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

Third Edition

NOTICE

These Standards are designed to provide minimum guidelines for facilities and individuals performing haematopoietic cell transplantation and therapy or providing support services for such procedures. These Standards are not intended to include all procedures and practices that a facility or individual should implement if the standard of practice in the community or governmental laws or regulations establish additional requirements. Each facility and individual should analyse its practices and procedures to determine whether additional standards apply. The Foundation for the Accreditation of Cellular Therapy and the Joint Accreditation Committee – ISCT and EBMT disclaim any responsibility for setting maximum standards and expressly do not represent or warrant that compliance with the Standards is an exclusive means of complying with the standard of care in the industry or community.

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INTRODUCTION

The major objective of the FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing, and Administration is to promote quality medical and laboratory practice in haematopoietic progenitor cell transplantation and other therapies using cellular products. These Standards apply to haematopoietic progenitor cells, defined as self-renewing and/or multi-potent stem cells capable of maturation into any of the haematopoietic lineages, lineage-restricted pluri-potent progenitor cells, and committed progenitor cells, regardless of tissue source (bone marrow, umbilical cord blood, peripheral blood, or other tissue source). These Standards also include Therapeutic Cells, defined as nucleated cells from any tissue source (marrow, peripheral blood, umbilical cord and placental blood) collected for therapeutic use other than as haematopoietic progenitor cells. Also, these Standards apply to all phases of collection, processing, storage, and administration of these cells that have been derived from marrow or peripheral blood, including various manipulations such as removal or enrichment of various cell populations, expansion of haematopoietic cell populations, and cryopreservation. For haematopoietic progenitor cells or therapeutic cells derived from umbilical cord and/or placental blood, these Standards apply only to the administration of the cellular product, applying the clinical standards for transplantation of allogeneic or autologous haematopoietic progenitor cells, as appropriate. These Standards do not apply to the collection, processing or banking of umbilical cord and placental blood cells. Standards for these processes are found in the NetCord-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release. The FACT-JACIE Standards also do not address the collection, processing, or administration of erythrocytes, platelets, mature granulocytes, plasma, or plasma-derived products intended for transfusion support.

Every effort has been made in these Standards to incorporate sound recommendations fostering quality medical and laboratory practice in haematopoietic cell therapy. However, no Standards can guarantee the successful outcome of such therapies. FACT-JACIE Standards are minimal performance guidelines that may be exceeded as deemed appropriate by the responsible personnel in individual facilities. Directors and Medical Directors of the Clinical Programme, Collection Facility, and Processing Facility assume responsibility for adopting FACT-JACIE Standards as appropriate to the programme or facility, and for setting more rigorous internal requirements where appropriate. Attempts have been made to conform these Standards to existing U.S. federal regulations and the requirements of the European Union Directives; however, compliance with these Standards does not guarantee compliance with all regulations. In all cases, personnel must follow the applicable laws and regulations.

This third edition of FACT-JACIE Standards has several notable changes from the Second Edition. First, it is published under a new title, the FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing, and Administration, which accurately reflects the contributions of the representatives from both organizations. The Foundation for the Accreditation of Cellular Therapy (FACT) was founded in 1996 by the American Society for Blood and Marrow Transplantation (ASBMT) and the International Society for Cellular Therapy (ISCT). The first edition of Standards was published that same year. The Inspection and Accreditation Programme based on these Standards was started in North America in 1997. The Joint Accreditation Committee of ISCT and EBMT (JACIE) was established in 1999. JACIE adopted the first edition of FACT-JACIE Standards in its entirety. The second edition of FACT-JACIE Standards was developed and published in 2002 following joint review by FACT and JACIE. This third edition was developed entirely by joint working groups, with representation from both FACT and JACIE. The final document was approved by the FACT and JACIE Boards of Directors and became effective from 27 October 2006 and 19 February 2007 respectively.

The third edition of the Standards is structured to align similar standards among the three primary functions within a transplantation programme: the clinical programme, collection facility, and processing facility. Similar standards were compared, and kept consistent wherever appropriate. The Quality Management section for each area in the transplant programme has been expanded, with specific requirements detailed. Standards were added to incorporate the new regulatory requirements for donor screening, testing, and eligibility determination, labelling, and current Good Tissue Practices as published by the U.S. FDA and as required by the European Union Tissue and Cells Directive 2004/23/EC and its associated implementing directives.

The Standards incorporate three labelling tables as appendices, detailing the requirements of labelling at each phase of manufacturing and transport, including the applicable biohazard and warning labels.

Both FACT and JACIE recognize the significant benefits of international standardization of coding and labelling in cellular therapy, and support the international efforts to implement *ISBT 128*, the international information standard for transfusion and transplantation. The product definitions and relevant product modifications defined in this edition of FACT-JACIE International Standards are consistent with the currently proposed product definitions and modifications in the *ISBT 128* Standard. These FACT-JACIE Standards require the use of this terminology for haematopoietic progenitor cell and therapeutic products as applicable. At an early stage in the implementation plan for introducing bar coding or other machine readable technology, the transplant programme, collection facility, and/or processing facility as appropriate, should register with ICCBBA, Inc., the organization charged with the international maintenance of this database, in order to obtain the necessary documents and databases. If the final approved product names in the *ISBT 128* Standard differ from those currently proposed, the FACT-JACIE definitions and product names will be revised to match those in the *ISBT 128* Standard. Further information is available from the ICCBBA web site at http://iccbba.org/.

ACCREDITATION

The basis for FACT or JACIE Accreditation is documented compliance with the current edition of these Standards. Although there are joint FACT-JACIE Standards, FACT and JACIE maintain separate and parallel accreditation processes. Accreditation is determined by evaluation of the written information provided by the applicant facility and by on-site inspection. All inspections are conducted by persons qualified by training and experience in haematopoietic cell therapy who are affiliated with an accredited or applicant facility, have attended inspector training, and who have a working knowledge of FACT-JACIE Standards and of their application to various aspects of the haematopoietic progenitor cell programme.

Facilities performing haematopoietic progenitor cell collection, processing, storage, and/or transplantation may apply for voluntary accreditation by FACT in North America or Australia, or by JACIE in Europe as described below. Applicants from other areas are encouraged to contact FACT or JACIE for direction in applying for accreditation.

1. A clinical haematopoietic progenitor cell transplantation programme may apply for accreditation alone or in conjunction with the collection facility and/or the cell processing laboratory with which it is associated. All facilities applying together should submit pre-inspection data together. If applying separately, a clinical transplant programme must use a collection facility and a processing laboratory that meet FACT-JACIE Standards and have a clearly defined contractual or reporting relationship.

2. A haematopoietic progenitor cell collection facility or service (peripheral blood or bone marrow) may apply for accreditation as an integral part of a clinical transplant programme, as a local or regional collection service providing haematopoietic progenitor cell collection services for one or more clinical transplant programs, or in conjunction with a cell processing laboratory if the services of haematopoietic progenitor cell collection and processing/storage are functionally linked. An accredited haematopoietic progenitor cell collection facility may provide services for clinical transplant programs that are or are not FACT or JACIE accredited, but shall use a processing laboratory that meets FACT-JACIE Standards.

3. A haematopoietic progenitor cell processing laboratory may apply for accreditation as an integral part of a clinical transplant programme, as part of a collection service or facility, or as an independent laboratory that processes and stores haematopoietic progenitor cell products for clinical programme(s) or collection facilities. An accredited laboratory may provide services for clinical transplant programs and/or collection services that are or are not FACT or JACIE accredited.

Accreditation of the clinical haematopoietic progenitor cell transplantation programme may be for allogeneic transplantation, autologous transplantation, or both. The accreditation may cover haematopoietic progenitor cells derived from bone marrow and/or peripheral blood. Transplantation of umbilical cord and/or placental blood is included in allogeneic or autologous transplantation Standards, as appropriate. Additionally, accreditation of the clinical programme may be for transplantation of adult patients, paediatric patients, or both. As detailed in the Standards, consultants and support services appropriate to the patient population are required.

An accreditation cycle is three years. Accredited facilities are reinspected routinely every three years, and may also be reinspected in response to complaints or information that a facility may be non-compliant with FACT-JACIE Standards, or as determined by the FACT or JACIE Boards. Accreditation may be suspended or terminated if a facility fails to comply with the Standards.

Accreditation for the collection and/or banking of cord blood cells is offered to facilities demonstrating compliance with the current edition of the NetCord-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release. There is a separate application and inspection process for NetCord-FACT accreditation. NetCord-FACT Standards for Cord Blood do not cover the clinical transplantation of umbilical cord and placental blood cells.

PART A: TERMINOLOGY, ABBREVIATIONS, AND DEFINITIONS

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PART A: TERMINOLOGY, ABBREVIATIONS, AND DEFINITIONS

A1 TERMINOLOGY

For purposes of these Standards, the term *shall* means that the Standard is to be complied with at all times. The term *should* indicates an activity that is recommended or advised, but for which there may be effective alternatives.

A2 ABBREVIATIONS

The following abbreviations cover terms used in these Standards:

ABO	Major human blood group including erythrocyte antigens, A, B, O
AC	Accompany
AF	Affixed
Anti-	Antibody to the antigen designated
ASHI	American Society for Histocompatibility and Immunogenetics
AT	Attached
CFR	Code of Federal Regulations
CIBMTR	Center for International Blood and Marrow Transplant Research
CMS	Centres for Medicare and Medicaid Services
CLIA	Clinical Laboratory Improvement Amendments
CMV	Cytomegalovirus
DNA	Deoxyribonucleic acid
EBMT	European Group for Blood and Marrow Transplantation
EFI	European Federation for Immunogenetics
FACT	Foundation for the Accreditation of Cellular Therapy
FDA	U.S. Food and Drug Administration
HLA	Human Leukocyte Antigen
HPC	Haematopoietic progenitor cells
IDE	Investigational device exemption
IND	Investigational new drug
ISCT	International Society for Cellular Therapy
JACIE	Joint Accreditation Committee – ISCT and EBMT
RBC	Red blood cell
Rh	Rhesus systems of human red cell antigens; used in this document to refer to the Rh(D) antigen only, unless otherwise specified
USDA	United States Department of Agriculture

A3 DEFINITIONS

Accompany: To go or be together with, but not attached. Information that must accompany a cellular therapy product in a sealed package, or alternatively, be attached or affixed.

Accreditation Cycle: The period of time from the awarding of accreditation until its expiration. At publication of these Standards, this period is three (3) years.

Advanced Practitioner: Advanced Practitioner of Nursing: includes certified nurse anaesthetist, nurse practitioner, certified nurse midwife, and clinical nurse specialist.

Adverse event: Any unintended or unfavourable sign, symptom, abnormality, or condition temporally associated with an intervention that may or may not have a causal relationship

with the intervention, medical treatment, or procedure. Adverse reaction is a type of adverse event.

Adverse reaction: A noxious and unintended response to the collection or infusion of any cellular therapy product for which there is a reasonable possibility that the cellular therapy product caused the response.

Affix: To attach in physical contact with the cellular therapy product container.

Allogeneic: Cellular therapy product obtained from a donor and intended for infusion into a genetically distinct recipient.

Apheresis: A medical technology in which the blood of a donor is separated into its component parts, the desired component is removed, and the remaining components are returned to the donor.

Aseptic technique: Practices designed to reduce the risk of microbial contamination of products, reagents, specimens, patients, or donors.

Attach: To fasten securely to the cellular therapy product container by means of a tie tag or comparable alternative. Any information required to be attached to a container may alternatively be affixed.

Audit: Documented, systematic evaluation to determine whether approved policies or procedures have been properly implemented and are being followed.

Autologous: Cellular therapy product obtained from a donor and intended for infusion back into the same individual.

Available for distribution: The point at which the cellular therapy product has been determined to meet all release criteria.

Biological product deviation: A deviation from applicable regulations, standards, or established specifications that relate to the prevention of communicable disease transmission or cellular therapy product contamination; or an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to cellular therapy product contamination.

Calibrate: To set measurement equipment against a known standard.

Calibration: Periodic scheduled activity to check and maintain the accuracy of measurements against a known standard.

CD34: The 115 kD glycoprotein antigen, expressed by 1-2% of normal bone marrow mononuclear cells, that is defined by a specific monoclonal antibody (anti-CD34) using the standardized cluster of differentiation (CD) terminology.

Cellular therapy: The administration of products with the intent of providing effector cells in the treatment of disease or support of other therapy.

Cellular therapy product: Somatic cell-based product (e.g. mobilized HPC, therapeutic

cells, cord blood cells, pancreatic islets) that is procured from a donor and intended for processing and administration.

Clinical Programme: An integrated medical team housed in geographically contiguous or proximate space with a single Clinical Programme Director and common staff training programs, protocols, and quality management systems. The Clinical Programme shall use haematopoietic cell collection and processing facilities that meet FACT-JACIE Standards with respect to their interactions with the Clinical Programme. Clinical Programs that include non-contiguous institutions in the same metropolitan area shall demonstrate evidence of regular interaction and common protocols, staff training procedures, quality management systems, and review of clinical results. Several clinical sites, particularly with different Directors, or outside a single metropolitan area, joining together for the purpose of meeting criteria to qualify as a Clinical Programme do not fulfil the intent of these Standards. In contrast, collection facilities and/or processing facilities serving one or more clinical programs are acceptable.

Collection: Any procedure for harvesting cellular therapy products, including labelling, regardless of technique or source.

Collection Facility: The site where a cellular therapy product is collected from a donor.

Competency: Ability to adequately perform a specific procedure or task according to direction.

Complaint: Any written, oral, or electronic communication about a problem associated with a distributed cellular therapy product or with a service related to the collection, processing, storage, distribution, or infusion of a cellular therapy product.

Cord blood: The whole blood, including HPC, collected from placental and umbilical cord blood vessels after the umbilical cord has been clamped.

Corrective action: Action taken to eliminate the causes of an existing discrepancy or other undesirable situation to prevent recurrence.

Current Good Tissue Practice: The methods used in, and the facilities and controls used for, the manufacture of HCT/Ps including recordkeeping and the establishment of a quality programme as required by the FDA for HCT/P establishments.

Designee: An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility.

