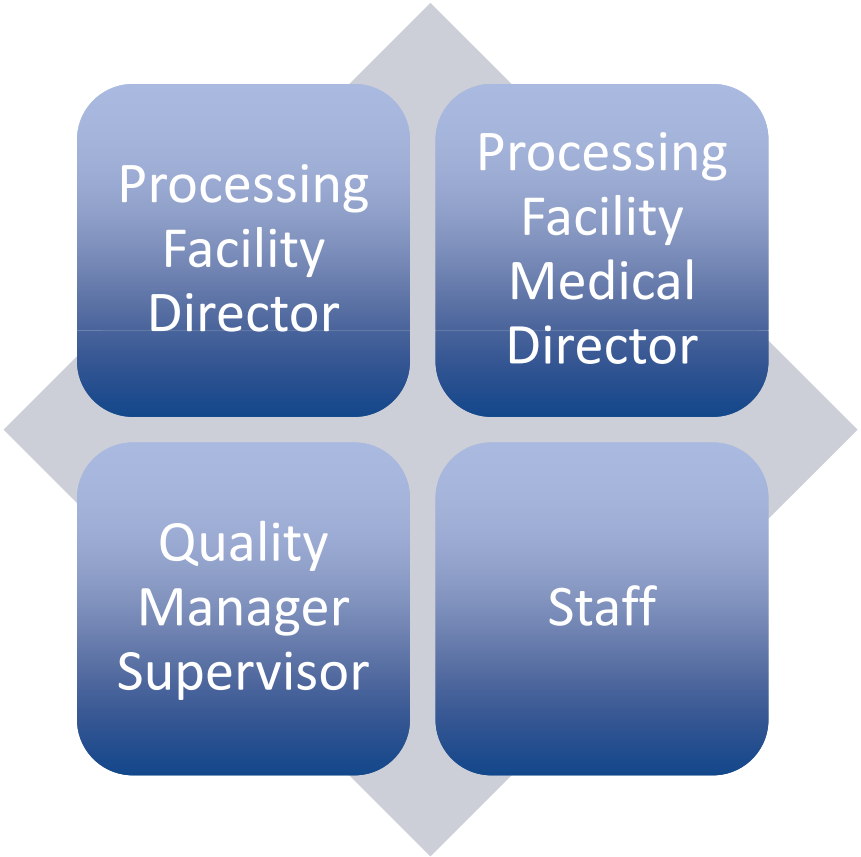
## *Critical facility parameters*

- Temperature
- Humidity
- Ventilation
- Air quality (particle counts and/or microbial colony counts)
- Surface contaminates

*"Open Systems"!!*

EUD /86/EC and GMP guidelines:
**Grade A** : envirovment to CTP are exposed during processing
**Grade D** background envirovment (as regard to air quality with particle counts and microbial colony counts)

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION




- ✓ Qualification
- ✓ Training
- ✓ Experience
- ✓ Responsability
- ✓ Continuing education

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Quality Manager Supervisor*

Acitive role in:

- ✓ Preparing, reviewing, approving and/or implementing QM policies and procedures in compliance with JACIE Standards
- ✓ Developing systems for auditing facility activities
- ✓ Defining the "**facility-defined time period**" for specific activities

