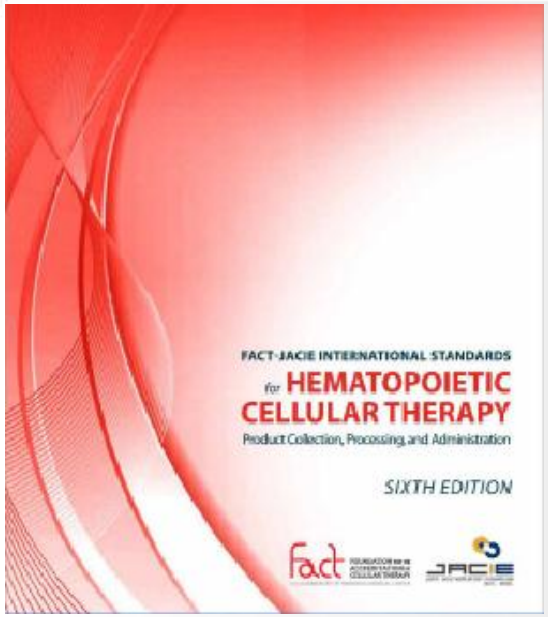


CLINICAL STANDARDS of the 6th Edition

JACIE TRAINING COURSE, 27-28 OCTOBER 2016

Thanks to: Dra. Christelle Ferrá

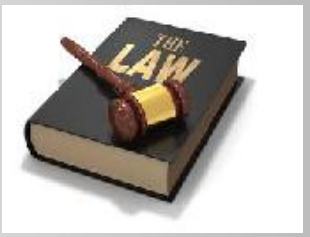
B1 GENERAL

- B1.1: Integrated medical team with Clinical Program Director
  - **More sites have to function as a single integrated program**
  - **One hour travelling within a single metropolitan area**
  - **Different patient groups…..handled by one physician group**

- B1.2: Collection and processing facilities that meet FACT-JACIE standards
  - **Regular interactions with the Clinical Program*****

B1 GENERAL

- B1.3: The clinical Program shall abide by all applicable laws and regulations
  - **But JACIE applies if more strict**



- B1.4 Designated **transplant team**
  - Clinical program Director
  - Quality Manager
  - > 1 additional attending transplant physician
  - > 12 months in place

B1 GENERAL

- B1.5: Minimal activity

Transplant Population	Clinical Site(s)	Type of Transplant	Twelve (12) Months Prior to Initial Accreditation	Average Per Year Within Accreditation Cycle
Adult OR Pediatric (only one of these two)	Single Clinical Site	Autologous only	5 autologous	5 autologous
		Allogeneic and Autologous	10 allogeneic recipients	10 allogeneic recipients
	Multiple Clinical Sites	Autologous only	5 autologous recipients at each site	5 autologous recipients at each site
		Allogeneic and Autologous	5 allogeneic recipients at each applicable site[2] 5 autologous at each applicable site[2]	5 allogeneic recipients at each applicable site[2] 5 autologous at applicable each applicable site[2]
Combined Adult AND Pediatric	Single Clinical Site	Autologous only	5 adult autologous And 5 pediatric autologous recipients	5 adult autologous and 5 pediatric autologous recipients
		Allogeneic and Autologous	5 adult allogeneic recipients 5 pediatric allogeneic recipients	5 adult allogeneic recipients 5 pediatric allogeneic recipients
	Multiple Clinical Sites	Autologous only	5 adult autologous at each applicable site 5 pediatric autologous recipients at each applicable site	5 adult autologous recipients at each applicable site 5 pediatric autologous recipients at each applicable site
		Allogeneic and Autologous	5 adult allogeneic recipients at each applicable site 5 pediatric allogeneic recipients at each applicable site 5 adult autologous at each applicable site[2] 5 pediatric autologous at each applicable site[2]	5 adult allogeneic recipients at each site 5 pediatric allogeneic recipients at each site 5 adult autologous at each applicable site[2] 5 pediatric autologous at each applicable site[2]

B2 CLINICAL UNIT

- B2.1: Appropriate location, adequate space, **minimized airborne microbial contamination➔** SOPs, procedures, policies and control registries for preventing, controlling and approaching specific infections.