Director: For purposes of these Standards, includes individuals with the following qualifications:

> *Clinical Programme Director* is the physician responsible for all administrative and clinical operations of the clinical transplantation programme, including compliance with these Standards. The Clinical Programme Director shall be appropriately licensed to practice medicine in the jurisdiction in which the programme is located and board certified (or non-U.S. equivalent) in one or more of the following specialties: Hematology, Medical Oncology, Adult or Paediatric Immunology, or Paediatric Hematology/Oncology. A non-board certified physician who completed

medical training prior to 1985 may serve as Clinical Programme Director if she/he has documented experience and published contributions in the field of haematopoietic cell transplantation extending over ten years. The Clinical Programme Director shall participate regularly in educational activities related to the field of haematopoietic cell transplantation. The Clinical Programme Director also has oversight of the care provided by the Clinical Programme.

Collection Facility Director is an individual with a medical degree or doctoral degree in a relevant science, qualified by postgraduate training or experience for the scope of activities carried out in the Collection Facility. The Collection Facility Director is responsible for all technical procedures, performance of the collection procedure, supervision of staff and administrative operations of the Collection Facility. The Collection Facility Director shall participate regularly in educational activities related to the field of cellular therapy product collection and/or transplantation. The Collection Facility Director may also serve as the Medical Director if appropriately credentialed.

Collection Facility Medical Director is a licensed physician with postgraduate training in cell collection and/or transplantation. This individual, or designee, is directly responsible for the medical care of patients undergoing apheresis or marrow harvest, including the pre-collection evaluation of the donor at the time of donation and care of any complications resulting from the collection procedure. The Collection Facility Medical Director shall participate regularly in educational activities related to the field of cellular therapy product collection and/or transplantation. The Collection Facility Medical Director may also serve as the Collection Facility Director if appropriately credentialed.

Processing Facility Director is an individual with a medical degree or a doctoral degree in a relevant science, qualified by training or experience for the scope of activities carried out in the Processing Facility. The Processing Facility Director is responsible for all procedures and administrative operations of the Processing Facility, including compliance with these Standards. The Processing Facility Director shall participate regularly in educational activities related to the field of cellular therapy processing and/or transplantation. The Processing Facility Director may also serve as the Processing Facility Medical Director if appropriately credentialed.

Processing Facility Medical Director is a licensed physician with postgraduate training and/or one year experience in the preparation and clinical use of cell therapy products. The Processing Facility Medical Director or designee is directly responsible for all medical aspects related to the Processing Facility. The Processing Facility Medical Director shall participate regularly in educational activities related to the field of cellular therapy product processing and/or transplantation. The Medical Director may also serve as the Processing Facility Laboratory Director if appropriately credentialed.

Distribution: Any conveyance or shipment (including importation and exportation) of a cellular therapy product that has been determined to meet appropriate release criteria, whether or not such conveyance or shipment is entirely intrastate.

Donor: A person who is the source of cells or tissue for a cellular therapy product.

Electronic record: Any record or document consisting of any combination of text, graphics, or other data that is created, stored, modified, or transmitted in digital form by a computer.

Eligible: A cellular therapy product donor who meets all donor screening and testing requirements related to transmission of infectious disease as defined by the FDA or non-U.S. equivalent.

Engraftment: The reconstitution of recipient haematopoiesis with blood cells and platelets from a donor.

Errors and Accidents: Any unforeseen or unexpected deviations from applicable regulations, standards, or established specifications that may affect the safety, purity, or potency of a cellular therapy product.

Establish and maintain: A process to define, document in writing or electronically, implement, follow, review, and, as needed, revise on an ongoing basis.

Expansion: Growth of one or more cell populations in an in vitro culture system.

Facility: A location where activities covered by these Standards are performed. Such activities include determination of donor eligibility or suitability, product collection, processing, storage, distribution, issue, and administration.

Fresh: A cellular therapy product that has never been cryopreserved.

Gene insertion: The introduction of one or more exogenous genes into one or more cell populations.

Haematopoietic progenitor cells (HPC): Self-renewing and/or multi-potent stem cells capable of maturation into any of the haematopoietic lineages, lineage-restricted pluripotent progenitor cells, and committed progenitor cells, regardless of tissue source (bone marrow, umbilical cord blood, peripheral blood, or other tissue source).

Haematopoietic progenitor cell therapy: The infusion of HPC product with the intent of providing effector functions in the treatment of disease or in support of other therapy.

Human cells, tissues, or cellular or tissue-based products (HCT/Ps): Articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.

Ineligible: A cellular therapy product donor who does not meet all donor screening and testing requirements related to transmission of infectious disease as defined by the FDA, or non-U.S. equivalent.

Institutional Review Board or Ethics Committee: A Board or Committee established by an institution in accordance with the regulations of the U.S. Department of Health and Human Services, or other governmental agency where applicable, to review biomedical and behavioural research involving human subjects conducted at or supported by that institution.

ISBT 128: The international information technology standard for transfusion medicine and transplantation.

Labelling: Steps taken to identify the original cellular therapy product collection and any products or product modifications; to complete the required reviews; and to attach the appropriate labels.

Manipulation: An ex vivo procedure(s) that selectively removes, enriches, expands, or functionally alters HPC products.

> *Minimally Manipulated:* Processing that does not alter the relevant biological characteristics of cells or tissues.
>
> *More than minimally manipulated:* Processing that does alter the relevant biological characteristics of cells or tissues.
>
> *Unmanipulated haematopoietic progenitor cells*: HPC as obtained at the time of collection and not subjected to any form of manipulation.

Manufacturing: Includes, but is not limited to, any or all steps in the recovery, processing, packaging, labelling, storage, or distribution of any human cellular or tissue-based product, and the screening and testing of a cell or tissue donor.

Microbial: Related to infectious agents including bacterial and fungal organisms.

Mid-Level Practitioner: Physician Assistant, Nurse Practitioner or other Advanced Practitioner who provides primary patient care with physician oversight.

Negative Selection: The manipulation of a cellular therapy product such that a specific cell population(s) is depleted.

Nurse Practitioner: A nurse with a graduate degree in advanced practice nursing providing patient services in defined areas of practice in collaboration with other health professionals.

New Patient: For purposes of these Standards, a New Patient refers to an individual undergoing the specified type (autologous, syngeneic, or allogeneic) of transplantation for the first time in the Clinical Programme whether or not that patient was previously treated by that Clinical Programme.

Outcome analysis: The process by which the results of a therapeutic procedure are formally assessed.

Partial label: The minimum essential elements that must be affixed to all cellular therapy product containers.

Physician Assistant: A person formally trained to provide diagnostic, therapeutic, and preventive health care services with physician supervision.

Policies: Documents that define the scope of an organization, explain how the goals of

the organization will be achieved, and/or serve as a means by which authority can be delegated.

Positive selection: The manipulation of a cellular therapy product such that a specific cell population(s) is enriched.

Potency: The therapeutic activity of a product as indicated by appropriate laboratory tests or adequately developed and controlled clinical data.

Preventive Action: Action taken to eliminate the cause of a potential discrepancy or other undesirable situation to prevent such an occurrence.

Procedure: A document that describes in detail, the process or chronological steps taken to accomplish a specific task; a procedure is more specific than a policy.

Process: A goal-directed, interrelated series of actions, events, or steps.

Process Control: The standardization of processes in order to produce predictable output.

Process development: The series of procedures performed in order to develop a final process that achieves the required results.

Processing: All aspects of manipulation, cryopreservation, packaging, and labelling of cellular therapy products regardless of source, including microbial testing, preparation for infusion or storage, and removal from storage. Processing does not include collection, donor screening, donor testing, storage, or distribution.

Processing Facility: A location where cellular therapy product processing activities are performed in support of the Clinical Programme. A Processing Facility may be part of the same institution as the Clinical Programme or may be part of another institution and perform these functions through contractual agreement.

Product sample: A quantity of product removed from the cellular therapy product.

*Products**:

The proper name of each product is as follows:
HPC, Apheresis: Haematopoietic Progenitor Cells obtained from a mobilized donor by an automated apheresis procedure.

HPC, Cord Blood: Haematopoietic Progenitor Cells obtained from umbilical cord and/or placental blood at the time of delivery.

HPC, Marrow: Haematopoietic Progenitor Cells aspirated from the iliac crests, sternum, or other bones of an autologous or allogeneic donor.

HPC, Whole Blood: Whole Blood collected for HPC contained within it.

TC, Apheresis: Nucleated cells obtained by an apheresis procedure intended for therapeutic use other than as HPC.

TC, Cord Blood: Nucleated cells collected from umbilical cord and/or placental

blood intended for therapeutic use other than as HPC.

TC, Marrow: Nucleated cells collected from bone marrow intended for therapeutic use other than as HPC.

TC, Whole Blood: Nucleated cells collected from whole blood intended for therapeutic use other than as HPC.

TC-T Cells: A therapeutic cell product from any source containing a quantified T lymphocyte population.

TC-Cytotoxic Lymphocytes: A therapeutic cell product containing an enriched preparation of Cytotoxic Lymphocytes.

TC-T Reg Cells: A therapeutic cell product containing an enriched population of regulatory T lymphocytes.

TC-DC: A therapeutic cell product containing dendritic cells prepared for therapeutic use.

TC-NK Cells: A therapeutic cell product containing an enriched preparation of Natural Killer Cells.

TC-Tumour Derived: A product containing malignant cells or elements derived from them.

TC-MSC: A therapeutic product containing mesenchymal stromal cells isolated by suitable technologies, expanded, and processed for therapeutic use.

**ISBT 128* official product nomenclature will be adopted when finalized.

*Product modifications**:

B-Cell Reduced: Cells processed by negative selection for B lymphocytes.

Buffy Coat Enriched: Cells remaining after removal of a portion of the mature erythrocytes and plasma by centrifugation and/or sedimentation using devices, supplies, and techniques validated for the procedure(s).

CD34-Enriched: Cells processed by positive selection for CD34-antigen bearing cells.

Cryopreserved: Cells frozen using devices, supplies, and techniques validated to maintain viability.

Density Enriched: Cells remaining after depletion of mature erythrocytes, polymorphonuclear leukocytes, and plasma by techniques using defined density gradient medium and devices and reagents validated for the separation of cells based on density.

Ex Vivo Expanded: Cells that have been cultured in vitro for the purpose of producing and/or enriching for a specific functional subset.

Gene-Manipulated: Cells that have been processed to alter their own genes or introduce new genetic material.

Plasma and RBC Reduced: Cells remaining after removal of a portion of the mature erythrocytes and plasma by sedimentation and/or centrifugation, using devices, supplies, and techniques validated for the process.

Plasma Reduced: Cells remaining after removal of a portion of the plasma by sedimentation and/or centrifugation using devices, supplies, and techniques validated for the procedure(s).

RBC Reduced: Cells remaining after removal of a portion of the mature erythrocytes by sedimentation, centrifugation, or lysis using devices, supplies, and techniques validated for the procedure(s).

T-Cell Depleted: Cells processed by negative selection for T lymphocytes.

Tumour Cell Depleted: Cells processed by negative selection for tumour cells.

**ISBT 128* official product nomenclature will be adopted when finalized.

Proficiency test: A test to ensure the adequacy of testing methods and equipment and the competency of personnel performing testing.

Protocol: A written document describing steps of a treatment or experimental procedure in sufficient detail such that the treatment or procedure can be reproduced repeatedly without variation.

Purity: Relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product.

Qualification: The establishment of confidence that processes, equipment, and reagents function consistently within established limits.

Quality: Conformance of a product or process with pre-established specifications or standards.

Quality assurance: The actions, planned and performed, to provide confidence that all systems and elements that influence the quality of the product or service are working as expected individually and collectively.

Quality assessment: The actions, planned and performed, to evaluate all systems and elements that influence the quality of the product or service.

Quality audit: A documented, independent inspection and review of a facility's activities. The purpose of a quality audit is to verify, by examination and evaluation of objective evidence, the degree of compliance with those aspects of the quality programme under review.

Quality control: A component of a quality management programme that includes the

activities and controls used to determine the accuracy and reliability of the establishment's personnel, equipment, reagents, and operations in the manufacturing of cellular therapy products, including testing and product release.

Quality improvement: The actions, planned and performed, to develop a system to review and improve the quality of a product or process.

Quality management: An integrated programme of quality assessment, assurance, control, and improvement.

Quality management plan: A written document that describes the systems in place to implement the quality management programme.

Quality management programme: An organization's comprehensive system of quality assessment, assurance, control, and improvement. A quality management programme is designed to prevent, detect, and correct deficiencies that may adversely affect the quality of the cellular therapy product or increase the risk of communicable disease introduction or transmission.

Quarantine: The identification or storage of a cellular therapy product in a physically separate area clearly identified for such use, or through use of other procedures such as automated designation to prevent improper release of that product. Also refers to segregated storage of products known to contain infectious disease agents to reduce the likelihood of cross-contamination.

Release: Removal of a product from quarantine or in-process status for distribution.

Responsible person: A person who is authorized to perform designated functions for which he or she is trained and qualified.

Safety: Relative freedom from harmful effects to persons or products.

Standard Operating Procedures Manual: A compilation of written detailed instructions required to perform procedures.

Standards: The current edition of the *International Standards for Cellular Therapy Product Collection, Processing, and Administration* published by FACT-JACIE.

Storage: Holding a cellular therapy product for future processing and/or distribution.

Syngeneic: Cellular therapy product collected from a donor and intended for infusion into a genetically identical twin.

Therapeutic cells (TC): Nucleated cells from any source (marrow, peripheral blood, or umbilical cord and or placental blood) intended for therapeutic use other than as HPC.

Time of collection: The time of day at the end of the cellular therapy product collection procedure.

Trace: To follow the history of a process, product, or service by review of documents.

Track: To follow a process or product from beginning to end.

Transplantation: The infusion of autologous, syngeneic, or allogeneic HPC with the intent of providing transient or permanent engraftment in support of therapy of disease.

Unique: Being the only one of its kind or having only one use or purpose.

Unique Identifier: A numeric or alphanumeric sequence used to designate a given cellular therapy product with reasonable confidence that it will not be used for another purpose.

Urgent medical need: A situation in which no comparable cellular therapy product is available and the recipient is likely to suffer death or serious morbidity without the cellular therapy product.