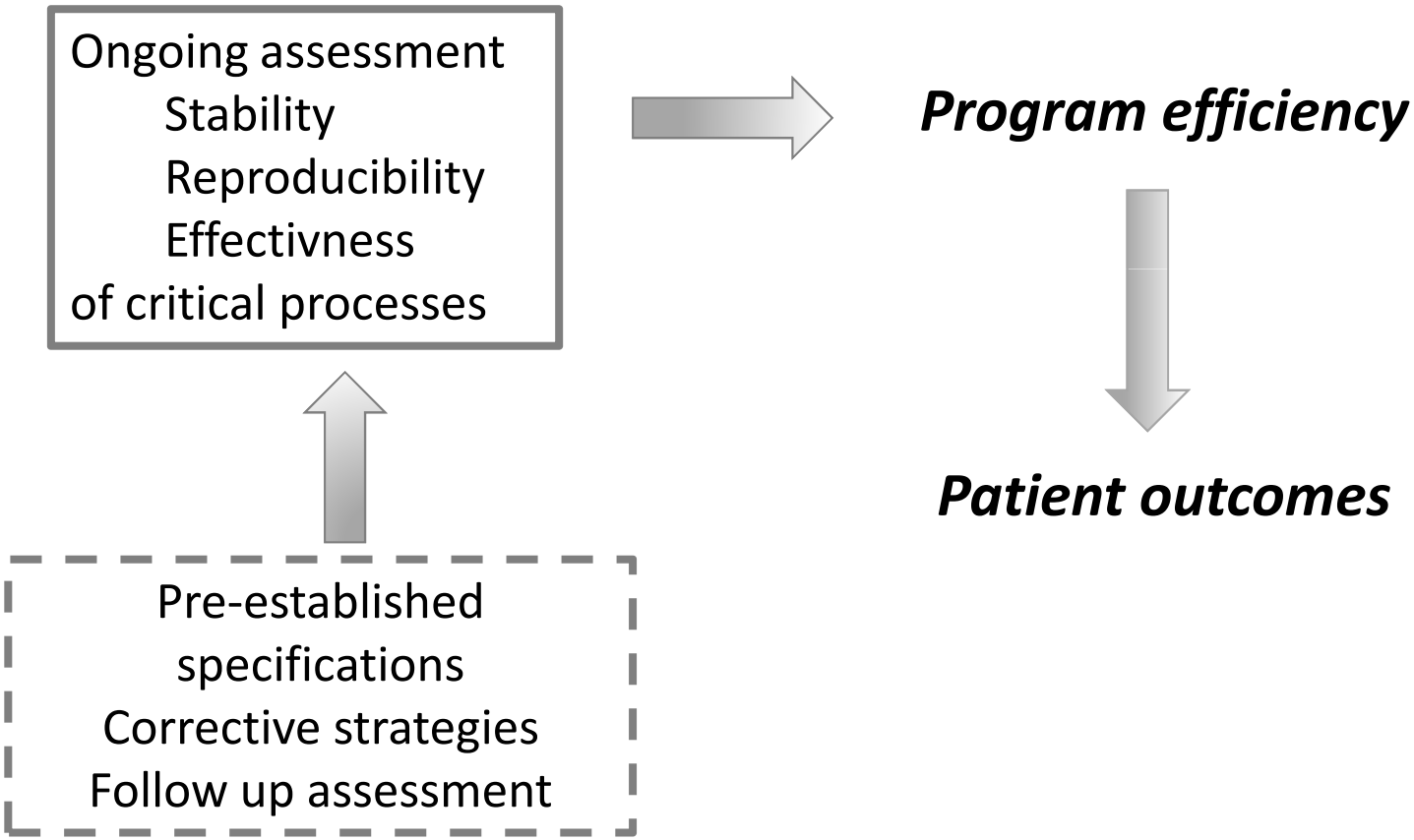
# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Quality Managment Plan*

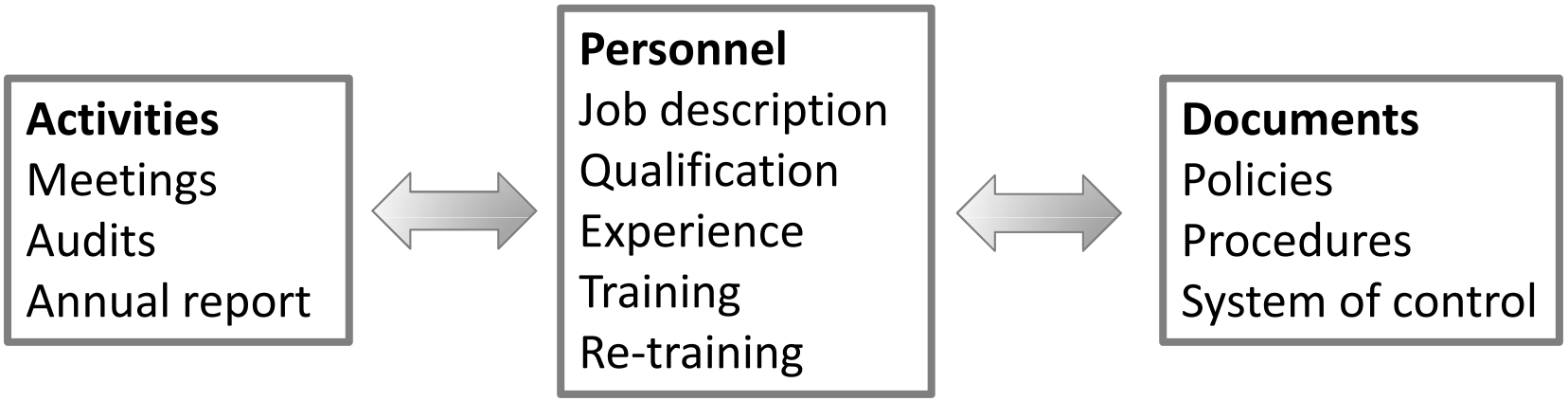
*"…. The most challenging and time-consuming exercise that the Processing Facility will encounter when preparing for JACIE inspection…."!!*

