
# JACIE clinical standards 7th edition

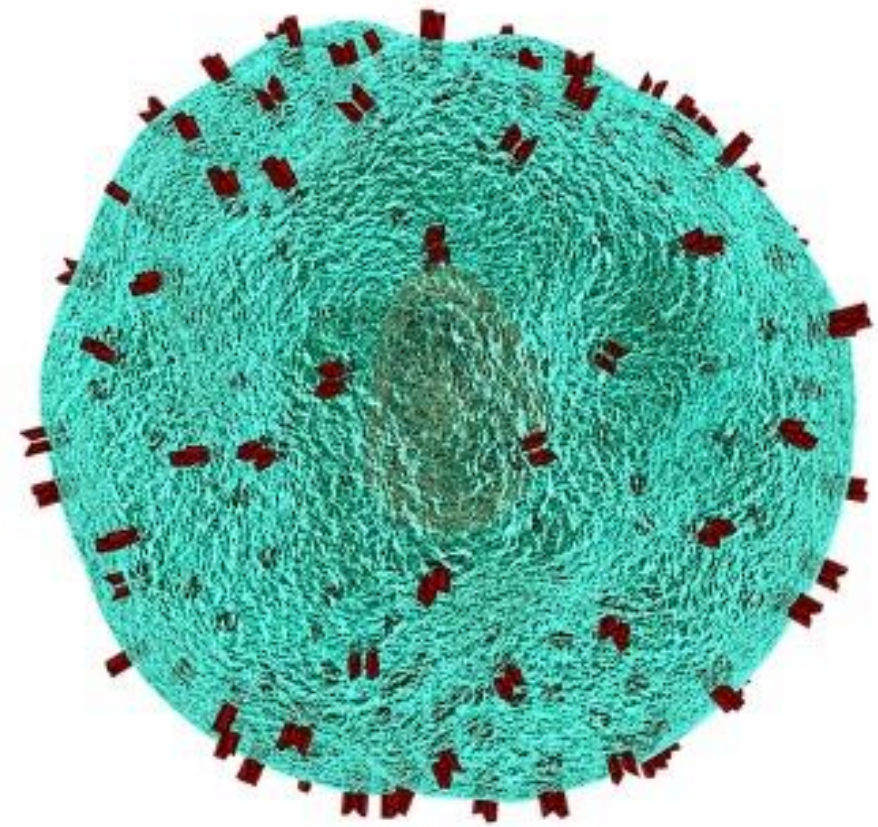
# PARTS


- A
  - TERMINOLOGY, TENETS, ABBREVIATIONS, AND DEFINITIONS
- B
  - **CLINICAL** PROGRAM STANDARDS
- CM/C
  - **COLLECTION** FACILITY STANDARDS
- D
  - **PROCESSING** FACILITY STANDARDS

| PART B CLINICAL | PART CM MARROW | PART C APHERESIS | PART D PROCESSING |
|---|---|---|---|
| B1 General | CM1 General | C1 General | D1 General |
| B2 Clinical Unit | CM2 Marrow Collection Facility | C2 Apheresis Collection Facility | D2 Processing Facility |
| B3 Personnel | CM3 Personnel | C3 Personnel | D3 Personnel |
| B4 Quality Management | CM4 Quality Management | C4 Quality Management | D4 Quality Management |
| B5 Policies and Standard Operating Procedures | CM5 Policies and Standard Operating Procedures | C5 Policies and Standard Operating Procedures | D5 Policies and Standard Operating Procedures |
| B6 Allogeneic and Autologous Donor Selection, Evaluation, and Management | CM6 Allogeneic and Autologous Donor Evaluation and Management | C6 Allogeneic and Autologous Donor Evaluation and Management | D6 Equipment, Supplies, and Reagents |
| B7 Recipient Care | CM7 Coding and Labeling of Cellular Therapy Products | C7 Coding and Labeling of Cellular Therapy Products | D7 Coding and Labeling of Cellular Therapy Products |
| | CM8 Process Controls | C8 Process Controls | D8 Process Controls |
| | CM9 Cellular Therapy Product Storage | C9 Cellular Therapy Product Storage | D9 Cellular Therapy Product Storage |
| | CM10 Cellular Therapy Product Transportation and Shipping | C10 Cellular Therapy Product Transportation and Shipping | D10 Cellular Therapy Product Transportation and Shipping |
| B8 Clinical Research | | | D11 Distribution and Receipt |
| B9 Data Management | | | D12 Disposal |
| B10 Records | CM11 Records | C11 Records | D13 Records |
| | CM12 Direct Distribution to Clinical Program | C12 Direct Distribution to Clinical Program | |