Validation: Confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled. A process is validated by establishing, by objective evidence, that the process consistently produces a cellular therapy product meeting its predetermined specifications.

Variance: A planned deviation from recommended practice or standard operating procedure.

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

Viability: Living cells as defined by dye exclusion, flow cytometry, or progenitor cell culture.

PART B: CLINICAL PROGRAMME STANDARDS

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PART B: CLINICAL PROGRAMME STANDARDS

B1. GENERAL

B1.1 The Clinical Transplantation Programme "Clinical Programme" consists of an integrated medical team housed in geographically contiguous or proximate space with a single Clinical Programme Director and common staff training programs, protocols, and quality management systems. The Clinical Programme shall use haematopoietic cell collection and processing facilities that meet FACT-JACIE Standards with respect to their interactions with the Clinical Programme. Clinical Programs that include non-contiguous institutions in the same metropolitan area shall demonstrate common protocols, staff training procedures, quality management systems, and review of clinical results and evidence of regular interaction. Several clinical sites, particularly with different Directors, or outside a single metropolitan area, joining together for the purpose of meeting criteria to qualify as a Clinical Programme do not fulfil the intent of these Standards.

B1.1.1 A Clinical Programme may have more than one clinical site in different hospitals if the other criteria in B1.1 are met.

B1.2 The Clinical Programme shall abide by all applicable governmental laws and regulations.

B1.3 If the Clinical Programme requests accreditation for allogeneic transplantation, a minimum of ten (10) new allogeneic patients shall have been transplanted during the twelve month period immediately preceding the application for programme accreditation and annually thereafter. A Clinical Programme that is accredited for allogeneic transplantation will be considered to have met the numeric requirement for autologous transplantation.

B1.3.1 For Clinical Programs utilizing more than one clinical site and requesting accreditation for allogeneic transplant, a minimum of five (5) new allogeneic patients shall have been transplanted at each site during the twelve month period immediately preceding the application and annually thereafter. A site that is accredited for allogeneic transplantation will be considered to have met the numeric requirement for autologous transplantation.

B1.3.2 For a combined Clinical Programme caring for paediatric and adult patients on the same site, Clinical Programs shall perform five (5) allogeneic transplants for each population.

B1.4 If the Clinical Programme requests accreditation for only autologous transplant, a minimum of five (5) new recipients of autologous transplant shall have been transplanted during the twelve month period immediately preceding the application for accreditation and annually thereafter at each site.

B2. CLINICAL UNIT

B2.1 There shall be a designated inpatient unit that minimizes airborne microbial contamination.

B2.2 The Clinical Programme's inpatient unit shall be located in a facility accredited by the Joint Commission on Accreditation of Healthcare Organizations or equivalent, if applicable.

B2.3 There shall be a designated area for outpatient care that reasonably protects the patient from transmission of infectious agents and allows, as necessary, for appropriate patient isolation, and administration of intravenous fluids, medications, and/or blood products.

B2.4 The following shall apply to both inpatient and outpatient care:

B2.4.1 There shall be provisions for prompt evaluation and treatment by a transplant attending physician available on a 24-hour basis.

B2.4.2 There shall be an adequate number of nurses experienced in the care of transplant patients.

B2.4.3 There shall be a nurse/patient ratio satisfactory to cover the severity of the patients' clinical status.

B2.4.4 There shall be a pharmacy providing 24-hour availability of medications needed for the care of transplant patients.

B2.4.5 There shall be the ability to perform dialysis under the direction of Nephrologists and trained personnel.

B2.4.6 There shall be a transfusion service providing 24-hour availability of CMV appropriate and irradiated blood products needed for the care of transplant patients.

B2.4.7 There shall be immediate access to an intensive care unit or equivalent coverage for critically ill patients.

B2.4.8 Clinical Programs performing allogeneic haematopoietic cell transplants shall use HLA testing laboratories accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or equivalent, with the capability of carrying out deoxyribonucleic acid (DNA) - based HLA-typing.

B2.5 SAFETY REQUIREMENTS

B2.5.1 The Clinical Programme shall be operated in a manner to minimize risks to the health and safety of employees, patients, donors, visitors, and volunteers.

B2.5.2 The Clinical Programme shall include instructions for action in case of exposure to communicable disease or to chemical, biologic, or radiological hazards in its safety manual.

B2.5.3 The Clinical Programme shall dispose of medical waste in a manner that minimizes any hazard to facility personnel and to the environment in accordance with applicable governmental laws and regulations.

B2.5.4 The Clinical Programme shall ensure that the Clinical Units are operated in a clean, sanitary, and orderly manner.

B2.5.5 Gloves shall be worn while handling biological specimens.

B3. PERSONNEL

B3.1 CLINICAL TRANSPLANT TEAM

B3.1.1 A dedicated transplant team including a Clinical Programme Director and at least one other physician trained and/or experienced in cell therapy shall have been in place for at least twelve (12) months prior to being eligible for initial accreditation.

B3.1.2 Clinical Programs performing paediatric transplantation shall have a transplant team trained in the management of paediatric patients.

B3.1.3 Clinical Programs performing paediatric transplantation shall have at least one attending physician who is board certified/eligible (or non-U.S. equivalent) in Paediatric Hematology/Oncology or Paediatric Immunology.

B3.1.4 For Clinical Programs performing adult transplantation, there shall be at least one attending physician who is board certified/eligible (or non-U.S. equivalent) in Hematology, Medical Oncology, or Immunology.

B3.1.5 The Clinical Programme shall have access to licensed physicians who are trained and competent in bone marrow harvesting and a bone marrow collection facility that meets FACT-JACIE Standards.

B3.1.6 The Clinical Programme shall have access to personnel who are trained and competent in cellular product collection by apheresis and an apheresis facility that meets FACT-JACIE Standards.

B3.2 CLINICAL PROGRAMME DIRECTOR

B3.2.1 The Clinical Programme Director shall be appropriately licensed to practice medicine in the jurisdiction in which the programme is located and board certified (or non-U.S. equivalent) in one or more of the following specialties: Hematology, Medical Oncology, Adult or Paediatric Immunology, or Paediatric Hematology/ Oncology. Non-board certified physicians who completed medical training prior to 1985 may serve as Clinical Programme Director if they have documented experience and published contributions in the field of haematopoietic cell transplantation extending over ten (10) years.

B3.2.2 The Clinical Programme Director shall have at least one year of specific clinical training in HPC transplantation as defined in B3.4, or two (2) years experience as an attending physician responsible for the clinical management of HPC transplant patients in the inpatient and outpatient settings. The Clinical Programme Director shall have written confirmation of his/her training or experience from the Director of the Clinical Programme, department, or institution in which that training or experience was obtained.

B3.2.3 The Clinical Programme Director shall be responsible for administrative and clinical operations, including compliance with these Standards.

B3.2.4 The Clinical Programme Director shall have oversight of all elements of the design of the Clinical Programme including quality management, the selection and care of patients and donors, cell collection, and processing, whether internal or contracted services.

B3.2.5 The Clinical Programme Director shall have oversight of the medical care provided by the Clinical Programme including medical care provided by the physicians on the transplant team. The Clinical Programme Director is responsible for verifying the knowledge and skills of the physicians of the transplant team. Management of the Clinical Unit may be delegated to a Medical Director who fulfils the requirements in B3.3.

B3.2.6 The Clinical Programme Director shall participate regularly in educational activities related to the field of HPC transplantation.

B3.3 ATTENDING PHYSICIANS

B3.3.1 Clinical Programme attending physicians shall be appropriately licensed to practice medicine in the jurisdiction of the Clinical Programme and should be board certified or eligible (or non-U.S. equivalent) in one of the specialties listed in B3.2.1.

B3.3.2 Clinical Programme attending physicians shall have specific clinical training in HPC transplant medicine as defined in B3.4.

B3.3.3 Clinical Programme attending physicians shall participate regularly in educational activities related to the field of HPC transplantation.

B3.4 TRAINING FOR CLINICAL PROGRAMME DIRECTORS AND ATTENDING PHYSICIANS

B3.4.1 Adequate specific clinical training in HPC transplant medicine shall be defined as a minimum of a one year experience in the management of transplant patients in both inpatient and outpatient settings.

B3.4.2 Clinical Programs transplanting paediatric patients shall have physicians experienced in treating paediatric patients as defined in B3.1.3.

B3.4.3 Clinical training and competency shall include the management of:

B3.4.3.1 Autologous transplant patients for physicians in Clinical Programs requesting accreditation for autologous transplantation.

B3.4.3.2 Allogeneic transplant patients for physicians in Clinical Programs requesting accreditation for allogeneic transplantation.

B3.4.3.3 Both autologous and allogeneic transplant patients for physicians in Clinical Programs requesting accreditation for autologous and allogeneic transplantation.

B3.4.4 Physicians in Clinical Programs requesting accreditation for autologous and/or allogeneic transplantation shall have specific training and competency in each of the following areas:

B3.4.4.1 Indications for HPC transplantation

B3.4.4.2 Selection of appropriate patients and preparative high dose therapy regimens

B3.4.4.3 Pre-transplant patient evaluation, including assessment of appropriate patient eligibility and HPC adequacy with respect to collection

B3.4.4.4 Administration of high-dose therapy

B3.4.4.5 Administration of growth factors for HPC mobilization and for post-transplant haematopoietic cell reconstitution

B3.4.4.6 Management of neutropenic fever

B3.4.4.7 Diagnosis and management of infectious and non-infectious pulmonary complications of transplantation

B3.4.4.8 Diagnosis and management of fungal disease

B3.4.4.9 Diagnosis and management of veno-occlusive disease of the liver

B3.4.4.10 Management of thrombocytopenia and bleeding

B3.4.4.11 Management of hemorrhagic cystitis

B3.4.4.12 Management of nausea and vomiting

B3.4.4.13 Management of pain

B3.4.4.14 Management of terminal care patients

B3.4.4.15 Documentation and reporting for patients on investigational protocols

B3.4.4.16 Diagnosis and management of HPC graft failure

B3.4.5 Specific clinical training and competency in each of the following additional areas required for physicians in Clinical Programs requesting accreditation for allogeneic haematopoietic cell transplantation shall include:

B3.4.5.1 Identification and selection of HPC source, including use of donor registries

B3.4.5.2 Methodology and implications of human leukocyte antigen (HLA) typing

B3.4.5.3 Management of patients receiving ABO incompatible HPC products

B3.4.5.4 Diagnosis and management of cytomegalovirus (CMV) infection and disease

B3.4.5.5 Diagnosis and management of other viral infections in immunocompromised hosts

B3.4.5.6 Diagnosis and management of acute and chronic graft versus host disease

B3.4.5.7 Diagnosis and management of post-transplant immunodeficiencies.

B3.4.5.8 Evaluation of chimerism

B3.4.6 The HPC transplant physicians shall be proficient in the HPC product infusion.

B3.4.7 The HPC transplant physicians shall be knowledgeable in the following procedures:

B3.4.7.1 HPC processing

B3.4.7.2 HPC cryopreservation

B3.4.7.3 Bone marrow harvest procedures

B3.4.7.4 Apheresis procedures

B3.5 MID-LEVEL PRACTITIONERS (Physician Assistants, Nurse Practitioners, Advanced Practitioner)

B3.5.1 Mid-level practitioners shall be licensed to practice in the jurisdiction of the Clinical Programme and shall be limited to scope of practice of license and within parameters of their training.

B3.5.2 Mid-level practitioners shall be trained and competent specifically in the transplant-related cognitive and procedural skills that they routinely practice. These skills may include but are not limited to those listed in B3.4.3 - B3.4.5.

B3.5.3 Mid-level practitioners shall participate regularly in educational activities related to the field of HPC transplantation.

B3.6 CONSULTING PHYSICIANS

B3.6.1 The Clinical Programme shall have access to board certified/eligible (or non-U.S. equivalent) consulting physicians from key disciplines who are capable of assisting in the management of patients requiring medical care, including but not limited to:

B3.6.1.1 Surgery

B3.6.1.2 Pulmonary medicine

B3.6.1.3 Intensive care

B3.6.1.4 Gastroenterology

B3.6.1.5 Nephrology

B3.6.1.6 Infectious disease

B3.6.1.7 Cardiology

B3.6.1.8 Pathology

B3.6.1.9 Psychiatry

B3.6.1.10 Radiation oncology with experience in large-field (e.g., total body or total lymphoid) irradiation treatment protocols, if radiation therapy is administered.

B3.6.2 A Clinical Programme treating paediatric patients shall have consultants, as defined in B3.6.1, qualified to manage paediatric patients.

B3.7 NURSES

B3.7.1 The Clinical Programme shall have nurses and nurse supervisors formally trained and experienced in the management of patients receiving HPC transplants.

B3.7.2 A Clinical Programme treating paediatric patients shall have nurses formally trained and experienced in the management of paediatric patients.

B3.7.3 Training shall include hematology/oncology patient care; administration of high-dose therapy, growth factors, and immunosuppressive medications; management of infectious complications associated with compromised host defence mechanisms; administration of blood products; and an appropriate degree of intensive medical/paediatric nursing care.

B3.7.4 There shall be written policies for all relevant nursing procedures, including, but not limited to, infection prevention and control, administration of the preparative regimen, transplantation of HPC, central venous catheter care, blood product transfusion, and transplant nurse competency evaluation process.

B3.8 SUPPORT SERVICES STAFF

B3.8.1 The Clinical Programme shall have one or more designated staff to assist in the provision of appropriate pre-transplant patient evaluation, treatment, and post-transplant follow-up and care.

B3.8.2 The Clinical Programme shall have pharmacy staff knowledgeable in the use and monitoring of pharmaceuticals used by the Clinical Programme.

B3.8.3 The Clinical Programme shall have dietary staff capable of providing dietary consultation regarding the nutritional needs of the transplant recipient, including enteral and parenteral support, and appropriate dietary advice to avoid food-borne illness.

B3.8.4 There shall be appropriate Social Services staff.

B3.8.5 There shall be appropriate Physical Therapy staff.

B3.8.6 There shall be Data Management staff sufficient to comply with Section B9.