**Purpose:** *to define **WHO** (Organizational chart) and **HOW** (meetings, partecipants, schedule, documentation) works and interacts to implement the quality managment acitivities)*

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION



# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION




***Process: a goal directed, interraletd series of actions, events or steps***

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## Efficacy and Outcome analysis

- ✓ Pre-established criteria for each CTP (***integrated approach!!!***)
- ✓ Collection
- ✓ Evaluation
- ✓ Distribution of patient outcome data
  - engraftment
  - adverse events/corrective action
- ✓ Documentation

| ***Efficacy*** | ***Outcome analysis*** |
|---|---|
| CD34 cell dose (median/range)<br>Viability<br>Sterility | Engraftment (ANC/PLT)<br>Adverse events (Graft Failure; adverse reaction during infusion) |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## CTPs with positive microbial cultures

- ✓ Documentation and product labeling
- ✓ Product quarantine
- ✓ Release (responsibility/criteria)
- ✓ Investigation of cause
- ✓ Notification
- ✓ Reporting to regulatory agencies
- ✓ Outcome analysis and preventive/corrective actions

**NOTIFICA AL DIRETTORE DEL PROGRAMMA**

Si notifica che la seguente unità:

Codice……Tipo di materiale……

data di raccolta……

Donatore……

Ricevente……

Sono risultate:

- ❒ positive per ricerca batteri aerobi, anaerobi e miceti positivi (vedi referto allegato)
- ❒ non hanno raggiunto l'endpoint previsto:……
- ❒ scadenza prodotto : ……
- ❒ Altro:……

Note:……

……

……

***Notificato da:*** ***Data / /***

*(timbro e firma)*

***Per accettazione***

*(timbro e firma)*

***Il Direttore del Programma***

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## CTPs with positive microbial cultures (II)

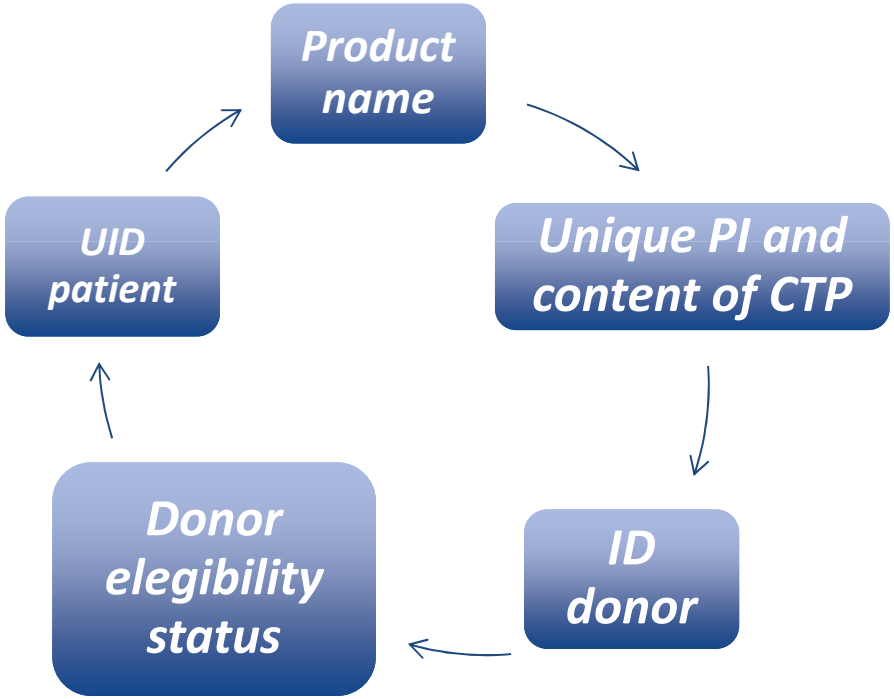
*Review of*

- ✓ Processing records
- ✓ Documentation of equipment cleaning ( biological safety cabinet)
- ✓ Environmental conditions
- ✓ Staff competency