- B2.2, B2.3: **Outpatient** area able to protect the patient from infectious agent transmission (isolation in **emergency department**,…)*

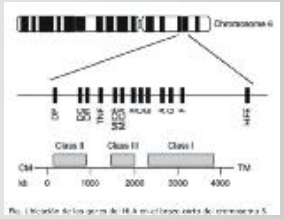
- B2.4: Facilities maintained in a clean, sanitary, a orderly manner

B2 CLINICAL UNIT

- B2.5: **24-h** a **transplant attending physician**.

- B2.6; B2.8; B2.9; B2.10; B2.13: **24-h** availability of **ICU, medication**, **CMV appropriate** and **irradiated blood products; renal support** under nephrologist control

B2 CLINICAL UNIT



- B2.11; B2.12: **EFI accredited HLA/ chimerism** testing
- B2.14, B2.15: policies to **minimize risks** to the health and safety of employees, patients, visitors and volunteers

B3 PERSONNEL

- B3.1: Clinical Program Director
- B3.2: Attending physicians
- B3.4: Physicians-in-training
- B3.5: Advanced practice providers/professionals
- B3.6: Clinical transplant team: **pediatrician**,...
- B3.7: Nurses
- B3.8: **Pharmacist**
- B3.9: **Consulting specialists**: ophtalmology; obstetrics/gyneacology; dermatology
- B3.10: Quality Manager
- B3.11: Support services staff: dietary, social services, ...

License
CV
Educational activities
On-the-job training 10 hrs*

- Specific knowledge*
- Training
- Competency

B3.1 Clinical Program Director's responsibilities

- Procedures
- Administrative operations
- Quality Management Program

  Compliance with Standards and laws and regulations
- Oversight of medical care provided
- Verifying the knowledge and skills the transplant team

B3.2 Attending physicians

Licensed	Specialist	Education
• Legal requirements to practice	• Hematology • Medical Oncology • Adult or Pediatric Immunology or Pediatric Hematology/ Oncology	• Participate regularly in HPC specific educational activities

B3.6 Nurses

- Adequate number of nurses **experienced** in the care of transplant patients
- **Nurse/Patient ratio** satisfactory to manage the severity of the patients' clinical status

Establish plan for:

- Increase nurse support when **case-load** increases
- Cover planned and unplanned **absences**
- **Training program** in transplant care for hematology nurses

Requirements concerning education

Redefined under:

B3.1.6, B3.2.2, B3.8.4, B3.10.2,
CM3.1.5, CM3.2.2, C3.1.5, C3.2.5, C3.3
D3.1.3, D3.2.3, D3.3.2

"Key personnel (directors, attending physicians, quality managers, and designated pharmacists) must participate in at least 10 hours of continuing education."

"Clinical Program Director, attending physicians, and designated pharmacists: Cellular therapy, to include (but not limited to) the field of HPC transplantation."