B4. QUALITY MANAGEMENT

B4.1 The Clinical Programme shall have a written Quality Management Plan that addresses, at a minimum:

B4.1.1 Organisational structure

B4.1.2 Process development and review

B4.1.3 Personnel qualifications, training, and competency

B4.1.4 Agreements

B4.1.5 Outcome analysis

B4.1.6 Audits

B4.1.7 Management of cellular therapy products with positive microbial culture results

B4.1.8 Detection and reporting of errors, accidents, and adverse events

B4.1.9 Record review and document control

B4.1.10 Product tracking

B4.2 The Clinical Programme Director shall be responsible for the Quality Management Plan as it pertains to the Clinical Programme. The performance of this activity may be delegated to a designated individual(s) with appropriate training, knowledge, and expertise.

B4.2.1 The designated individual(s) shall have authority over and responsibility for ensuring that the Quality Management Plan is effectively established and maintained.

B4.2.2 The designated individual(s) shall not have oversight of his/her own work if this person also performs other tasks in the Clinical Programme.

B4.2.3 The designated individual(s) shall report on quality management activities, at a minimum, quarterly.

B4.2.3.1 The results of Quality Management activities shall be reviewed and approved by the Clinical Programme Director.

B4.2.4 The designated individual(s) shall provide a report on the performance of the Quality Management Plan, at a minimum, annually to the Clinical Programme Director.

B4.2.5 There shall be an overall Clinical Programme Quality Management Programme that incorporates the information from clinical, collection, and processing facility quality management.

B4.3 The Quality Management Plan shall include an organisational chart of key personnel and functions within the Clinical Programme.

B4.3.1 The Quality Management Plan shall include a description of how these key personnel interact to implement the quality management activities.

B4.4 The Quality Management Plan shall include policies and procedures for development and implementation of written agreements with third parties whose services impact the cellular therapy product.

B4.5 The Quality Management Plan shall include methods for process development, approval, implementation, review, revision, and archiving for all critical processes, policies, and procedures.

B4.5.1 There shall be a defined process improvement plan that includes policies or procedures for the recognition and investigation of the cause of all issues that require corrective and preventive action.

B4.6 The Quality Management Plan shall include personnel requirements for each key position in the Clinical Programme. Personnel requirements shall include at a minimum:

B4.6.1 A system to document the following for all medical, nursing, and pharmacy staff:

B4.6.1.1 Initial qualifications and training

B4.6.1.2 Annual performance review

B4.6.1.3 Provisions for continuing education

B4.7 The Quality Management Plan shall include a process for documentation and review of outcome analysis and product efficacy, as appropriate, including at least:

B4.7.1 For HPC products, a process for documentation and review of time to engraftment following product administration.

B4.8 The Quality Management Plan shall include a process and timetable for conducting independent quality audits of the Programme's activities to verify compliance with elements of the Quality Management Programme.

B4.8.1 Audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not solely responsible for the process being audited.

B4.8.2 Audit results shall be reviewed, reported, and documented, at a minimum, on a quarterly basis.

B4.8.3 The results of audits shall be used to recognize problems, detect trends, and identify improvement opportunities.

B4.9 The Quality Management Plan shall include policies and procedures on the management of cellular therapy products with positive microbial culture results that address at a minimum:

B4.9.1 Documentation and product labelling.

B4.9.2 Release of the product from the distribution facility, including identification of authorized individuals and criteria for product release.

B4.9.3 Investigation of cause.

B4.9.4 Notification of transplant physician, Collection Facility and/or Cell Processing Facility as applicable.

B4.9.5 Notification of the recipient prior to infusion.

B4.9.6 Recipient follow-up and outcome analysis.

B4.9.7 Follow-up of the donor, if relevant.

B4.9.8 Reporting to regulatory agencies if appropriate.

B4.10 The Quality Management Plan shall include a system for detecting, evaluating, documenting, and reporting errors, accidents, suspected adverse events, biological product deviations, and complaints.

B4.10.1 Documentation of each adverse event that occurs in the Clinical Programme shall be reviewed by the Clinical Programme Director as appropriate.

B4.10.2 Adverse events in the Clinical Programme shall be documented in a manner that complies with institutional requirements and applicable governmental laws and regulations.

B4.10.3 Deviations from key Standard Operating Procedures (B5.1.1, B5.1.7, B5.1.8) shall be documented.

B4.10.3.1 Planned deviations shall be pre-approved by the Clinical Programme Director or designee.

B4.10.3.2 Unplanned deviations and associated corrective actions shall be reviewed by the Clinical Programme Director or designee.

B4.10.4 Corrective actions shall be implemented, as appropriate.

B4.10.5 Effectiveness of corrective actions shall be verified.

B4.10.6 A written description of adverse events shall be made available to the recipient's and/or donor's physician and the collection and processing facilities, if appropriate.

B4.10.7 When applicable, the event shall be reported to the appropriate regulatory agencies.

B4.10.8 There shall be policies and procedures to document and follow up customer-reported product failures, concerns, or complaints.

B4.11 The Quality Management Plan shall include a mechanism for document control and for the regular review of records relating to HPC transplantation and cellular product infusion. The document control system shall include at a minimum the following elements:

B4.11.1 Definition and current listing of all critical documents that must adhere to the document control system requirements.

B4.11.2 Assignment of a numeric or alphanumeric identifier to each document regulated within the system.

B4.11.3 A procedure for document approval, including the approval date, signature of approving individual(s), and the effective date.

B4.11.4 A system to ensure that controlled documents cannot undergo accidental or unauthorized modification.

B4.11.5 A system for documentation of training associated with each procedure and its revisions.

B4.11.6 A system for document change control that includes a description of the change, the signature of approving individual(s), approval, date, and effective date.

B4.11.7 A system for the retraction of obsolete documents to prevent unintended use.

B4.11.7.1 Obsolete documents shall be archived for a minimum of ten (10) years.

B4.11.8 A system for record creation, assembly, storage, archival, and retrieval.

B4.12 The Quality Management Plan shall include a process for product tracking that allows tracking from the donor to the recipient or final distribution and from the recipient, or final disposition, to the donor.

B4.13 The Quality Management Plan shall include a mechanism to ensure continuous operations in the event that the Clinical Programme's computer system ceases to function, including a plan for data backup and a mechanism to ensure compliance with applicable laws.

B5. POLICIES AND PROCEDURES

B5.1 The Clinical Programme shall have documented policies and procedures addressing all appropriate aspects of operations and management including, at a minimum:

B5.1.1 Donor and patient evaluation, selection, and treatment

B5.1.2 Donor consent

B5.1.3 Patient consent

B5.1.4 Emergency and safety procedures

B5.1.5 Donor and patient confidentiality

B5.1.6 Infection prevention and control

B5.1.7 Administration of the preparative regimen

B5.1.8 Transplantation of haematopoietic progenitor cells

B5.1.9 Blood product transfusion

B5.1.10 Quality management and improvement

B5.1.11 Errors, accidents, and adverse events

B5.1.12 Biological product deviations

B5.1.13 Corrective actions

B5.1.14 Personnel training

B5.1.15 Competency assessment

B5.1.16 Outcome analysis

B5.1.17 Audits

B5.1.18 Facility maintenance and monitoring

B5.1.19 Disposal of medical and biohazard waste

B5.1.20 Disaster response

B5.2 The Clinical Programme shall maintain a detailed Standard Operating Procedures Manual. The Standard Operating Procedures Manual shall include:

B5.2.1 A procedure for preparation, approval, implementation, review, and revising all procedures.

B5.2.2 A standardized format for procedures, including worksheets, reports, and forms.

B5.2.3 A system of numbering and/or titling of individual procedures, policies, worksheets, and forms.

B5.3 Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual procedure shall include:

B5.3.1 A clearly written description of the objectives of the procedure.

B5.3.2 A description of equipment and supplies used.

B5.3.3 Acceptable end-points and the range of expected results, where applicable.

B5.3.4 A stepwise description of the procedure, including diagrams and tables as needed.

B5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

B5.3.6 A reference section listing appropriate literature.

B5.3.7 Documented approval of each procedure and procedural modification by the Clinical Programme Director or designated physician prior to implementation and annually thereafter.

B5.3.8 Copies of current versions of orders, worksheets, reports, labels, and forms, where applicable.

B5.4 Copies of the Standard Operating Procedures Manual shall be readily available to the facility staff at all times.

B5.5 All personnel in the facility shall follow the Standard Operating Procedures.

B5.6 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.

B5.7 Archived policies and procedures, the inclusive dates of use, and their historical sequence shall be maintained for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

B5.8 All Standard Operating Procedures shall comply with these Standards and all applicable governmental regulations.

B5.9 There shall be a process to address age specific issues in the Standard Operating Procedures, as appropriate.

B6. DONOR SELECTION, EVALUATION, AND MANAGEMENT

B6.1 There shall be written criteria for donor selection, evaluation, and management by trained medical personnel.

B6.2 There shall be donor evaluation procedures in place to protect the safety of the cellular product donor.

B6.2.1 The donor shall be evaluated for potential risks of the collection procedure, including:

B6.2.1.1 Possible need for central venous access and/or mobilization therapy for collection of peripheral blood cells.

B6.2.1.2 Anaesthesia for collection of marrow.

B6.2.2 The risk of donation and informed consent shall be documented.

B6.2.3 The use of a donor who does not meet the Clinical Programme donor safety criteria shall require documentation of the rationale for his/her selection by the transplant physician.

B6.2.4 Issues of donor health that pertain to the safety of the collection procedure shall be communicated in writing to the Collection Facility staff.

B6.3 There shall be donor evaluation procedures in place to protect the recipient from the risk of disease transmission from the donor.

B6.3.1 There shall be procedures for all steps in screening, testing, and determining donor eligibility, and for all regulatory requirements related to cellular therapy donors.

B6.3.2 Within thirty (30) days prior to collection, all HPC donors shall be tested for evidence of clinically relevant infection by the following communicable disease agents:

B6.3.2.1 Human immunodeficiency virus, type 1

B6.3.2.2 Human immunodeficiency virus, type 2

B6.3.2.3 Hepatitis B virus

B6.3.2.4 Hepatitis C virus

B6.3.2.5 Human T-cell lymphotropic virus I (per governmental regulations)

B6.3.2.6 Human T-cell lymphotropic virus II (per governmental regulations)

B6.3.2.7 Treponema pallidum (syphilis)

B6.3.3 Additional tests shall be performed as required to assess the possibility of transmission of other infectious or non-infectious diseases.

B6.3.4 For viable, lymphocyte rich cells, including therapeutic cells, each donor shall be tested for communicable disease agents listed in section B6.3.2 within seven (7) days prior to or after collection, or in accordance with applicable governmental regulations.

B6.4 Any abnormal findings shall be reported to the prospective donor with documentation in the donor record of recommendations made for follow-up care.

B6.5 All donors shall be tested for ABO group and Rh type.

B6.5.1 Allogeneic donors shall be tested for ABO group and Rh type on each day of collection.

B6.5.2 Autologous donors shall be tested for ABO group and Rh type at least on the first day of collection.

B6.6 A pregnancy assessment shall be performed for all female donors of childbearing potential within seven (7) days prior to initiation of recipient's conditioning regimen or of donor starting mobilization regimen.

B6.7 Laboratory testing on all donors shall be performed by a laboratory credited or licensed in accordance with applicable U.S. or non U.S. equivalent regulations using one or more donor screening tests approved or cleared by the FDA or non- U.S. equivalent.

B6.8 ALLOGENEIC DONORS

B6.8.1 In addition to laboratory testing for relevant communicable disease agents as defined in B6.3.2, allogeneic donors shall be evaluated for risk factors for disease transmission by medical history, examination of relevant medical records, and physical examination.

B6.8.2 The medical history shall include at least the following:

B6.8.2.1 Vaccination history

B6.8.2.2 Travel history

B6.8.2.3 Blood transfusion history

B6.8.2.4 Questions to identify persons at high risk for transmission of communicable disease as defined by the FDA or non-U.S. equivalent

B6.8.2.5 Questions to identify persons at risk of transmitting inherited conditions

B6.8.2.6 Questions to identify persons at risk of transmitting a haematological or immunological disease

B6.8.2.7 Questions to identify a past history of malignant disease

B6.8.3 Allogeneic donors shall be tested for Cytomegalovirus (unless previously documented to be positive).

B6.8.4 Allogeneic donors shall be tested at a minimum for HLA-A, B, DR type by a laboratory accredited by ASHI, EFI, or an affiliate.

B6.8.5 Allogeneic donors shall be tested for red cell compatibility where appropriate.

B6.8.6 Allogeneic donor eligibility, as defined by FDA donor eligibility regulation or non-U.S. equivalent governmental regulation, shall be determined by a physician and shall be documented in the recipient's medical record before the recipient's high dose therapy is initiated and before the donor is mobilized.

B6.8.7 The use of an ineligible allogeneic donor shall require an urgent medical need documentation, including the rationale for his/her selection and suitability by the transplant physician, and the documented informed consent of the donor and the recipient.

B6.8.8 Allogeneic donor eligibility and suitability shall be communicated in writing to the collection and cell processing facilities.

B6.8.9 The donor shall confirm that all the information provided is true to the best of his/her knowledge.

B6.9 DONOR CONSENT

B6.9.1 The collection procedure shall be explained in terms the donor can understand, and shall include information about:

B6.9.1.1 The significant risks and benefits of the procedure

B6.9.1.2 Tests performed to protect the health of the donor and recipient

B6.9.1.3 The rights of the donor to review the results of such tests

B6.9.1.4 Alternatives to donation

B6.9.1.5 Alternative modalities of donation.

B6.9.2 The donor shall have an opportunity to ask questions and the right to refuse to donate.

B6.9.3 Informed consent from the donor shall be obtained and documented by a licensed physician or other health care provider familiar with the collection procedure.

B6.9.4 In the case of a minor donor, informed consent shall be obtained from the donor's parents or legal guardian in accord with applicable law and shall be documented.

B6.9.5 The allogeneic donor shall give informed consent and authorization in advance to release the donor's health information to the transplant physician and recipient as appropriate

B6.9.6 Documentation of consent shall be available to the Collection Facility staff prior to the collection procedure.

B7. THERAPY ADMINISTRATION

B7.1 There shall be a written policy to ensure that the preparative regimen is administered safely.

B7.1.1 There shall be a written policy to ensure that chemotherapy is administered safely.