# Immune Effector Cells

- Covered in separate presentation



ALLINONEMOVIE, PIXABAY

https://www.the-scientist.com/?articles.view/articleNo/50231/title/First-CAR-T-Cell-Therapy-Approved-in-U-S-/

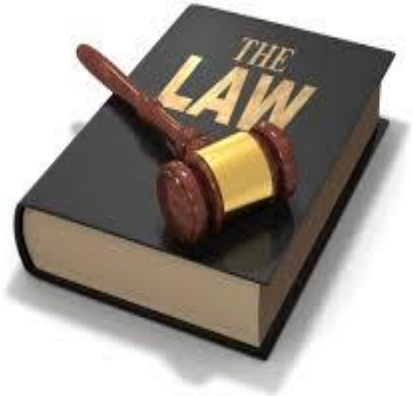
# B1 GENERAL

- B1.1: Integrated medical team with Clinical Program Director
  - More sites - have to function as a single integrated program
  - 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

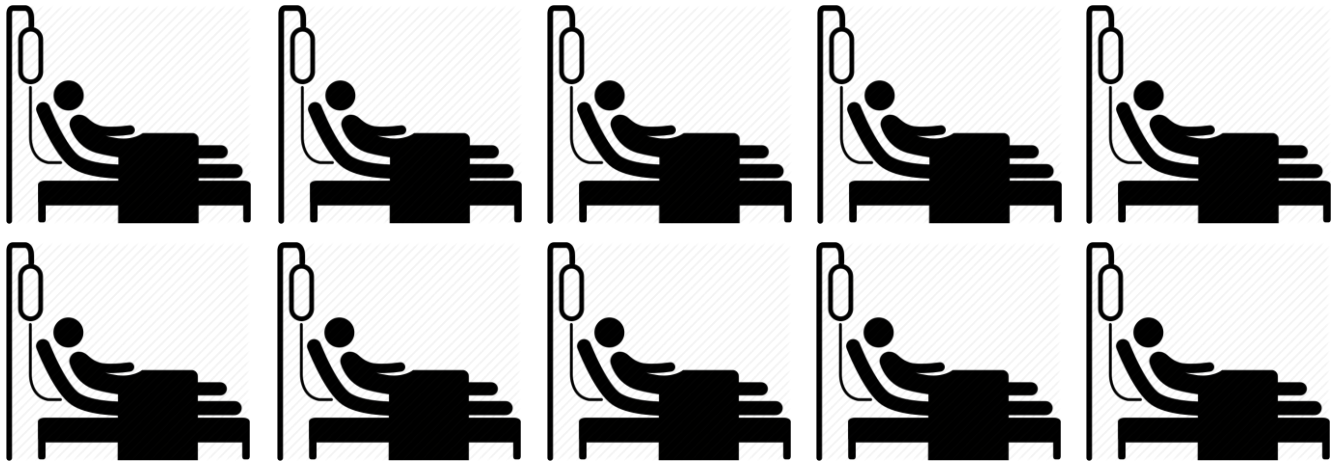



- B1.4 **Designated transplant team**
  - 1 x Clinical program Director
  - 1 x Quality Manager
  - Min 1 x additional attending transplant physician