| FASE | Data<br>Firma Operatore | Indagine eseguita<br>SI/NO | Esito<br>P/N |
|---|---|---|---|
| Emocoltura paziente/donatore pre-aferesi | | | |
| Disinfezione cute<br>Nursing CVC | | | |
| Emocoltura pre-manipolazione | | | |
| Emocoltura post-manipolazione | | | |
| Emocoltura allo scongelamento pre-infusione | | | |
| Etichetta Biohazard | | | |
| Quarantena | | | |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Tracking and tracing*




- ✓ *Outcome information to other facilities*
- ✓ *Final disposition of CTP*

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Interruption of Processing Facility's operations*

- ✓ Electronic record systems failure
- ✓ Drug shortage
- ✓ Power outages
- ✓ Equipment failure

### *To identify*

- ➢ Personnel ( key personnel to be involved )
- ➢ Documents (Policies, Procedures, worksheet etc)

### *To monitor*

- ➢ Staff training
- ➢ Alternate systems

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Qualification of critical supplies, reagents , equipment and facilities*

" The establishment of confidence in equipment, supplies, and reagents function consistently with established limits"

- ✓ SOP
- ✓ Minimal standards for the acceptance
- ✓ Qualification of the manner in which they are used
- ✓ Control of vendors as regard to the provision according to applicable governmental laws and regulations and FACT-JACIE Standards

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Validation and/or verification of critical procedures*

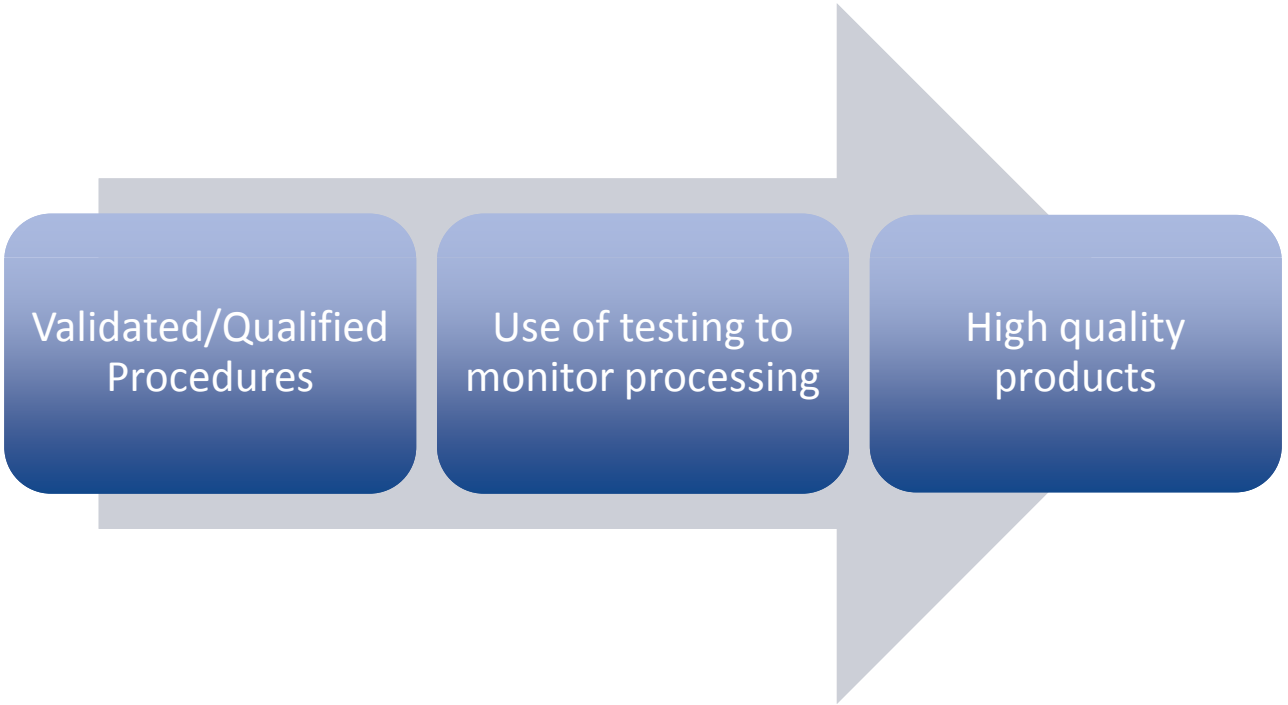
**Validation**: confirmation by examination and provision of objective evidence that particular requirements can be consistently fulfilled
Retrospective, concurrent or prospective