B7.1.1.1 The treatment orders shall include the patient height and weight, specific dates, daily doses (if appropriate), and route of each agent.

B7.1.1.2 Pre-printed orders or electronic equivalent should be used for protocols and standardized regimens.

B7.1.1.3 The pharmacist preparing the chemotherapy shall verify the doses against the protocol or standardized regimen listed on the orders.

B7.1.1.4 Prior to administration of chemotherapy, two (2) persons qualified to administer chemotherapy shall verify the drug and dose in the bag or pill against the orders and the protocol, and the identity of the patient to receive the chemotherapy.

B7.1.2 There shall be a written policy to ensure that radiotherapy is administered safely.

B7.1.2.1 There shall be a written request for radiotherapy including details of diagnosis, any prior radiotherapy that the patient has received, and any other factors that may increase the toxicity of radiotherapy.

B7.1.2.2 There shall be a consultation with a radiation therapist prior to initiation of therapy. The consult should include radiotherapy planning.

B7.1.2.3 Prior to administration of each dose of radiotherapy treatment, dose should be verified and documented as per radiation therapy standards.

B7.1.2.4 A final report of the radiotherapy details administered should be filed in the patient's records.

B7.2 There shall be a written policy to ensure safe administration of haematopoietic cell products.

B7.2.1 Two (2) qualified persons shall verify the identity of the recipient and the product prior to the infusion of the product.

B7.2.1.1 Verification of identity shall be documented.

B7.2.2 There shall be documentation in the patient medical record of the unit identifier and a copy of the distribution record (i.e. product infusion form).

B7.2.3 The Circular of Information for Cellular Therapy Products shall be available to staff.

B8. CLINICAL RESEARCH

B8.1 If required by applicable regulations, Clinical Programs shall have formal review of investigational treatment protocols and patient consent forms by a mechanism that is approved by the Office for Human Research Protections under the Department of Health and Human Services, by the FDA, or by the equivalent agencies outside of the U.S., as applicable.

B8.1.1 Those programs utilizing applicable investigational treatment protocols shall have in place a pharmacy equipped for research activities, including a mechanism for tracking, inventory, and secured storage of investigational drugs.

B8.2 Documentation for all research protocols performed by the Programme, including all audits, documentation of approval by the Institutional Review Board, Ethics Committee or equivalent, correspondence with regulatory agencies, and any adverse outcomes, shall

be maintained in accordance with institutional policies and applicable laws and regulations.

B8.3 For clinical research, informed consent shall be obtained from each research subject or legally authorized representative, in language he or she can understand, and under circumstances that minimize the possibility of coercion or undue influence.

B8.3.1 The research subject shall be given the opportunity to ask questions and to have their questions answered to his/her satisfaction, and to withdraw from the research without prejudice.

B8.3.2 Informed consent for a research subject shall contain at least the following elements and comply with applicable laws and regulations:

B8.3.2.1 An explanation of the research purposes, a description of the procedures to be followed, and the identification of experimental procedures.

B8.3.2.2 The expected duration of the subject's participation.

B8.3.2.3 A description of the reasonably expected risks, discomforts, benefits to the subject or others, and alternative procedures.

B8.3.2.4 A statement of the extent to which confidentiality will be maintained.

B8.3.2.5 An explanation of the extent of compensation for injury.

B8.4 There shall be a mechanism in place to ensure, as appropriate, the financial disclosure of any issues that may represent a conflict of interest in clinical research.

B9. DATA MANAGEMENT[1]

B9.1 The Programme shall collect all the data contained in the Transplant Essential Data Forms of the CIBMTR or the Minimum Essential Data-A forms of the EBMT (See Appendix IV).

B9.2 Each transplant programme shall periodically audit, at a minimum, the following data: patient outcomes, donor screening and testing, and recipient Day 100 treatment related mortality.

B9.2.1 Collection and analysis of data related to the audit shall be reviewed, reported, and documented, at a minimum, on an annual basis.

B10. RECORDS

B10.1 Clinical Programme records related to quality control, personnel training or competency, facility maintenance, facility management, or other general facility issues shall be retained in accordance with applicable laws or regulations, or a defined programme or institution policy, unless otherwise specified in these standards. Not all records need be immediately available.

[1] See Appendix IV for further details

B10.2 Patient and donor records including, but not limited to, consents and records of care, shall be maintained in a confidential manner as required by applicable governmental laws and regulations, but no less than ten (10) years after the administration of the cellular therapy product, or, if not known, ten (10) years after the date of the distribution, disposition, or expiration, whichever is latest.

B10.3 Employee records shall be maintained in a confidential manner and as required by applicable governmental laws and regulations.

B10.4 Research records shall be maintained in a confidential manner as required by applicable governmental laws and regulations, but no less than ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.

B10.5 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

B10.5.1 If two (2) or more facilities participate in the collection, processing, or transplantation of the cellular therapy product, the records of each facility shall show plainly the extent of its responsibility.

B10.5.2 The Clinical Programme shall furnish to other facilities involved in the collection or processing of the cellular therapy product, transplant outcome data in so far as they concern the safety, purity, and potency of the product involved.

PART C: CELLULAR THERAPY PRODUCT COLLECTION STANDARDS

C1 General

C2 Collection Facility

C3 Personnel

C4 Quality Management

C5 Policies and Procedures

C6 Donor Selection, Evaluation, and Management

C7 Labels

C8 Cellular Therapy Product Collection Procedure

C9 Cellular Therapy Product Storage

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PART C: CELLULAR THERAPY PRODUCT COLLECTION STANDARDS

C1. GENERAL

C1.1 These Standards apply to all HPC, Marrow; HPC, Apheresis; and other cellular therapy product collection activities performed within the Collection Facility.

C1.2 The Collection Facility shall abide by all applicable governmental laws and regulations.

C1.3 The Collection Facility, including the Medical Director and at least one staff member, shall have been in place and performing cellular therapy product collections for at least twelve (12) months prior to being eligible for initial accreditation.

C1.3.1 For apheresis collection facilities, a minimum of ten (10) apheresis collection procedures shall have been performed in the twelve (12) months preceding application for accreditation.

C1.3.2 For bone marrow collection facilities, a minimum of one bone marrow collection procedure shall have been performed in the twelve (12) months preceding application for accreditation.

C1.4 For renewal accreditation of apheresis collection facilities, a minimum of thirty (30) apheresis collection procedures shall have been performed within an accreditation cycle.

C1.5 For renewal accreditation of bone marrow collection facilities, a minimum of three (3) bone marrow collection procedures shall have been performed within an accreditation cycle.

C2. COLLECTION FACILITY

C2.1 Where required, the Collection Facility shall be registered with the FDA or non-U.S. equivalent for the activities performed.

C2.2 There shall be appropriate designated areas for collection of cellular therapy products, for the product collected, and for storage of supplies and equipment.

C2.2.1 The Collection Facility shall be divided into defined areas of adequate size to prevent improper labelling, mix-ups, contamination, or cross-contamination of cellular therapy products.

C2.2.2 There shall be suitable and confidential space for donor examination and evaluation.

C2.2.3 There shall be a designated area for appropriate preparation and storage of the reagents and equipment needed for the performance of the collection procedure.

C2.2.4 The Collection Facility shall provide adequate lighting, ventilation, plumbing, drainage, and access to sinks and toilets to prevent the introduction, transmission, or spread of communicable disease.

C2.3 There shall be adequate equipment for the procedures performed at the facility.

C2.4 There shall be a process to control storage areas to prevent mix-ups, contamination, and cross contamination of products during quarantine, prior to release or transport to the Processing Facility, and for non-conforming products.

C2.5 There shall be a transfusion service providing 24-hour availability of CMV appropriate and irradiated blood products.

C2.6 There shall be access to an intensive care unit and/or emergency services.

C2.7 SAFETY REQUIREMENTS

C2.7.1 The Collection Facility shall be operated in a manner to minimize risks to the health and safety of employees, patients, donors, and visitors.

C2.7.2 Instructions for action in case of exposure to communicable disease or to chemical, biologic, or radiological hazards shall be included in the safety manual.

C2.7.3 Medical waste shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment, in accordance with applicable governmental laws and regulations.

C2.7.4 The Collection Facility shall be maintained in a clean, sanitary, and orderly manner.

C2.7.5 Gloves shall be worn while handling biological specimens.

C3. PERSONNEL

C3.1 COLLECTION FACILITY DIRECTOR

C3.1.1 There shall be a Collection Facility Director who is an individual with a medical degree or doctoral degree in a relevant science, qualified by postgraduate training or experience for the scope of activities carried out in the Collection Facility. The Collection Facility Director may also serve as the Collection Facility Medical Director, if appropriately credentialed.

C3.1.2 The Collection Facility Director shall be responsible for all technical procedures, performance of the collection procedure, supervision of staff, and administrative operations of the Collection Facility.

C3.1.3 The Collection Facility Director shall have at least one year experience in the cellular therapy product collection procedure; and shall have performed or supervised at least ten (10) collection procedures of each type (HPC, Apheresis and/or HPC, Marrow) for which the collection facility is requesting accreditation.

C3.1.4 The Collection Facility Director shall participate regularly in educational activities related to cellular therapy product collection and/or transplantation.

C3.2 COLLECTION FACILITY MEDICAL DIRECTOR

C3.2.1 There shall be a Collection Facility Medical Director who is a licensed physician with postgraduate training in cell collection and/or transplantation. The

Collection Facility Medical Director may also serve as the Collection Facility Director, if appropriately credentialed.

C3.2.2 The Collection Facility Medical Director or designee shall be directly responsible for the medical care of patients undergoing apheresis or marrow harvesting, including the pre-collection evaluation of the donor at the time of donation and care of any complications resulting from the collection procedure.

C3.2.3 The Collection Facility Medical Director shall have at least one year experience in cellular therapy product collection procedures, and shall have performed or supervised at least ten (10) such collection procedures of each type (HPC, Apheresis and/or HPC, Marrow) for which the Collection Facility is requesting accreditation.

C3.2.4 The Collection Facility Medical Director shall participate regularly in educational activities related to cellular therapy product collection and/or transplantation.

C3.3 OTHER STAFF

C3.3.1 There shall be adequate numbers of trained support personnel available at the Collection Facility.

C3.4 For Collection Facilities collecting cellular therapy products from paediatric donors, physicians and collection staff shall have documented training and experience in performing these procedures.

C4. QUALITY MANAGEMENT

C4.1 The Collection Facility shall have a written Quality Management Plan that addresses, at a minimum:

C4.1.1 Organisational structure

C4.1.2 Agreements

C4.1.3 Process development and review

C4.1.4 Personnel qualifications, training, and competency

C4.1.5 Outcome analysis

C4.1.6 Audits

C4.1.7 Management of cellular therapy products with positive microbial culture results

C4.1.8 Detection and reporting of errors, accidents, and adverse events

C4.1.9 Record review and document control

C4.1.10 Validation of reagents, equipment, and procedures

C4.1.11 Qualification of facilities, reagents, supplies, and equipment

C4.1.12 Inventory control

C4.1.13 Product tracking

C4.1.14 Process control

C4.2 There shall be a Collection Facility Director who is responsible for the Quality Management Plan as it pertains to the Collection Facility. The performance of this activity may be delegated to a designated individual(s) with appropriate training, knowledge, and expertise.

C4.2.1 The designated individual(s) shall have authority over and responsibility for ensuring that the Quality Management Plan is effectively established and maintained.

C4.2.2 The designated individual(s) shall not have oversight of his/her own work if this person also performs other tasks in the Collection Facility.

C4.2.3 The designated individual(s) shall report on quality management activities, at a minimum, quarterly.

C4.2.4 The designated individual(s) shall provide a report on the performance of the Quality Management Plan, at a minimum, annually to the Collection Facility Director and, if applicable, the Clinical Programme Director.

C4.3 The Quality Management Plan shall include an organisational chart of key personnel and functions within the Collection Facility.

C4.3.1 The Quality Management Plan shall include a description of how these key personnel interact to implement the quality management activities.

C4.4 The Quality Management Plan shall include policies and procedures for development and implementation of written agreements with third parties whose services impact the cellular therapy product.

C4.5 The Quality Management Plan shall include methods for process development, approval, validation, implementation, review, revision, and archiving for all critical processes, policies, and procedures.

C4.5.1 There shall be a defined process improvement plan that includes policies or procedures for the recognition and investigation of the cause of all issues that require corrective and preventive action.

C4.6 The Quality Management Plan shall include personnel requirements for each key position in the Collection Facility. Personnel requirements shall include at a minimum:

C4.6.1 Current job description for all staff

C4.6.2 A system to document the following for each staff member:

C4.6.2.1 Initial qualifications

C4.6.2.2 Orientation

C4.6.2.3 Initial training

C4.6.2.4 Competency for each function performed

C4.6.2.5 Continued competency at least annually

C4.6.2.6 Provisions for continuing education, training, and retraining

C4.6.3 A description of minimal trainer qualifications and a uniform plan for staff training.

C4.7 The Quality Management Plan shall include a process for documentation and review of outcome analysis and product efficacy, as appropriate, including at least:

C4.7.1 For HPC products, a process for documentation and review of time to engraftment following product administration.

C4.8 The Quality Management Plan shall include a process and timetable for conducting independent quality audits of the Collection Facility's activities to verify compliance with elements of the Quality Management Programme.

C4.8.1 Audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not solely responsible for the process being audited.

C4.8.2 Audit results shall be reviewed, reported, and documented at a minimum, on a quarterly basis.

C4.8.3 The results of audits shall be used to recognize problems, detect trends, and identify improvement opportunities.

C4.8.4 Audits shall include, at a minimum, documentation of proper donor eligibility and determination.

C4.9 The Quality Management Plan shall include policies and procedures on the management of cellular therapy products with positive microbial culture results that address at least:

C4.9.1 Documentation and product labelling.

C4.9.2 Release of the product from the distribution facility, including identification of authorized individuals and criteria for product release.

C4.9.3 Investigation of cause.

C4.9.4 Notification of transplant physician, Collection Facility and/or Cell Processing Facility, as applicable.

C4.9.5 Notification of the recipient prior to infusion.

C4.9.6 Recipient follow-up and outcome analysis.