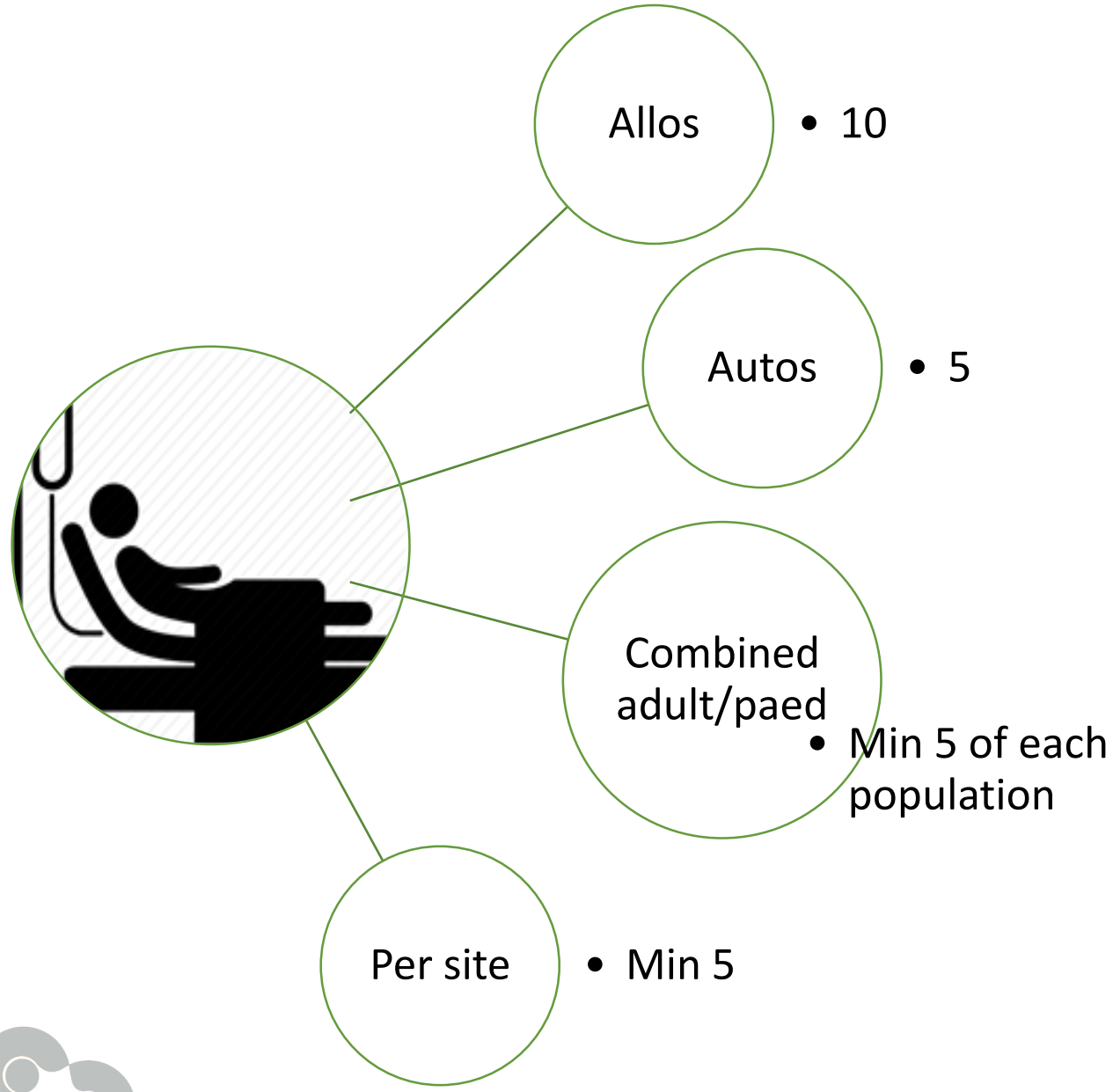
- Active for **min > 12 months** in place before accreditation