B4 QUALITY MANAGEMENT

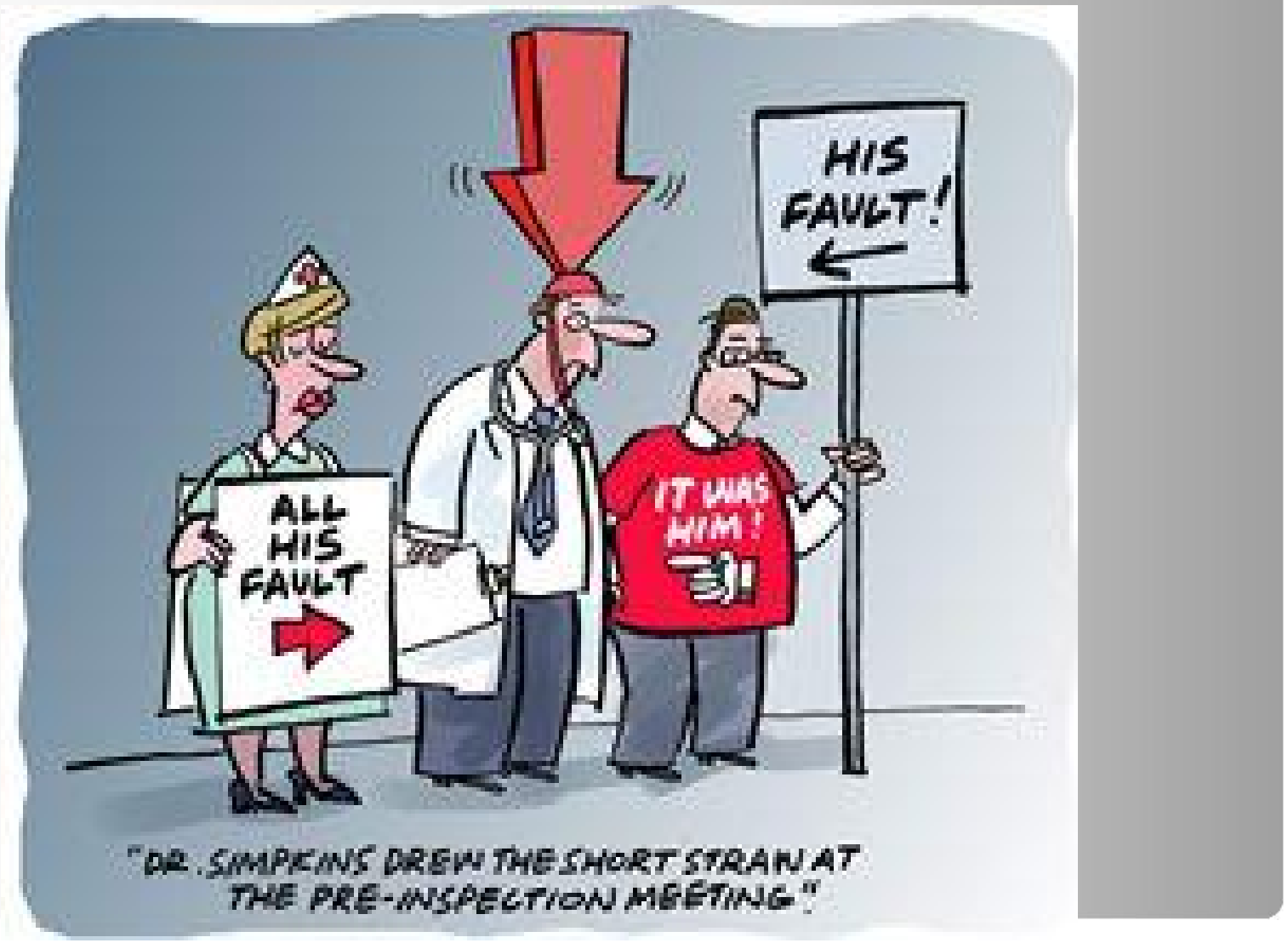
B4 QUALITY MANAGEMENT

- B4.1; B4.2: **Quality management program:** incorporates key performance

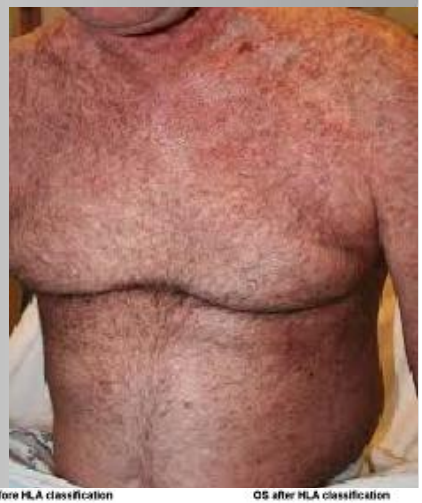
- B4.2.2:
  - **Quarterly quality report** to Clinical Program Director
  - **Organizational chart** of key positions (job description and interactions)
  - **Control document** and management: Policies, protocols and SOPs // Worksheets // Forms // Labels
  - **Third parties agreements** (B4.6)

New*: Annual review of Quality Management program

Documentation must be provided.