C4.9.7 Follow-up of the donor, if relevant.

C4.9.8 Reporting to regulatory agencies, if appropriate.

C4.10 The Quality Management Plan shall include a system for detecting, evaluating, documenting, and reporting errors, accidents, suspected adverse events, biological product deviations, and complaints.

C4.10.1 Documentation of each adverse event that occurs in the Collection Facility shall be reviewed by the Collection Facility Director and/or Medical Director, as appropriate.

C4.10.2 Adverse events in the Collection Facility shall be documented in a manner that complies with institutional requirements and applicable governmental laws and regulations.

C4.10.3 Deviations from Standard Operating Procedures shall be documented.

C4.10.3.1 Planned deviations shall be pre-approved by the Collection Facility Director or designee.

C4.10.3.2 Unplanned deviations and associated corrective actions shall be reviewed by the Collection Facility Director or designee.

C4.10.4 Corrective actions shall be implemented, as appropriate. These shall include both short-term action to address the immediate problem and long-term action to prevent the problem's recurrence.

C4.10.5 Effectiveness of corrective actions shall be verified.

C4.10.6 A written description of adverse events shall be made available to the donor's physician, the recipient's physician, and the Processing Facility, if appropriate.

C4.10.7 When applicable, the event shall be reported to appropriate regulatory agencies.

C4.10.8 There shall be policies and procedures to document and follow-up customer-reported product failures, concerns, or complaints.

C4.11 The Quality Management Plan shall include a mechanism for document control and for the regular review of records relating to cell collection and transportation. The document control system shall include at a minimum the following elements:

C4.11.1 Definition and current listing of all critical documents that must adhere to the document control system requirements.

C4.11.2 Assignment of a numeric or alphanumeric identifier to each document regulated within the system.

C4.11.3 A procedure for document approval, including the approval date, signature of approving individual(s), and the effective date.

C4.11.4 A system to ensure that controlled documents cannot undergo accidental or unauthorized modification.

C4.11.5 A system for documentation of training associated with each procedure and its revisions.

C4.11.6 A system for document change control that includes a description of the change, the signature of approving individual(s), approval date, and effective date.

C4.11.7 A system for the retraction of obsolete documents to prevent unintended use.

C4.11.7.1 Obsolete documents shall be archived for a minimum of ten (10) years.

C4.11.8 A system for record creation, assembly, storage, archival, and retrieval.

C4.12 The Quality Management Plan shall include a process for product tracking that allows tracking from the donor to the recipient or final distribution and from the recipient, or final disposition, to the donor.

C4.13 The Quality Management Plan shall include a mechanism to ensure continuous operations in the event that the electronic record system ceases to function, including a plan for data backup, and a mechanism to ensure compliance with applicable laws.

C4.14 The Quality Management Plan shall include a process for validation and verification of critical reagents, equipment, and procedures.

C4.14.1 There shall be documentation of review and acceptance of validation studies by the appropriate individual from Quality Management.

C4.14.2 Changes to a process shall be verified or validated to ensure that they do not create an adverse impact anywhere in the operation.

C4.15 The Quality Management Plan shall include a process for qualification of critical reagents, equipment, procedures and facilities.

C4.15.1 Critical procedures shall include at least the following: collection procedures, labelling, storage conditions, and transportation.

C4.15.2 Equipment, supplies, and reagents used to collect cellular therapy products shall be used in a manner that prevents product mix-ups, contamination and cross-contamination, and that does not compromise cellular product function and integrity.

C4.15.3 Supplies and reagents used in collection of cellular therapy products shall be stored at the appropriate temperature in a secure, sanitary, and orderly manner.

C4.15.4 All supplies and reagents coming into contact with cellular therapy products during collection, storage, or transportation shall be sterile and shall be of appropriate grade for the intended use.

C4.15.4.1 Reagents that are not of the appropriate grade shall undergo qualification for the intended use.

C4.15.4.2 Non-disposable supplies or instruments shall be cleaned and sterilized using a procedure validated to remove infectious agents.

C4.15.5 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

C4.15.6 There shall be a process to prevent the use of expired reagents, supplies, and obsolete labels.

C4.15.7 There shall be a system to uniquely identify and track all critical equipment used in the collection of cellular therapy products.

C4.15.8 Equipment used in the collection, testing, storage, or transportation of cellular therapy products shall be maintained in a clean and orderly manner and located to facilitate cleaning, calibration, and maintenance.

C4.15.9 Equipment shall be standardized and calibrated on a regularly scheduled basis as described in Standard Operating Procedures and in accordance with the Manufacturer's recommendations.

C4.15.10 Equipment shall conform to existing legislation/regulations, where applicable.

C4.15.11 Critical facility parameters that may affect cellular therapy product viability, integrity, contamination, sterility, or cross-contamination during collection shall be identified, controlled, monitored, and recorded to demonstrate ongoing compliance.

C4.15.12 There shall be documentation of facility cleaning and sanitation, environmental conditions, and inspection of environmental control systems to ensure adequate conditions for proper operations.

C4.15.12.1 Records of all cleaning and sanitation activities performed to prevent product contamination shall be maintained ten (10) years after their creation.

C4.16 The Quality Management Plan shall include a process for inventory control that encompasses reagents, supplies, and labels.

C4.16.1 There shall be a system to uniquely identify and track all critical reagents, supplies, and labels used in the collection of cellular therapy products.

C4.16.2 Each supply and reagent used to collect cellular therapy products shall be examined visually for damage or evidence of contamination upon receipt.

C4.17 The Quality Management Plan shall include a process for controlling and monitoring the collection of products to ensure products meet predetermined release specifications.

C4.17.1 The Collection Facility Director shall define processes for assessing quality of cellular therapy products to ensure their safety, viability, and integrity and to document that products meet predetermined release specifications. Results of all such assessments shall become part of the permanent record of the product processed.

C4.17.2 Communicable disease testing required by these Standards shall be performed using FDA approved tests in an FDA registered laboratory or non-U.S. equivalent that is accredited or licensed in accordance with applicable governmental regulations.

C4.17.3 Other tests required by these Standards, not performed by the Collection Facility, shall be performed by a laboratory certified by CMS, CLIA, or non-U.S. equivalent.

C5. POLICIES AND PROCEDURES

C5.1 The Collection Facility shall have documented policies and procedures addressing all appropriate aspects of operations and management including at a minimum:

C5.1.1 Donor and recipient confidentiality

C5.1.2 Donor treatment

C5.1.3 Donor screening

C5.1.4 Donor consent

C5.1.5 Management of paediatric donors, if applicable

C5.1.6 Product collection

C5.1.7 Labelling (including associated forms and samples)

C5.1.8 Expiration dates

C5.1.9 Storage

C5.1.10 Release and exceptional release

C5.1.11 Biological product deviations

C5.1.12 Product tracking

C5.1.13 Transportation

C5.1.14 Quality management and improvement

C5.1.15 Personnel training and competency assessment

C5.1.16 Reagent and supply management

C5.1.17 Equipment maintenance, monitoring, and corrective actions in the event of failure

C5.1.18 Errors, accidents, adverse events, and complaints

C5.1.19 Corrective actions

C5.1.20 Outcome analysis

C5.1.21 Audits

C5.1.22 Facility management and monitoring

C5.1.23 Cleaning and sanitation

C5.1.24 Disposal of medical and biohazard waste

C5.1.25 Emergency and safety

C5.1.26 Disaster plan

C5.2 The Collection Facility shall maintain a detailed Standard Operating Procedures Manual. The Standard Operating Procedures Manual shall include:

C5.2.1 A procedure for preparation, approval, implementation, review, and revision of all procedures.

C5.2.2 A standardized format for procedures, including worksheets, reports, and forms.

C5.2.3 A system of numbering and/or titling of individual procedures, policies, worksheets, and forms.

C5.3 Procedures shall be sufficiently detailed and unambiguous to allow qualified technical staff to follow and complete the procedures successfully. Each individual procedure requires:

C5.3.1 A clearly written description of the objectives.

C5.3.2 A description of equipment and supplies used.

C5.3.3 Acceptable end-points and the range of expected results, where applicable.

C5.3.4 A stepwise description of the procedure, including diagrams and tables as needed.

C5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

C5.3.6 A reference section listing appropriate literature.

C5.3.7 Documented approval of each procedure and procedural modification by the Collection Facility Director or designated physician prior to implementation and annually thereafter.

C5.3.8 Copies of current versions of orders, worksheets, reports, labels, and forms, where applicable.

C5.4 Copies of the Standard Operating Procedures Manual shall be readily available to the facility staff at all times.

C5.5 All personnel in the facility shall follow the Standard Operating Procedures.

C5.6 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.

C5.7 Archived policies and procedures, the inclusive dates of use, and their historical sequence, shall be maintained for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

C5.8 All Standard Operating Procedures shall comply with these Standards and all applicable governmental regulations.

C5.9 There shall be a process to address age specific issues in the Standard Operating Procedures as appropriate.

C6. DONOR SELECTION, EVALUATION, AND MANAGEMENT

C6.1 There shall be written criteria for donor selection, evaluation, and management by trained medical personnel.

C6.2 There shall be donor evaluation procedures in place to protect the safety of the cellular product donor.

C6.2.1 The donor shall be evaluated for potential risks of the collection procedure, including:

C6.2.1.1 Possible need for central venous access and/or mobilization therapy for collection of peripheral blood cells.

C6.2.1.2 Anaesthesia for collection of marrow.

C6.2.2 The risk of donation and informed consent shall be documented.

C6.2.3 The use of a donor who does not meet the Clinical Programme donor safety criteria shall require documentation of the rationale for his/her selection by the transplant physician.

C6.2.4 Issues of donor health that pertain to the safety of the collection procedure shall be communicated in writing to the Collection Facility staff.

C6.3 There shall be donor evaluation procedures in place to protect the recipient from the risk of disease transmission from the donor.

C6.3.1 There shall be procedures for all steps in screening, testing, and determining donor eligibility, and for all regulatory requirements related to cellular therapy donors.

C6.3.2 Within thirty (30) days prior to collection, all HPC donors shall be tested for evidence of clinically relevant infection by the following communicable disease agents:

C6.3.2.1 Human immunodeficiency virus, type 1

C6.3.2.2 Human immunodeficiency virus, type 2

C6.3.2.3 Hepatitis B virus

C6.3.2.4 Hepatitis C virus

C6.3.2.5 Human T-cell lymphotropic virus I (per governmental regulations)

C6.3.2.6 Human T-cell lymphotropic virus II (per governmental regulations)

C6.3.2.7 Treponema pallidum (syphilis)

C6.3.3 Additional tests shall be performed as required to assess the possibility of transmission of other infectious or non-infectious diseases.

C6.3.4 For viable, lymphocyte rich cells, including therapeutic cells, each donor shall be tested for communicable disease agents listed in section B6.3.2 within seven (7) days prior to or after collection, or in accordance with applicable governmental regulations.

C6.4 Any abnormal findings shall be reported to the prospective donor with documentation in the donor record of recommendations made for follow-up care.

C6.5 All donors shall be tested for ABO group and Rh type.

C6.5.1 Allogeneic donors shall be tested for ABO group and Rh type on each day of collection.

C6.5.2 Autologous donors shall be tested for ABO group and Rh type at least on the first day of collection.

C6.6 A pregnancy assessment shall be performed for all female donors of childbearing potential within seven (7) days prior to initiation of recipient's conditioning regimen or of donor starting mobilization regimen.

C6.7 Laboratory testing on all donors shall be performed by a laboratory accredited or licensed in accordance with applicable U.S. or non U.S. equivalent regulations using one or more donor screening tests approved or cleared by the FDA or non-U.S. equivalent.

C6.8 ALLOGENEIC DONORS

C6.8.1 In addition to laboratory testing for relevant communicable disease agents as defined in B6.3.2, allogeneic donors shall be evaluated for risk factors for disease transmission by medical history, examination of relevant medical records, and physical examination.

C6.8.2 The medical history shall include at least the following:

C6.8.2.1 Vaccination history.

C6.8.2.2 Travel history.

C6.8.2.3 Blood transfusion history.

C6.8.2.4 Questions to identify persons at high risk for transmission of communicable disease as defined by the FDA or non-U.S. equivalent.

C6.8.2.5 Questions to identify persons at risk of transmitting inherited conditions.

C6.8.2.6 Questions to identify persons at risk of transmitting a haematological or immunological disease.

C6.8.2.7 Questions to identify a past history of malignant disease.

C6.8.3 Allogeneic donors shall be tested for Cytomegalovirus (unless previously documented to be positive).

C6.8.4 Allogeneic donors shall be tested at a minimum for HLA-A, B, DR type by a laboratory accredited by ASHI, EFI, or an affiliate.

C6.8.5 Allogeneic donors shall be tested for red cell compatibility where appropriate.

C6.8.6 Allogeneic donor eligibility, as defined by FDA donor eligibility regulation or non-U.S. equivalent governmental regulation, shall be determined by a physician and shall be documented in the recipient's medical record before the recipient's high dose therapy is initiated and before the donor is mobilized.

C6.8.7 The use of an ineligible allogeneic donor shall require an urgent medical need documentation, including the rationale for his/her selection and suitability by the transplant physician, and the documented informed consent of the donor and the recipient.

C6.8.8 Allogeneic eligibility and suitability shall be communicated in writing to the collection and cell processing facilities.

C6.8.9 The donor shall confirm that all the information provided is true to the best of his/her knowledge.

C6.9 DONOR CONSENT

C6.9.1 The collection procedure shall be explained in terms the donor can understand and shall include information about:

C6.9.1.1 The significant risks and benefits of the procedure.

C6.9.1.2 Tests performed to protect the health of the donor and recipient.

C6.9.1.3 The rights of the donor to review the results of such tests.

C6.9.1.4 Alternatives to donation.

C6.9.1.5 Alternative modalities of donation.

C6.9.2 The donor shall have an opportunity to ask questions and the right to refuse to donate.

C6.9.3 Informed consent from the donor shall be obtained and documented by a licensed physician or other health care provider familiar with the collection procedure.

C6.9.4 In the case of a minor donor, informed consent shall be obtained from the donor's parents or legal representative in accord with applicable law and shall be documented.