# B1.5 Minimum transplant activity

ALLO TRANSPLANTS = 10 **NEW** PATIENTS



AUTO TRANSPLANTS = 5 **NEW** PATIENTS




**APPENDIX I**

MINIMUM NUMBER OF NEW PATIENTS FOR ACCREDITATION

Clinical Programs shall transplant at least the following number of new patients[1] before initial accreditation and annually thereafter:

| 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]<br>• 5 autologous at each applicable site[2] | • 5 allogeneic recipients at each applicable site[2]<br>• 5 autologous at applicable each applicable site[2] |
| Combined Adult AND Pediatric | Single Clinical Site | Autologous only | • 5 adult autologous<br>• 5 pediatric autologous recipients | • 5 adult autologous<br>• 5 pediatric autologous recipients |
| | | Allogeneic and Autologous | • 5 adult allogeneic recipients<br>• 5 pediatric allogeneic recipients | • 5 adult allogeneic recipients<br>• 5 pediatric allogeneic recipients |
| | Multiple Clinical Sites | Autologous only | • 5 adult autologous at each applicable site<br>• 5 pediatric autologous recipients at each applicable site | • 5 adult autologous recipients at each applicable site<br>• 5 pediatric autologous recipients at each applicable site |
| | | Allogeneic and Autologous | • 5 adult allogeneic recipients at each applicable site<br>• 5 pediatric allogeneic recipients at each applicable site<br>• 5 adult autologous at each applicable site[2]<br>• 5 pediatric autologous at each applicable site[2] | • 5 adult allogeneic recipients at each site<br>• 5 pediatric allogeneic recipients at each site<br>• 5 adult autologous at each applicable site[2]<br>• 5 pediatric autologous at each applicable site[2] |

[1]The term "new allogeneic patient" or "new autologous patient" includes only a patient who received his/her first transplant of that type during the period of time in question.

[2]Programs performing allogeneic and autologous transplantation that have more than one clinical site may or may not perform both types of transplant at each site. The requirement for five autologous transplant recipients per site only applies to those sites that do not perform allogeneic transplant.

# 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,…)*, ambulatory setting

- B2.16: Facilities maintained in a clean, sanitary, and orderly manner – **MINIMISE RISKS**

# B2 CLINICAL UNIT

- B2.6: **24-h attending physician**
  - Not necessarily transplant specialist but needs planning and oversight

- B2.7; B2.11; B2.12; B2.13: 24-h availability of **ICU**, **pharmacy** support, **renal support** under nephrologist control, **CMV appropriate** and irradiated blood products

# Safety

- B2.16, B2.17: policies to minimize risks to the health and safety of employees, patients, visitors and volunteers -> SAFETY MANUAL