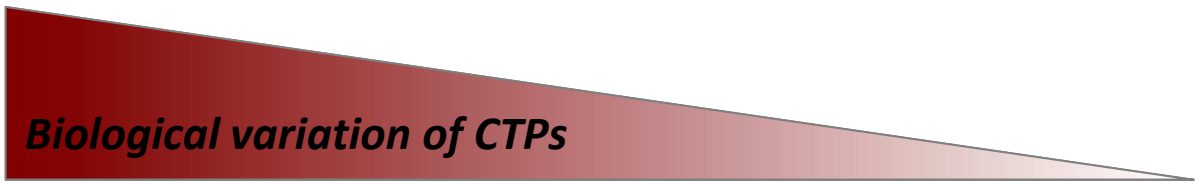
**Verification:** confirmation of the accuracy of something or that specified requirements have been fulfilled

| | | |
|---|---|---|
| Processing<br>Cryopreservation<br>Labeling<br>Storage<br>Distribution | Equipments<br>Reagents<br>Supplies<br>Electronic record systems | Pre-established specifications<br>Format/Report<br>Validation studies:<br>Analysis<br>Review<br>Acceptance<br>Changes/Implementation |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Process Controls*



# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Process Controls*

- ✓ Tests to ensure safety, viability and integrity of CTPs (***Release and exceptional release criteria)***
- ✓ Identification and handling of test samples (representative of CTP)
- ✓ Required validated assays and procedures for evaluation of CTP
  - ➢ TNC
  - ➢ Viability
  - ➢ CD34 testing ( manipulation other than minimal)
  - ➢ Monitoring assays for target populations after enrichment or depletion
  - ➢ Post-processing microbial cultures
  - ➢ AB0/RH (allogeneic donors)
  - ➢ Communicable disease testing (specifically for cGTP facilities)

***Standard V Edition***: minimal tests required: TNC count and CTP viability (not specified when they are to be performed)

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Release/Exceptional Release*

**Expansion in the V Edition of Standards**

- ✓ Notification of the transplant physician of all nonconforming CTPS *( in the IV edition testing and screening results of inelegible products)* and documented approval for their release

- ✓ All products disribuited from the Processing Facility are required to meet pre-determined criteria whether or not destinated to the administration *(in the IV Edition: only those distribuited for administration)*

- ✓ Quarantine for products with positive infection disease results and/or positive microbial cultures also with products with incomplete donor eligibility determination *( in the IV Edition)*

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Process Controls*

### Cord Blood Administration

***Shall:***

- ✓ To communicate with registries and/or third parties regarding the manufacturer's instructions for preparation and administration and follow these to the extent possible
- ✓ To verify the processing procedure utilizing practice units similar to the CTP.
- ✓ Do not perform processing on a type of product (cord blood) for the first time on a unit intended for administration to a patient

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *ISBT 128 CODING and LABELING*

Developed and mantained by ICCBBA (www.iccbba.com) supported by CTCLAG (
*Ashford P et Al. Transfusion 2007; 47:1319-27 and . Transfusion 2007; 47: 1312-8)*

*Advantages*

- ✓ Unique identification, coding and labeling of CTPs worldwide
- ✓ Standard for the transfer of informations
- ✓ Provides standard data structure for bar coding and electonic data interchange

IV Standard Edition: ISBT128 **terminology** mandatory
V Standard Edition: implementation plan of ISBT 128 **coding and labeling** mandatory

Pending decision by the EU on a European Coding System
Regulation of Bone Marrow Facilities?!