C6.9.5 The allogeneic donor shall give informed consent and authorization in advance to release the donor's health information to the transplant physician and recipient as appropriate.

C6.9.6 Documentation of consent shall be available to the Collection Facility staff prior to the collection procedure.

C7. LABELS

C7.1 LABELLING OPERATIONS

C7.1.1 Labelling operations shall be conducted in a manner adequate to prevent mislabelling or misidentification of products and product samples.

C7.1.2 The labelling operation shall include, at a minimum, the following controls:

C7.1.2.1 Labels shall be held upon receipt from the manufacturer pending review and proofing against a copy or template approved by the Collection Facility Director or designee to ensure accuracy regarding identity, content, and conformity.

C7.1.2.2 Labels printed on demand at the Collection Facility shall be reviewed against a copy or template approved by the Collection Facility Director or designee to ensure accuracy regarding identity, content, and conformity.

C7.1.2.3 Stocks of unused labels for different products shall be stored in a controlled manner to prevent errors.

C7.1.2.4 Stocks of obsolete labels shall be destroyed.

C7.1.2.5 A system for container label version control shall be employed.

C7.1.2.6 Representative obsolete labels shall be archived for ten (10) years with inclusive dates of use.

C7.1.2.7 A system of checks in labelling procedures shall be used to prevent errors in transferring information to labels.

C7.1.2.8 The information entered on a container label shall be verified by at least two (2) staff members.

C7.1.2.9 All labelling shall be clear, legible, and completed using indelible ink.

C7.1.2.10 The label shall be validated as reliable for storage under the conditions in use.

C7.1.3 Cellular therapy products that are subsequently re-packaged into new containers shall be labelled with new labels when appropriate.

C7.1.4 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.

C7.1.5 All data fields on labels shall be completed.

C7.1.6 Labelling elements required by applicable governmental regulations, if any, shall be observed.

C7.1.7 Records to allow tracking of products shall be maintained indefinitely, and include collection or processing facility identity, unique numeric or alphanumeric identifier, collection date and time, product identity, and donor and recipient information as found on the original container.

C7.2 PRODUCT IDENTIFICATION

C7.2.1 Each cellular therapy product shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any product to its donor, the donor's medical record, and to all records describing the handling and final disposition of the product.

C7.2.1.1 If a single cellular collection is stored in multiple containers, there shall be a system to identify each container.

C7.2.2 Collection Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the cellular product.

C7.2.2.1 Supplementary identifiers shall not obscure the original identifier.

C7.2.2.2 The facility associated with each identifier shall be noted on the label.

C7.2.3 Cellular therapy products shipped by registries may obscure the donor name and collection facility identifiers to maintain confidentiality as long as there is sufficient documentation to allow tracking to the donor.

C7.2.4 Cellular therapy products shall be identified according to the proper name of the product as defined in A3, including the appropriate product modifiers.

C7.3 LABEL CONTENT

C7.3.1 At the end of any cell collection, the product label on the primary container shall bear the information in the Cellular Therapy Product Labelling Table in Appendix I.

C7.4 BIOHAZARD LABEL

C7.4.1 Biohazard labels, as required by applicable laws and regulations, shall be affixed or attached to the product if the collection facility also distributes the product. (See Appendices I and III).

C7.4.2 A biohazard label shall be used if there are reactive test results for relevant communicable disease agents as designated in B6.3.2 or if donor screening indicates the presence of risk factors for relevant communicable disease or disease agents.

C7.5 WARNING LABELS

C7.5.1 Warning labels as defined in Appendices I and III shall be used as applicable.

C7.5.2 If required by applicable regulations, the following shall be included:

C7.5.2.1 The statement: "Caution: New drug limited by federal law for investigational use only" for products under IND or IDE.

C7.5.2.2 The statement: "Rx Only" for licensed products.

C7.6 Products collected for autologous use shall carry the label: "FOR AUTOLOGOUS USE ONLY" prior to release from the Collection Facility.

C7.7 LABEL AT COMPLETION OF COLLECTION

C7.7.1 Labelling at the end of collection shall occur before the product is removed from the proximity of the donor.

C7.8 ACCOMPANYING DOCUMENTATION AT DISTRIBUTION

C7.8.1 According to FDA and non-U.S. regulations, as applicable, the following shall accompany the cellular therapy product:

C7.8.1.1 A statement based upon the results of donor screening and testing that the donor has been determined to be eligible or ineligible.

C7.8.1.2 A summary of records used to make the donor eligibility determination.

C7.8.1.3 The name and address of the establishment that made the donor eligibility determination.

C7.8.1.4 A listing and interpretation of the results of all communicable disease screening and testing performed.

C7.8.1.5 A statement that the communicable disease testing was performed by a laboratory certified under CLIA of 1988, as amended from time to time, or has met equivalent requirements as determined by the Centres for Medicare and Medicaid Services (CMS) or has met equivalent non-U.S. requirements.

C7.8.1.6 Instructions for use to prevent the introduction, transmission, or spread of communicable diseases.

C7.8.2 In the case of a donor who has been determined to be ineligible based upon screening or testing there shall be:

C7.8.2.1 A statement noting the reason(s) for the determination of ineligibility.

C7.8.2.2 Documentation of notification of the physician using the product of the results of all testing and screening.

C7.8.3 Product distributed before completion of donor eligibility determination shall be accompanied by:

C7.8.3.1 A statement that the donor eligibility determination has not been completed.

C7.8.3.2 The results of required donor screening or testing that have been completed.

C7.8.3.3 A listing of any required screening or testing that has not yet been completed.

C7.8.3.4 Documentation that the physician using the cellular therapy product was notified that testing or screening was not complete.

C7.9 ADDITIONAL DOCUMENTATION AT OR IMMEDIATELY AFTER DISTRIBUTION

C7.9.1 For products distributed before completion of donor eligibility determination, there shall be documentation that donor eligibility determination was completed during or after the use of the product.

C8. CELLULAR THERAPY PRODUCT COLLECTION PROCEDURE

C8.1 Collection of cellular therapy products shall be performed according to written procedures in the Collection Facility's Standard Operating Procedures Manual.

C8.2 Before cell collection is undertaken, there shall be a written order from a physician specifying timing, procedural details, and goals of collection.

C8.3 There shall be written documentation of an interim assessment of donor suitability for the collection procedure performed by a qualified person immediately prior to each collection procedure.

C8.3.1 A complete blood count, including platelet count, shall be performed within 24 hours prior to each HPC collection by apheresis.

C8.3.2 There shall be peripheral blood count criteria to proceed with collection.

C8.4 General or regional anaesthesia, if required, shall be performed or supervised by a licensed, board-certified, or board-eligible anaesthesiologist or non-U.S. equivalent.

C8.5 Central venous catheters, where applicable, shall be placed by a licensed physician qualified to perform the procedure.

C8.5.1 Adequacy of line placement shall be verified by the Collection Facility.

C8.6 Administration of mobilization agents shall be under the supervision of a physician experienced in their administration and in the management of complications in persons receiving these agents.

C8.7 Methods for collection shall employ procedures validated to result in acceptable cell viability and recovery.

C8.8 Collection methods shall employ aseptic technique to ensure that cell products do not become contaminated during collection.

C8.9 Collection methods for paediatric donors shall employ appropriate age and size adjustments to the procedures.

C8.10 Cellular therapy products shall be packaged in a closed sterile transfer pack appropriate for blood and marrow products.

C8.11 HPC, Marrow products shall be filtered to remove particulate material prior to final packaging, distribution, or transplantation using filters that are non-reactive with blood.

C9. CELLULAR THERAPY PRODUCT STORAGE

C9.1 Collection Facilities storing cellular therapy products shall control storage areas to prevent mix-ups, deterioration, contamination, cross-contamination, and improper release of products.

C9.2 Collection Facilities storing cellular therapy products shall establish policies for the duration and conditions of storage prior to transfer to a Processing Facility or distribution to a Clinical Programme.

C10. CELLULAR THERAPY PRODUCT TRANSPORTATION

C10.1 Procedures for transportation of the cellular therapy product shall be designed to protect the integrity of the product and the health and safety of facility personnel.

C10.1.1 The primary product container shall be placed in a secondary container that is sealed to prevent leakage.

C10.1.2 The cellular therapy product shall be shipped to the Processing Facility at a temperature defined in the Collection Facility Standard Operating Procedure Manual.

C10.1.3 Cellular therapy products that are transported from the collection site to any non-contiguous Processing Facility shall be transported in an outer container made of material adequate to withstand leakage of contents, impact shocks, pressure changes, temperature changes, puncture, and other conditions incident to ordinary handling.

C10.2 The cellular therapy product shall be transported with required accompanying records, as appropriate.

C10.3 There shall be a record of the date and time of product distribution.

C11. RECORDS

C11.1 Collection Facility records related to quality control, personnel training or competency, facility maintenance, facility management, or other general facility issues shall be retained for at least ten (10) years by the Collection Facility, or longer in accordance with applicable laws or regulations, or a defined programme or institution policy, unless otherwise specified in these standards. Not all records need be immediately available.

C11.2 Patient and donor records including, but not limited to, consents and records of care, shall be maintained in a confidential manner, as required by applicable governmental laws and regulations, but no less than ten (10) years after the administration of the cellular therapy product, or, if not known, ten (10) years after the date of the distribution, disposition, or expiration of the product, whichever is latest.

C11.3 Employee Records shall be maintained in a confidential manner, as required by applicable governmental laws and regulations.

C11.4 Research records shall be maintained in a confidential manner, as required by applicable governmental laws and regulations, but no less than ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.

C11.5 ELECTRONIC RECORDS

C11.5.1 If a computer record-keeping system is used, there shall be a system to ensure the authenticity, integrity, and confidentiality of all records.

C11.5.2 There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.

C11.5.3 There shall be a back-up or alternative system for all electronic records that ensures continuous operation in the event that primary electronic data are not available. The alternative system shall be tested periodically.

C11.5.4 There shall be written procedures for record entry, verification, and revision. A system shall be established for review of data before final acceptance.

C11.5.4.1 The Quality Management Programme shall include an assessment of electronic functions to ensure that errors and problems are reported and resolved.

C11.5.5 There shall be a system whereby access to the electronic records is limited to authorized individuals.

C11.5.6 There shall be the ability to generate true copies of the records in both paper and computer format suitable for inspection and review.

C11.5.7 When an electronic system is used, there shall be validated procedures for and documentation of:

C11.5.7.1 Systems development

C11.5.7.2 Numerical designation of system versions if applicable

C11.5.7.3 Prospective validation of system including hardware, software, and databases

C11.5.7.4 Installation of the system

C11.5.7.5 Training and continuing competency of personnel in the use of the system

C11.5.7.6 Monitoring of data integrity

C11.5.7.7 Back-up of the electronic records system on a regular schedule

C11.5.7.8 System maintenance and operations

C11.5.8 All system modifications shall be authorized, documented, and validated prior to implementation.

C11.5.9 The electronic system shall ensure that all donor, product, and patient identifiers are unique.

C11.6 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

C11.6.1 If two (2) or more facilities participate in the collection, processing, or transplantation of the product, the records of each facility shall show plainly the extent of its responsibility.

C11.6.2 The Collection Facility shall furnish to the facility of final disposition a copy of all records relating to the collection and processing procedures performed in so far as they concern the safety, purity, and potency of the product involved.

C12. DIRECT DISTRIBUTION TO CLINICAL PROGRAMME

C12.1 Where cellular therapy products are distributed directly from the Collection Facility to the Clinical Programme, without transit via a Processing Facility, the Standards related to labelling, documentation, distribution, transportation, and recordkeeping in Sections D7, D8, D10, D12, and the Appendices apply.

PART D: CELLULAR THERAPY PRODUCT PROCESSING STANDARDS

D1 General

D2 Processing Facility

D3 Personnel

D4 Quality Management

D5 Policies and Procedures

D6 Process Controls

D7 Labels

D8 Distribution

D9 Storage

D10 Receipt and Transportation

D11 Disposal

D12 Records

PART D: CELLULAR THERAPY PRODUCT PROCESSING STANDARDS

D1. GENERAL

D1.1 These Standards apply to all processing, storage, and distribution activities performed in the Processing Facility.

D1.2 The Processing Facility shall abide by all applicable national and international governmental laws and regulations.

D1.3 The Processing Facility and staff, including a Processing Facility Director and Processing Facility Medical Director, shall have been in place and performing cellular therapy product processing for at least twelve (12) months prior to being eligible for accreditation.

D2. PROCESSING FACILITY

D2.1 Where required, the Processing Facility shall be registered with the FDA or non-U.S. equivalent for the activities performed.

D2.2 The Processing Facility shall be of adequate space, design, and location for the intended procedures.

D2.2.1 The Processing Facility shall be divided into defined areas of adequate size to prevent improper labelling, mix-ups, contamination, or cross-contamination of cellular therapy products.

D2.2.2 The Processing Facility shall be secure to prevent the admittance of unauthorized personnel.

D2.2.3 The Processing Facility shall provide adequate lighting, ventilation, plumbing, drainage, and access to sinks and toilets to prevent the introduction, transmission, or spread of communicable disease.

D2.3 There shall be adequate equipment for the procedures performed at the Processing Facility.

D2.4 There shall be a process to control storage areas to prevent mix-ups, contamination, and cross contamination of all products during quarantine and prior to release or transport.

D2.5 SAFETY REQUIREMENTS

D2.5.1 The Processing Facility shall be operated in a manner to minimize risks to the health and safety of employees, patients, donors, and visitors.

D2.5.2 Instructions for action in case of exposure to communicable disease or to chemical, biologic, or radiological hazards shall be included in the safety manual.

D2.5.3 Medical waste shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with applicable governmental laws and regulations.

D2.5.4 The Facility shall be maintained in a clean, sanitary, and orderly manner.

D2.5.5 Gloves and protective clothing shall be worn while handling biological specimens. Such protective clothing shall not be worn outside the work area.

D3. PERSONNEL

D3.1 PROCESSING FACILITY DIRECTOR

D3.1.1 There shall be a Processing Facility Director who is an individual with a medical degree or doctoral degree in a relevant science, qualified by training or experience for the scope of activities carried out in the Processing Facility. The Processing Facility Director may also serve as the Medical Director, if appropriately credentialed.