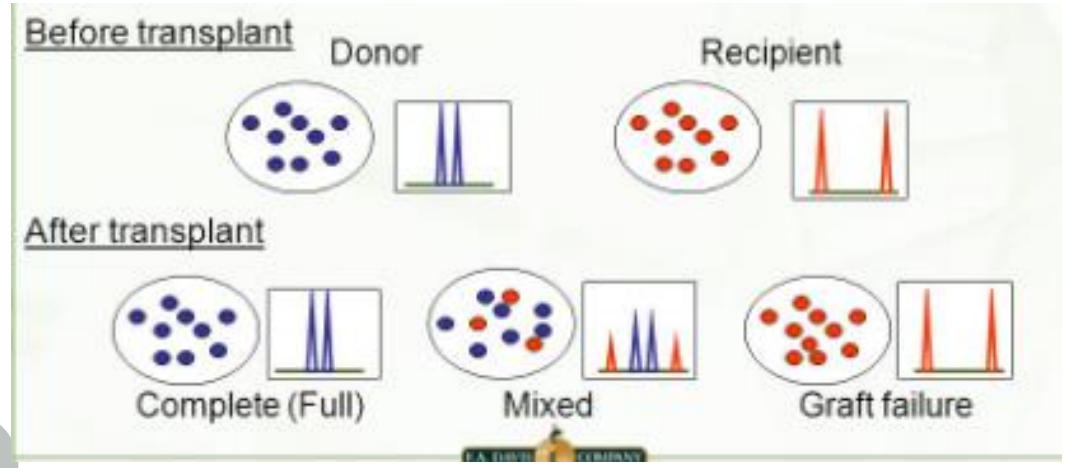


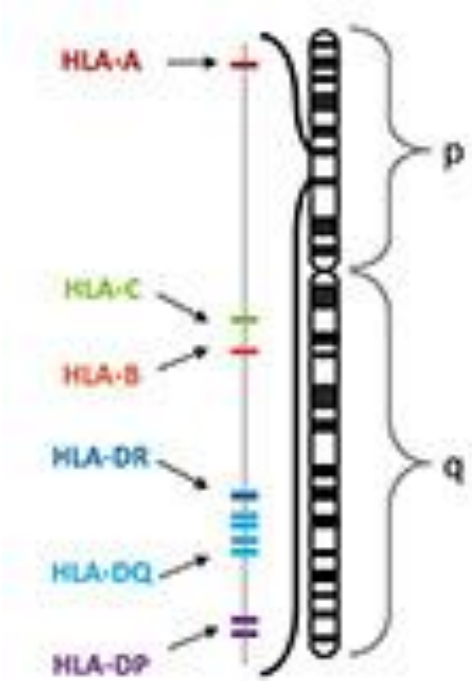

# B2 CLINICAL UNIT

FOR ALLOGENEIC

USE ACCREDITED SERVICES FOR:

- B2.14 EFI accredited HLA
- B2.15: Chimerism testing




| MHC Class I |
| --- |
| HLA-A |
| HLA-B |
| HLA-C |
| **MHC Class II** |
| HLA-DRB1 |
| HLA-DRB3 |
| HLA-DRB4 |
| HLA-DRB5 |
| HLA-DQA1 |
| HLA-DQB1 |
| HLA-DPA1 |
| HLA-DPB1 |

# 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 etc.
- B3.10: Quality Manager
- B3.11: Support services staff: dietary, social services, etc.

- Specific knowledge*
- Training
- Competency

# B3 Clinical Program Director's responsibilities

- Administrative operations
- Clinical operations
- Quality Management Program
- Selection and care of recipients and donors
- Cell collection and processing, whether internal or contracted services.
- Compliance with Standards and laws and regulations
- Oversight of medical care provided
- Verifying the knowledge and skills the transplant team

# B3 Physician training

| Licensed | Specialist | Education |
|---|---|---|
| • Legal requirements to practice | • Hematology<br>• Medical Oncology<br>• Immunology<br>• or Pediatric Hematology/Oncology | • Min 10 hours per year<br>• Participate regularly in HPC specific educational activities |

# 33 areas of requried specific training (*as applicable*) B3.3.4.1-B3.3.4.33

| | | | | | | |
|---|---|---|---|---|---|---|
| Indications for allogeneic and autologous HPC transplantation. | Selection of suitable recipients and appropriate preparative regimens. | Donor selection, evaluation, and management. | Donor and recipient informed consent. | Administration of preparative regimens. | Administration of growth factors for HPC mobilization and for post-transplant hematopoietic cell reconstitution. | Cellular therapy product administration and patient management. |
| Management of neutropenic fever. | Diagnosis and management of infectious and non-infectious pulmonary complications of transplantation. | Diagnosis and management of fungal disease. | Diagnosis and management of sinusoidal obstruction syndrome and other causes of hepatic dysfunction. | Management of thrombocytopenia and bleeding, including recognition of disseminated intravascular coagulation. | Management of hemorrhagic cystitis. | Blood transfusion management. |
| Use of irradiated blood products. | Management of mucositis, nausea, and vomiting. | Monitoring and management of pain. | Cytokine release syndrome. | Tumor lysis syndrome and macrophage activation syndrome. | Cardiac dysfunction. | Renal dysfunction. |
| Respiratory distress. | Neurologic toxicity. | Anaphylaxis. | Infectious and noninfectious processes. | Diagnosis and management of HPC graft failure. | Evaluation of post-transplant cellular therapy outcomes. | Evaluation of late effects of cellular therapy. |

| | | | |
|---|---|---|---|
| Documentation and reporting for patients on investigational protocols. | Applicable regulations and reporting responsibilities for adverse events. | Palliative and end of life care. | Age-specific donor and recipient care. |