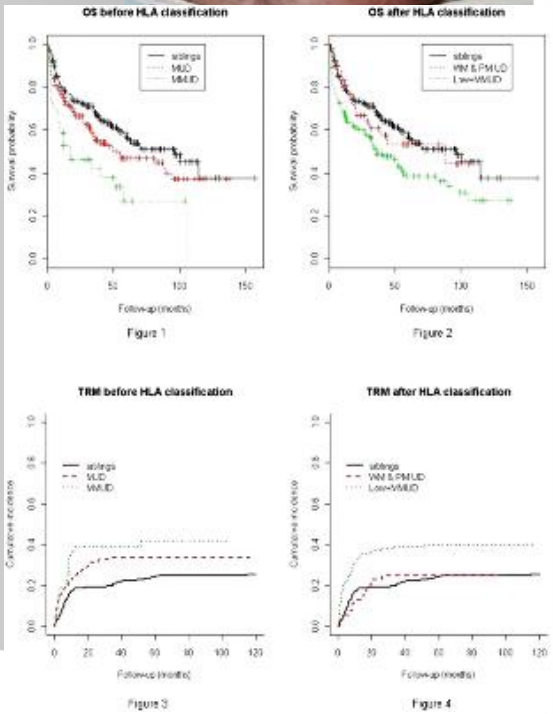

ALL HIS FAULT
IT WAS HIM!
HIS FAULT!
"DR. SIMPKINS DREW THE SHORT STRAW AT THE PRE-INSPECTION MEETING."

B4 QUALITY MANAGEMENT



- **B4**

  R**eview outcome analysis**
  - Hematopoietic reconstitution, time to engraftment (ANC and platelet)
  - TRM and mortality at 100d and 1y
  - **aGVHD at 100d***
  - **cGVHD at 1y***
  - **Central venous catheter infection***
  - Adverse events
  - Overall survival at 1y **compared to (inter)national outcome data ***



M. Michallet et al. Blood 2009

Analysis (B4.7, C4.7, D4.7):

Evaluation of individual products but also of ag
for types of cellular therapies and of types of r
Transplantation programs have to compare 1-
data with national and international outcome d

Outcome analysis

1. With the introduction of national and international comparative outcome data, Clinical Programs have additional resources to evaluate their one-year survival rates and improve upon them when they fall below expected ranges.
2. Clinical Programs should begin evaluating their one-year survival rates in comparison with published data soon, before it could have an impact on their accreditation. This new recommendation will also give programs, FACT, and JACIE experience with this type of evaluation before any decisions are made to officially require outcomes within expected ranges in future Standards editions.

Country	Teams (n.)*	Summary of responses
Australia¥	40	No scheme available
Austria	12	No scheme available
Belgium	20	No national benchmark or scheme, but comparison with EBMT or CIBMTR data is done; Belgian Transplant Registry; MDPB-registry with BHS-working party yearly reporting activity and outcome data National registry; ProMise of the EBMT
Bulgaria	2	No scheme available
Croatia	3	No scheme available
Czech Republic	9	CIBMTR data; Annual morbidity,mortality meeting 2 days with other pediatric Tx team in Slovakia
Denmark	4	We have the possibility to compare with the other Nordic contries (NOPHO) regardin leukemia
Finland	7	No scheme available
France	79	Agence de BioMédecine and EBMT; agence de biomedecine survey; SFGM-TC; it was a national rtrospective analysis of all sct center by a state institution; Periodical statistical analysis of all allotransplant in France by the Agence de la BIOMEDECINE (every 3-5 years)
Germany	110	EBMT registry; drst; Deutsches (Pädiatrisches) Register Stammzelltransplantation
Greece	14	No scheme available
Hungary	5	No scheme available
Ireland	4	No scheme available
Israel	9	No scheme available
Italy	97	GITMO accreditation; AIEOP, PROMISE; GITMO; EMBT; As pediatric Centre, part of a Mixed EBMT center, I can compare the local results with data of OS, EFS and especially 100-day TRM of the HSCT Italian Registry of AIEOP (Italian Association of Pediatric Hematology Oncology) gitmo
Netherlands	15	No scheme available
Pakistan	3	No scheme available
Poland	18	No scheme available
Portugal	6	No scheme available
Saudi Arabia	5	No scheme available
Singapore »	6	No scheme available
Spain	73	ONT (National Transplant Organization)
Sweden	7	national allo-SCT group; National diagnostic registries
Switzerland	10	annual outcome report delivered to competent authorities; Swiss Blood Stem Cells (SBSC) Registry; EBMT data
Turkey	53	turkpediatrikkit; KIBS (National Bone Marrow Transplantation Data Base; Ministry of Health)
United Kingdom	51	BSBMT outcomes survey; EBMT annual report; CQUINS benchmarking; UKBBMT group: specialist commissioning dashboard; UK Paediatriic BMT group BSBMT outcomes survey; EBMT annual report; CQUINS benchmarking; UKBBMT group: specialist commissioning dashboard; UK Paediatric BMT group