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Labeling Operations*

- ✓ Finalized to prevent mislabeling or misidentification of CTP
- ✓ Approved/Validated “pre-printed” or “on-demand” labels
- ✓ Label version and labeling control system

| Element[3] | Partial label | Label at completion of collection | Label at completion of processing | Label at distribution for administration[2] |
|---|---|---|---|---|
| Unique numeric or alphanumeric identifier | AF | AF | AF | AF |
| Proper name of product [1] | AF | AF | AF | AF |
| Product modifiers [1] | AF | | AF | AF |
| Product attributes (manipulations) [1] | | | AC | AC |
| Recipient name and identifier (if applicable) | AF | AT | AT | AT |
| Identity and address of collection facility or donor registry | | AT | AC | AC |
| Date, time collection ends, and (if applicable) time zone | | AT | AC | AC |
| Approximate volume | | AT | AT | AT |
| Name and volume or concentration of anticoagulant and other additives | | AT | AT | AT |
| Donor identifier and (if applicable) name | | AT | AT | AT |
| Recommended storage temperature range | | AT | AT | AT |
| Biohazard and/or Warning Labels (as applicable, see CM7.4, C7.4, D7.4). | | AT | AT | AT |
| If applicable:<br>Statement "NOT EVALUATED FOR INFECTIOUS SUBSTANCES"<br>Statement "WARNING: Advise Patient of Communicable Disease Risks"<br>Statement "WARNING: Reactive Test Results for [name of disease agent or disease]" | | AT<br>AT<br>AT | AT<br>AT<br>AT | AT<br>AT<br>AT |
| Identity and address of processing and distribution facility(ies) | | | AC | AC |
| Statement "Do Not Irradiate" | | | AT | AT |
| Expiration Date (if applicable) | | | AT | AT |
| Expiration Time (if applicable) | | | AC | AT |
| ABO and Rh of donor (if applicable) | | | AC | AC |
| RBC compatibility testing results (if applicable) | | | | AC |
| Statement "Properly Identify Intended Recipient and Product" | | | | AT |
| Statement indicating that leukoreduction filters should not be used. | | | | AT |
| Statement "FOR AUTOLOGOUS USE ONLY" (if applicable) | | AT | AT | AT |
| Statement "For Use By Intended Recipient Only" (if for allogeneic recipient) | | | | AT |
| Statement "For Nonclinical Use Only" (if applicable) | | | | AT |
| Date of distribution | | | | AC |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *CTP Labels for shipping and transport on public roads*

- ✓ Release and exceptional release criteria
- ✓ CTP integrity and safety
  - Temperature-controlled envirovment
  - Outer container (material, labeling)
- ✓ Method of transportation/shipping
  - Time
  - Qualified courier
  - Alternative means

| Element | Inner container document | Outer container label |
|---|---|---|
| Date of distribution and time, if appropriate | AC | AF |
| Statement "Do Not X-Ray" and /or "Do Not Irradiate", if applicable | AC | AF |
| Statements "Human Cells for Administration" or equivalent and "Handle with Care" | AC | AF |
| Shipper handling instructions | AC | AF |
| Shipping facility name, street address, contact person, and phone number | AC | AF |
| Receiving facility name, street address, contact person, and phone number | AC | AF |
| Biohazard and/or Warning Labels (as applicable, see CM7.4, C7.4, D7.4). | AC | |
| If applicable:<br>Statement "NOT EVALUATED FOR INFECTIOUS SUBSTANCES"<br><br>Statement "WARNING: Advise Patient of Communicable Disease Risks"<br><br>Statement "WARNING: Reactive Test Results for [name of disease agent or disease]" | AC<br><br>AC<br><br>AC | |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Accompaniyng Documents at Distribution*

| Documentation | Allogeneic Donors-Eligible | Allogeneic Donor-Ineligible[1] | Allogeneic Donor-Incomplete[1] | Autologous Donors[5] |
|---|---|---|---|---|
| Statement that the donor has been determined to be either eligible or ineligible, based upon results of donor screening and testing | X | X | | X (if positive) |
| Summary of records used to make the donor-eligibility determination[2] | X | X | | X (if positive) |
| Name and address of the establishment that made the donor-eligibility determination | X | X | | X (if positive) |
| Listing and interpretation of the results of all communicable disease testing performed | X | X | X | X (if positive) |
| Statement that the communicable disease testing was performed by a laboratory meeting regulatory requirements[3] | X | If applicable | If applicable | If applicable |
| Statement noting the reason(s) for the determination of ineligibility | | X | | If applicable |
| Statement that the donor-eligibility determination has not been completed | | | X | |
| Statement that the product must not be transplanted or infused until completion of the donor-eligibility determination, except under condition of urgent medical need | | | X | |
| Listing of any required screening or testing that has not yet been completed | | | X | |
| Results of donor screening that has been performed | | | X | |
| Documentation that the physician using the cellular therapy product was notified of incomplete testing or screening | | | X | |
| Instructions for product use to prevent the introduction, transmission, or spread of communicable diseases | X | X | X | X |
| Instructions for reporting serious adverse reactions or events to the distributing facility[4] | X | X | X | X |