# B3 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

# B3 Pharmacist

- Must be qualified
- Standard specifies training and knowledge requirements
- Shall be involved in the development and implementation of controlled documents related to the pharmaceutical management of cellular therapy recipients

http://victoryoncology.com/wp-content/uploads/2015/11/pharmo.jpg

# B3 Pharmacist training including

**Hematology/oncology patient care**, including the process of cellular therapy.

**Therapeutic drug monitoring**, including, but not limited to, anti-infective agents, immunosuppressive agents, anti-seizure medications, and anticoagulants.

**Adverse events** including, but not limited to, cytokine release syndrome and neurological toxicities.

Monitoring for and recognition of **drug/drug and drug/food interactions** and necessary dose modifications.

Recognition of **medications** that require **adjustment for organ dysfunction**.

# B3 Requirements concerning education

## Minimum 10 hours of continuing education per annum

# B3 Quality Manager

- There shall be a Clinical Program Quality Manager **to establish and maintain systems to review, modify, and approve all policies** and Standard Operating Procedures intended to **monitor compliance with these Standards or the performance of the Clinical Program**.
- Min continuous education = 10 hours / year

# B3 Support Staff

Dietary

Data Management

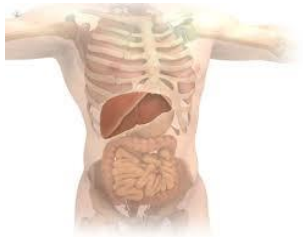

Social Services

Support staff

Physical Therapy

Psychology Services

# B3 Consulting specialists



- Surgery
- Pulmonary medicine
- Intensive care
- Gastroenterology
- Nephrology
- Infectious disease
- Obstetrics/Ginecology
- Dermatology
- Palliative and end of life care

- Cardiology
- Pathology
- Psychiatry
- Radiology
- Radiation Oncology
- Infectious disease
- Transfusion medicine
- Neurology
- Ophtalmology

# B4 QUALITY MANAGEMENT

# B4 Quality Management standards

- General quality management (QM) standards covered in separate presentation
- Some specific QM ítems discussed here

# B4 Review of outcome analysis and/or product efficacy shall include at a minimum:

- B4.7.3.1 For HPC products intended for hematopoietic reconstitution, **time to engraftment** following cellular therapy product administration.
- B4.7.3.3 **Overall survival and treatment-related morbidity and mortality** at thirty (**30**) days, one hundred (**100**) days, and **one** (1) **year** after cellular therapy product administration.
- B4.7.3.4 **Acute GVHD** grade within one hundred (100) days after allogeneic transplantation.
- B4.7.3.5 **Chronic GVHD** grade within one (1) year after allogeneic transplantation.
- B4.7.3.6 Central venous **catheter infection**.

# B4 Outcome

- The Clinical Program should achieve **one-year survival** outcome within or above the expected range when **compared to national or international outcome data**.
  - B4.7.5.1 If expected one-year survival outcome is not met, the Clinical Program shall implement a corrective action plan that meets FACT or JACIE requirements.
- B4.7.6 The Clinical Program should set **benchmarks for non-relapse mortality** at one hundred (100) days after cellular therapy product administration and describe the rationale and process for review in the Quality Management Plan.



# B5 POLICIES AND STANDARD OPERATING PROCEDURES

- Mantain policies and SOPs addressing critical aspects of operations and management.
- Detailed list of all controlled documents.
- Documents must be controlled, detailed and unambiguous.
- Identified critical documents.
- Revised every two years.
- Current literature (when appropriate).

# B6 Allogeneic and autologous donor selection, evaluation and management

- Allogeneic and autologous donor selection, evaluation, and management covered in separate presentation

# B7 RECIPIENT CARE

- **Informed consent**
- Confirm the **availability and suitability** of a donor or cellular therapy product **prior to initiating the recipient's preparative regimen.**
- Records shall be made concurrently with **each step of recipient care** in such a way that all steps may be **accurately traced**.