* Data from http://www.nature.com/bmt/journal/v51/n6/extref/bmt201620x1.pdf

¥ Australia - Nivison-Smith et al http://doi.org/10.1016/j.bbmt.2015.09.009

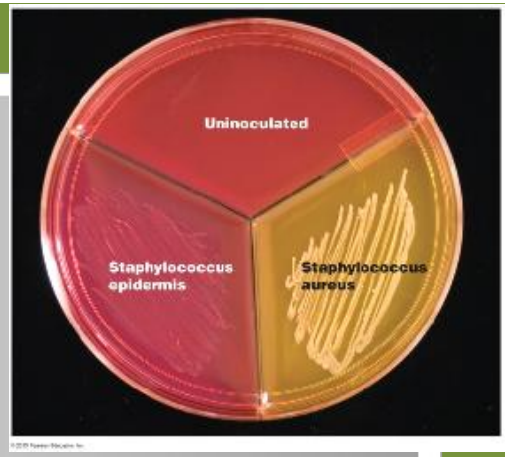
» Singapore - https://bmdp.org/recipients-caregivers/

B4 QUALITY MANAGEMENT

- **B4**
  - **Audits**→ audit plan, assessment and audit results, actions taken, and follow-up assessments and audits
    - Adherence to policies and procedures

1. Accuracy of data contained in MED-A forms
2. Donor screening and testing
3. Verification of radiotherapy/ chemotherapy and dose against the prescription ordering system
4. Management of cellular therapy products with positive microbiological culture

B4 QUALITY MANAGEMENT



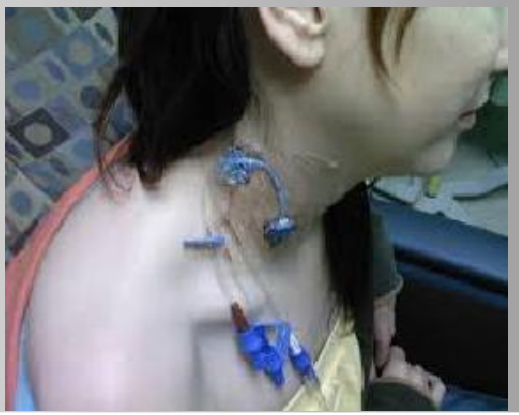
- **B4**
  - Policies and procedures on **positive microbiological cultures**
  - Policies and procedures **for errors, accidents, biological product deviations, serious adverse events and complaints**
    - Detection
    - Investigation: root cause
    - Documentation
    - Reporting: to competent authorities, accrediting agencies, Ethic committees,...
    - Correcting and preventing actions

B4 QUALITY MANAGEMENT

- **B4**
  - Policies and procedures for cellular therapy **product tracking and tracing** from the donor to the recipient or final disposition
  - Policies in the event the Clinical Program's operations are interrupted→ **Contingency plan**
  - Policies and procedures for qualification of **supplies** and validation and/or verification of the **procedure** for **marrow collection (quantity, quality)**

B5 POLICIES AND PROCEDURES

- **B5.1: CRITICAL ASPECTS OF OPERATIONS AND MANAGEMENT**
  - **Recipient evaluation, selection and treatment**
  - Donor and recipient **confidentiality and consent**
  - **Donor** screening, testing, eligibility determination, **selection**.
  - Management of **need of CVC***.
  - Administration of **preparative regimen·**



B5 POLICIES AND PROCEDURES

- **B5.1: CRITICAL ASPECTS OF OPERATIONS AND MANAGEMENT**
  - Administration of **HPC and other cellular products**: ABO-incompatible products, duration and conditions of cellular therapy product storage and indications for disposal
  - Administration of **blood products**
  - Disposal of medical and **biohazard waste**
  - Hygiene and use of **personal protective equipment**
  - **Emergency and disaster plan**