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## Storage/Disposal

- ✓ Clinical and Processing facilities agreement as regard to the duration and conditions of storage and indication of disposal

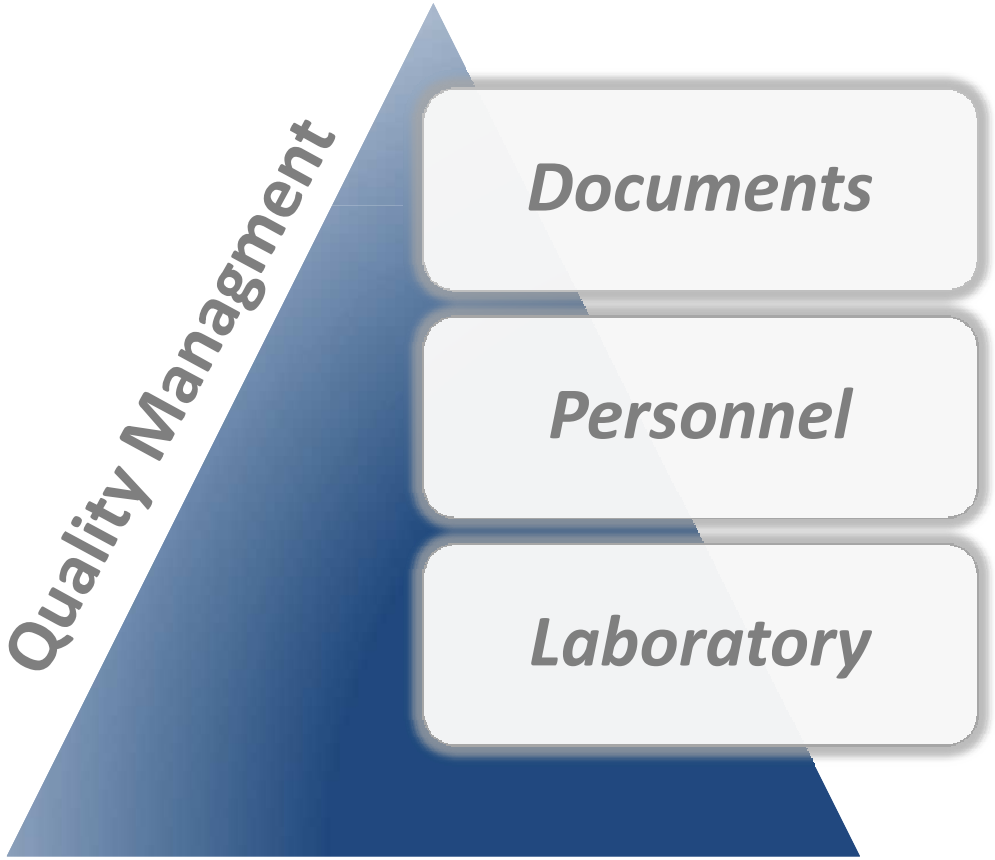
- ✓ Informed consent by donor/recipient to storage/disposal policy before CTP collection
  - Lenght of storage
  - Circumstances of CTP disposal (death of the recipient, no further need for CTPs, written agreements with donor registries)
  - Option to transfer CTP

- ✓ Documentation of recipient's death or no further need of CTP before proudct discarding

- ✓ Approval by PF Medical Director or recipient's physician for discard, other disposition and method of disposal

# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION

## *Application/Accreditation*



# INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION
# **ACCREDITATION MANUAL**

FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY
AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER

JACIE
joint accreditation committee
isct-ebmt

***Standard B 1.2***

The Clinical Program **shall** use cell collection and processing facilities that meet FACT-JACIE Standards with respect to their **interactions** with the Clnical Program