# B7 Policies in place for:

- Administration of the **preparative regimen**
- Administration of **radiation therapy**
- Administration of **cellular therapy products**
- Indications for and safe administration of **ECP** *if utilized*
- Administration of **immune effector cells** and management of complications *if utilized*

# B7 Policies in place for:

- Provision of appropriate **long-term follow-up**, treatment, and plans of care.
- Monitoring by appropriate specialists of recipients for post-cellular therapy **late effects**
- Describing the transition of long-term **pediatric recipients** to adult care as appropriate.
- Describing the **acceptance** of pediatric recipients into a long-term follow-up **clinic for adults.**

# B7 Planned discharge

- There shall be **policies or Standard Operating Procedures** in place for planned discharges and provision of post-transplant care.
- **Discharges should normally take place after hematopoietic engraftment**.
- A Clinical Program may adopt a policy for **discharging recipients before engraftment**, with ongoing inpatient care undertaken at another facility.
- It may be necessary to **collaborate with health care providers in local or regional facilities** to provide a portion of post-transplant care.

https://www.uzdaily.com/img/people/jigar-op.jpg

# B7 Planned discharge to another facility:

Clinical Program shall verify that the following elements are available:

A consult between the attending physician and the receiving health care professionals regarding the applicable elements in Standard B7.7.

Facilities that provide appropriate location, adequate space, and protection from airborne microbial contamination.

Appropriate medications, blood products, and additional care required by the recipient.

# B7 Inspecting planned discharge

JACIE's approach

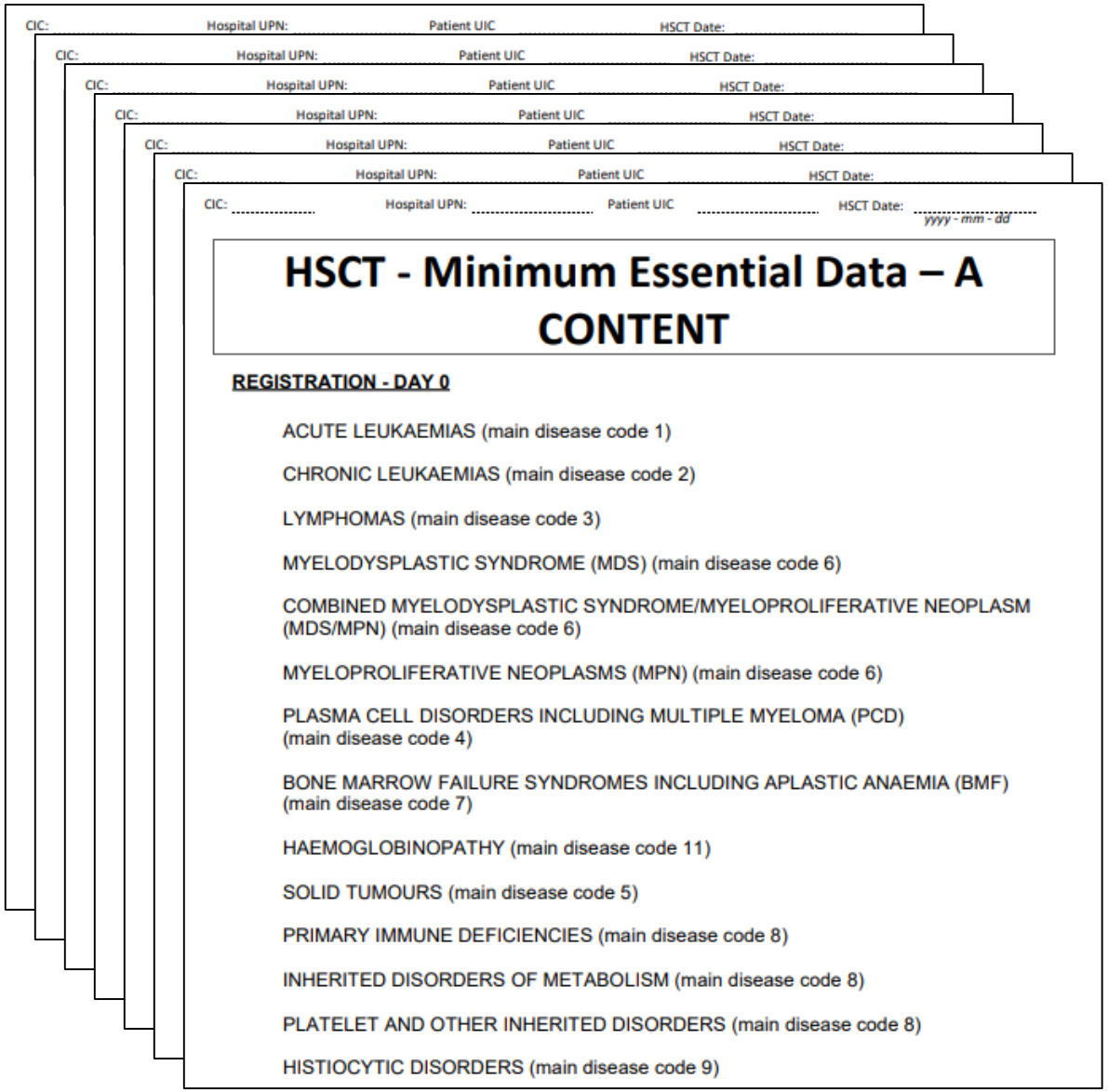
- All **locations providing critical patient care** are considered by JACIE to be part of the transplant process and therefore **fall within the scope of the accreditation**
- These locations must be described in the application form
- These clinical units must complete the inspection checklist and provide pre-audit documentation
- These locations will be subject to an onsite inspection