B5 POLICIES AND PROCEDURES

- **B5.2 - B5.7: About SOPs:**
  - Detailed **list**
  - **Reference**s
  - Revised every **two years**
  - Documented approval of each modification
  - Reference to **current versions**
  - SOPs etc **available**
  - Evidence of staff's **knowledge, training in new procedures**
  - Approved by the **Clinical program Director** and reviewed by the Quality Manager

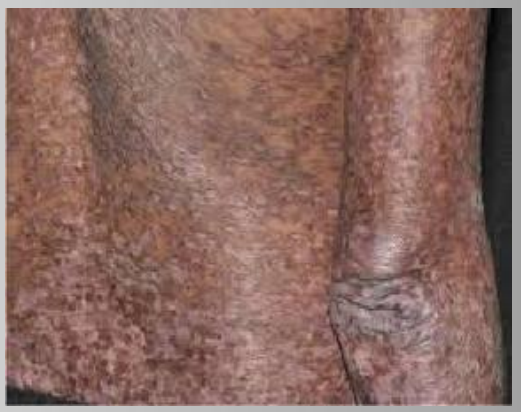
B6 ALLOGENEIC AND AUTOLOGOUS DONOR SELECTION, EVALUATION AND MANAGEMENT

- **WILL BE COVERED IN SEPARATE PRESENTATION TOMORROW MORNING**

B7 RECIPIENT CARE

- **B7.1: Informed consent**
- **B7.2:** Confirm the **availability of donor or cellular therapy product** prior conditioning therapy
- **B7.3: Records and traceability**
- **B7.4, B7.5: Safe administration of the preparative regimen:** protocols, double chemotherapy verification*, radiation therapy administration
- **B7.6: safe administration of cellular therapy products:** policies (adequate volume, additives, ABO-incopatibility, double check,...), cord blood recommendations, adverse events,....

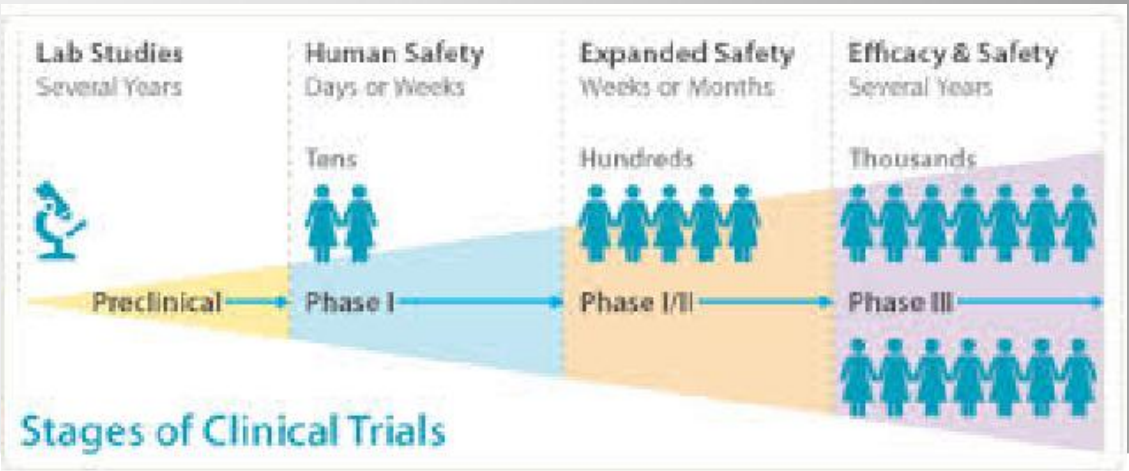
B7 RECIPIENT CARE



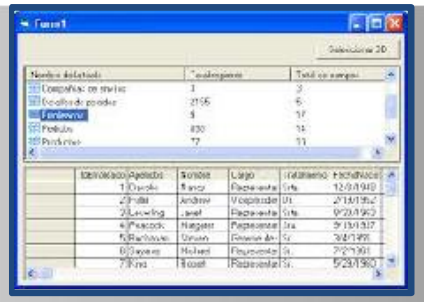
- **B7.7: Additional requirements**
  - Acute GVHD assessment (d100)*
  - Chronic GHVD assessment (1y)*
  - Procedures for vaccination
  - Central venous catheter infection*
- **B7.8: Post-transplant care and discharge**