# B8 CLINICAL RESEARCH


# B9 DATA MANAGEMENT

- The Clinical Program shall collect all the data necessary to complete the Transplant Essential Data Forms of the CIBMTR or the **Minimum Essential Data-A forms** of the EBMT

  - Reporting not obligatory but strongly recommended
  - Centre would have to ***justify*** why they **DON'T** report data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**HSCT - Minimum Essential Data – A CONTENT**

**REGISTRATION - DAY 0**

ACUTE LEUKAEMIAS (main disease code 1)

CHRONIC LEUKAEMIAS (main disease code 2)

LYMPHOMAS (main disease code 3)

MYELODYSPLASTIC SYNDROME (MDS) (main disease code 6)

COMBINED MYELODYSPLASTIC SYNDROME/MYELOPROLIFERATIVE NEOPLASM (MDS/MPN) (main disease code 6)

MYELOPROLIFERATIVE NEOPLASMS (MPN) (main disease code 6)

PLASMA CELL DISORDERS INCLUDING MULTIPLE MYELOMA (PCD) (main disease code 4)

BONE MARROW FAILURE SYNDROMES INCLUDING APLASTIC ANAEMIA (BMF) (main disease code 7)

HAEMOGLOBINOPATHY (main disease code 11)

SOLID TUMOURS (main disease code 5)

PRIMARY IMMUNE DEFICIENCIES (main disease code 8)

INHERITED DISORDERS OF METABOLISM (main disease code 8)

PLATELET AND OTHER INHERITED DISORDERS (main disease code 8)

HISTIOCYTIC DISORDERS (main disease code 9)

# B10 RECORDS: Electronic records

**Critical electronic record systems** shall include at a minimum systems

- under the control of the Clinical Program
- that are used as a substitute
  - for paper
  - to make decisions
  - to perform calculations
  - or to create or store information used in critical procedures.

# Revised: "Validation of Computerised Systems" Guideline

Back

AGENDA

- https://www.edqm.eu/en/news/revised-validation-computerised-systems-guideline

The revised guidelines are the following

- Validation of Computerised Systems - Core Document
- Validation of Computerised Systems Annex 1: Validation of Excel Spreadsheets
- Validation of Computerised Systems Annex 2: Validation of Complex Computerised Systems

# ANY QUESTIONS