B8 CLINICAL RESEARCH

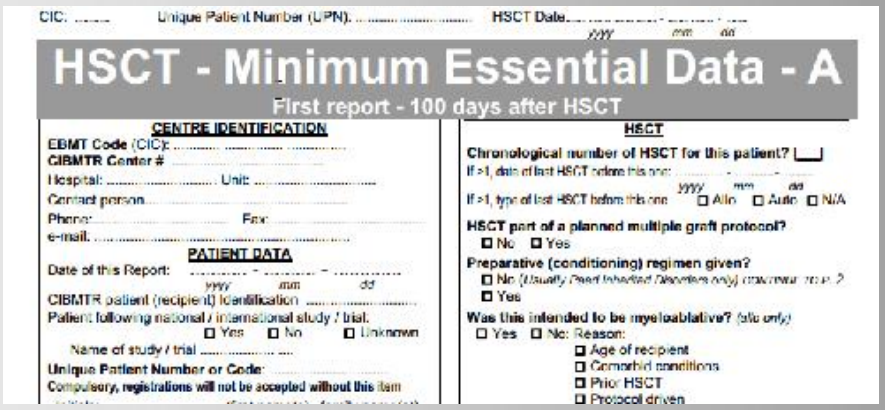
- **B8.1: Review of investigational treatment protocols, informed consents, pharmacy requirements, …..**
- **B8.2: Documentation management**
- **B8.3: Informed consent**
- **B8.4: Conflict of interest**



B9 DATA MANAGEMENT



- **Submit data to national and international database**
- **MEDA**



B10 RECORDS

- **Minimum 10 years**
- **Confidentiality, accessibility**

PART CM: MARROW COLLECTION FACILITY STANDARDS

CM1 GENERAL

- **CM1.5: Minimal activity** 1 BM harvest/year (average)

CM2 MARROW COLLECTION FACILITY

- **CM2.1;2.2;2.3 : “Appropriate” facility**

CM3 PERSONNEL

- **CM3.1:** Marrow Collection Facility Medical Director
- **CM3.2:** Marrow Collection Facility Quality Manager
- **CM3.3:** Marrow Collection Facility Staff

CM4 QUALITY MANAGEMENT

- Comply with B4 if it operates independently of a Clinical Program

CM5 POLICIES AND PROCEDURES

CM5.1:

- Donor and patient **confidentiality**
- Donor consent; donor screening, testing, eligibility determination and management
- Cellular therapy product **collection**
- Prevention of **mix-ups and cross-contamination**
- **Labelling**
- **Cellular therapy product** expiration dates, storage, release and exceptional release
- **Transportation and shipping**, critical equipment
- Hygiene and use of protective attire
- **Emergency and disaster plan**

CM7 CODING AND LABELING OF CELLULAR THERAPY PRODUCTS

- **CM7.1**: **ISBT 128** coding and labelling (Standard terminology for Blood, Cellular Therapy, and Tissue Product descriptions
- **CM7.2; CM7.3:** Labelling operations (obsolete labels,....) product identification

Class: cells, comma, source of cells

- HPC, APHERESIS
- HPC, CORD BLOOD
- HPC, MARROW
- CONCURRENT PLASMA, APHERESIS
- T CELLS, APHERESIS

For autologous use only

Not evaluated for infectious substances

CM8 PROCESS CONTROLS

- **CM8.1:** Written collection procedures
- **CM8.2; CM8.3:** Equipment, reagents, supplies and labels
- **CM8.4:** Autologous or/and CMV-appropiate/irradiated for the donor
- **CM8.5: Anesthesiology supervision**
- **CM8.10:** Controlling and monitoring the collection and cellular therapy product

CM9 CELLULAR THERAPY PRODUCT STORAGE

- Prevent mix-ups, deterioration, contamination, cross-contamination and improper release or distribution

CM10 CELLULAR THERAPY PRODUCT TRANSPORTATION AND SHIPPING

- Transported or shipped in a validated container

CM11 RECORDS