D3.1.2 The Processing Facility Director shall be responsible for all procedures and administrative operations of the Processing Facility, including compliance with these Standards.

D3.1.3 The Processing Facility Director shall participate regularly in educational activities related to the field of cellular processing and/or transplantation.

D3.2 PROCESSING FACILITY MEDICAL DIRECTOR

D3.2.1 There shall be a Processing Facility Medical Director who is a licensed physician with postgraduate training and/or one year's experience in the preparation and clinical use of cellular therapy products. The Medical Director may also serve as the Processing Facility Director, if appropriately credentialed.

D3.2.2 The Processing Facility Medical Director or designee shall be directly responsible for all medical aspects related to the Processing Facility.

D3.2.3 The Processing Facility Medical Director shall participate regularly in educational activities related to the field of cellular processing and/or transplantation.

D3.3 There shall be a Processing Facility Quality Management supervisor approved by the Processing Facility Director to establish and maintain systems to review, modify, and approve all policies and procedures intended to monitor compliance with these Standards and/or the performance of the Processing Facility.

D3.3.1 The Processing Facility Quality Management Supervisor shall participate regularly in educational activities related to the field of cellular processing and/or quality management.

D3.4 OTHER STAFF

D3.4.1 The Processing Facility shall have an adequate number of trained staff for the volume and complexity of all operations.

D4. QUALITY MANAGEMENT

D4.1 The Processing Facility shall establish and maintain a written Quality Management Plan that includes a process for controlling and monitoring the manufacturing of cellular therapy products that ensures that products conform to specifications, are not contaminated, and maintain function and integrity. The plan shall address, at a minimum:

D4.1.1 Organisational structure

D4.1.2 Agreements

D4.1.3 Process development and review

D4.1.4 Personnel qualifications, training, and competency

D4.1.5 Outcome analysis

D4.1.6 Audits

D4.1.7 Management of cellular therapy products with positive microbial cultures

D4.1.8 Detection and reporting of errors, accidents, and adverse events

D4.1.9 Record review and document control

D4.1.10 Validation of reagents, equipment, and procedures

D4.1.11 Qualification of facilities, reagents, supplies, and equipment

D4.1.12 Inventory control

D4.1.13 Product tracking

D4.1.14 Process control

D4.2 The Processing Facility Director shall be responsible for the Quality Management Plan as it pertains to the Processing Facility. The performance of this activity may be delegated to a designated individual(s) with the appropriate training, knowledge, and expertise.

D4.2.1 The designated individual(s) shall have authority over and responsibility for ensuring that the Quality Management Plan is effectively established and maintained.

D4.2.2 The designated individual(s) shall not have oversight of his/her own work if this person also performs other tasks in the Processing Facility.

D4.2.3 The designated individual(s) shall report on quality management activities, at a minimum, quarterly.

D4.2.4 The designated individual(s) shall provide a report on the performance of the Quality Management Plan, at a minimum, annually to the Processing Facility Director and, if applicable, the Clinical Programme Director.

D4.3 The Quality Management Plan shall include an organisational chart of key personnel and functions within the Processing Facility.

D4.3.1 The Quality Management Plan shall include a description of how these key personnel interact to implement the Quality Management activities.

D4.4 The Quality Management Plan shall include policies and procedures for development and implementation of written agreements with third parties whose services impact the cellular therapy product.

D4.5 The Quality Management Plan shall include methods for process development, approval, validation, implementation, review, revision, and archiving for all critical processes, policies, and procedures.

D4.5.1 There shall be a defined process improvement plan that includes policies or procedures for the recognition and investigation of the cause of all issues that require corrective and preventive action.

D4.6 The Quality Management Plan shall include personnel requirements for each position in the Processing Facility. Personnel requirements shall include at a minimum:

D4.6.1 Current job description for all staff

D4.6.2 A system to document the following for each staff member:

D4.6.2.1 Initial qualifications

D4.6.2.2 Orientation

D4.6.2.3 Initial training

D4.6.2.4 Competency for each function performed

D4.6.2.5 Continued competency at least annually

D4.6.2.6 Provisions for continuing education, training, and retraining

D4.6.3 The Quality Management Plan shall include a description of minimal trainer qualifications and a uniform plan for staff training.

D4.7 The Quality Management Plan shall include a process for documentation and review of product efficacy, and outcome analysis, as appropriate, including at least:

D4.7.1 For HPC products, a process for documentation and review of time to engraftment following product administration.

D4.8 The Quality Management Plan shall include a process and timetable for conducting independent quality audits of the Processing Facility's activities to verify compliance with elements of the Quality Management Programme.

D4.8.1 Audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not solely responsible for the process being audited.

D4.8.2 Audit results shall be reviewed, reported, and documented, at a minimum, on a quarterly basis.

D4.8.3 The results of audits shall be used to recognize problems, detect trends, and identify improvement opportunities.

D4.9 The Quality Management Plan shall include policies and procedures on the management of cellular therapy products with positive microbial culture results that address at least:

D4.9.1 Documentation and product labelling

D4.9.2 D4.9.2 Release of the product from the distribution facility, including identification of authorized individuals and criteria for product release

D4.9.3 Investigation of cause

D4.9.4 Notification of transplant physician, Collection Facility and/or Cell Processing Facility, as applicable

D4.9.5 Notification of the recipient prior to infusion

D4.9.6 Recipient follow-up and outcome analysis

D4.9.7 Follow up of the donor, if relevant

D4.9.8 Reporting to regulatory agencies, if appropriate

D4.10 The Quality Management Plan shall include a system for detecting, evaluating, documenting, and reporting errors, accidents, suspected adverse events, biological product deviations, variances, and complaints.

D4.10.1 Documentation of each adverse event associated with the cellular therapy product shall be reviewed by the Processing Facility Director and/or Medical Director, as appropriate.

D4.10.2 Adverse events associated with the cellular therapy product shall be documented in a manner that complies with institutional requirements and applicable governmental laws and regulations.

D4.10.3 A written description of adverse events shall be made available to the recipient's physician and the Collection Facility, if appropriate.

D4.10.4 Deviations from Standard Operating Procedures shall be documented.

D4.10.4.1 Planned deviations shall be pre-approved by the Processing Facility Director or designee and if medically relevant, by the Processing Facility Medical Director.

D4.10.4.2 Unplanned deviations and associated corrective actions shall be reviewed by the Processing Facility Director or designee, or Processing Facility Medical Director or designee, as appropriate.

D4.10.5 Corrective actions shall be implemented as appropriate. These shall include both short-term action to address the immediate problem and long-term action to prevent the problem's recurrence.

D4.10.6 Effectiveness of corrective actions shall be verified.

D4.10.7 When applicable, the event shall be reported to appropriate regulatory agencies.

D4.10.8 There shall be policies and procedures to document and follow-up customer-reported product failures, concerns, or complaints.

D4.11 The Quality Management Plan shall include a mechanism for document control and for regular review of records relating to cellular product processing, storage, release, and transportation. The document control system shall include at a minimum the following elements:

D4.11.1 Definition and current listing of all critical documents that must adhere to the document control system requirements.

D4.11.2 Assignment of a numeric or alphanumeric identifier to each document regulated within the system.

D4.11.3 A procedure for document approval, including the date, signature of approving individual(s), and the effective date.

D4.11.4 A system to ensure that controlled documents cannot undergo accidental or unauthorized modification.

D4.11.5 A system for documentation of training associated with each procedure and its revisions.

D4.11.6 A system for document change control that includes a description of the change, the signature of approving individual(s), approval dates, and effective date.

D4.11.7 A system for the retraction of obsolete documents to prevent unintended use.

D4.11.7.1 Obsolete documents shall be archived for a minimum of ten (10) years.

D4.11.8 A system for record creation, assembly, storage, archival, and retrieval.

D4.12 The Quality Management Plan shall include a process for product tracking that allows tracking from the donor to the recipient or final distribution and from the recipient, or final disposition, to the donor.

D4.13 The Quality Management Plan shall include a mechanism to ensure continuous operations in the event that the electronic record system ceases to function, including a plan for data backup, and to ensure compliance with applicable laws.

D4.14 The Quality Management Plan shall include a process for validation and verification of critical reagents, equipment, and procedures.

D4.14.1 There shall be documentation of review and acceptance of validation studies by the appropriate individual from Quality Management.

D4.14.2 Changes to a process shall be verified or validated to ensure that they do not create an adverse impact anywhere in the operation.

D4.14.3 Procedures for manufacturing reagents in-house shall be validated.

D4.15 The Quality Management Plan shall include a process for qualification of critical supplies, reagents, equipment, procedures, and facilities.

D4.15.1 Critical procedures shall include at least the following: processing techniques, cryopreservation protocols, storage conditions, and transportation.

D4.15.2 Equipment, supplies, and reagents used to process cellular therapy products shall be used in a manner that prevents product mix-ups, contamination and cross-contamination, and that does not compromise cellular product function and integrity.

D4.15.3 Supplies and reagents used in the processing, testing, cryopreservation, storage, and administration of cellular therapy products shall be stored at the appropriate temperature in a secure, sanitary, and orderly manner.

D4.15.4 All supplies and reagents coming into contact with cellular therapy products during processing, storage, and/or administration shall be sterile and of appropriate grade for the intended use.

D4.15.4.1 Reagents that are not of the appropriate grade shall undergo qualification for the intended use.

D4.15.4.2 Non-disposable supplies or instruments shall be cleaned and sterilized using a procedure verified to remove infectious agents.

D4.15.5 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

D4.15.6 There shall be a process to prevent the use of expired reagents, supplies, and obsolete labels.

D4.15.7 There shall be a system to uniquely identify and track all critical equipment used in the processing of cellular therapy products.

D4.15.8 Equipment used in the processing, testing, cryopreservation, storage, transportation, and administration of cellular therapy products shall be maintained in a clean and orderly manner and located to facilitate cleaning, calibration, and maintenance.

D4.15.9 The equipment shall be standardized and calibrated on a regularly scheduled basis as described in Standard Operating Procedures and in accordance with the Manufacturer's recommendations.

D4.15.10 Equipment shall conform to applicable governmental laws, legislation, and regulations.

D4.15.11 Critical facility parameters that may affect cellular therapy product processing, storage, or release shall be identified, controlled, monitored, and recorded to demonstrate ongoing compliance.

D4.15.12 There shall be documentation of facility cleaning and sanitation, environmental conditions, and inspection of environmental control systems to ensure adequate conditions for proper operations.

D4.15.12.1 Records of all cleaning and sanitation activities performed to prevent product contamination shall be maintained ten (10) years after their creation.

D4.16 The Quality Management Plan shall include a process for inventory control that encompasses reagents, supplies, labels, products, and product samples.

D4.16.1 There shall be a system to uniquely identify and track all critical reagents, supplies, and labels used to manufacture cellular therapy products.

D4.16.2 Each supply and reagent used to manufacture and administer cellular therapy products shall be examined visually for damage or evidence of contamination upon receipt.

D4.17 The Quality Management Plan shall include a process for controlling and monitoring the manufacturing of cellular therapy products to ensure products meet predetermined release specifications.

D4.17.1 The Processing Facility Director shall define tests and procedures for measuring and assaying cellular therapy products to ensure their safety, viability, and integrity and to document that products meet predetermined release specifications. Results of all such tests and procedures shall become part of the permanent record of the product processed.

D4.17.2 Communicable disease testing required by these Standards shall be performed using FDA approved tests in an FDA or non-U.S. equivalent registered laboratory, that is accredited or licensed in accordance with applicable governmental regulations.

D4.17.3 Other tests required by these Standards, not performed by the Processing Facility, shall be performed by a laboratory certified by CMS, CLIA, or non-U.S. equivalent.

D4.17.4 For tests performed within the Processing Facility, there shall be documentation of on-going proficiency testing as designated by the Processing Facility Director. The results shall be reviewed by the Processing Facility Director or designee and outcomes reviewed with the staff.

D4.17.5 Cellular therapy products that do not meet release or donor eligibility requirements shall be distributed only if there is documented urgent medical need for the product. Documentation shall include, at a minimum, the approval

of the recipient's physician and the Processing Facility Medical Director or other designated physician.

D4.17.5.1 Notification of the recipient's physician of testing and screening results for ineligible donors shall be documented.

D5. POLICIES AND PROCEDURES

D5.1 The Processing Facility shall have documented policies and procedures addressing all appropriate aspects of operations and management including at a minimum:

D5.1.1 Product receipt

D5.1.2 Processing and process control

D5.1.3 Prevention of cross-contamination

D5.1.4 Red cell compatibility testing and processing of ABO incompatible products

D5.1.5 Cryopreservation and thawing

D5.1.6 Labelling (including associated forms and samples)

D5.1.7 Expiration dates

D5.1.8 Storage (including alternative storage if the primary storage device fails)

D5.1.9 Release and exceptional release

D5.1.10 Product recall

D5.1.11 Biological product deviations

D5.1.12 Product tracking

D5.1.13 Transportation

D5.1.14 Quality management and improvement

D5.1.15 Personnel training and competency assessment

D5.1.16 Reagent and supply management

D5.1.17 Equipment maintenance, monitoring, and corrective actions in the event of failure

D5.1.18 Errors, accidents, and adverse events

D5.1.19 Complaints

D5.1.20 Corrective actions

D5.1.21 Outcome analysis

D5.1.22 Audits

D5.1.23 Facility management

D5.1.24 Cleaning and sanitation procedures

D5.1.25 Environmental control

D5.1.26 Hygiene and use of personal protective attire

D5.1.27 Infection control, biosafety, chemical, and radiological safety

D5.1.28 Decontamination and disposal of medical and biohazard waste

D5.1.29 Emergency and safety

D5.1.30 Disaster plan

D5.1.31 Donor and recipient confidentiality

D5.2 The Processing Facility shall maintain a detailed Standard Operating Procedures Manual. The Standard Operating Procedures Manual shall include:

D5.2.1 A procedure for preparing, reviewing, disseminating, implementing, and revising procedures.

D5.2.2 A standardized format for procedures, including worksheets, reports, and forms.

D5.2.3 A system of numbering and/or titling of individual procedures, policies, worksheets, and forms.

D5.3 Procedures shall be sufficiently detailed and unambiguous to allow qualified technical staff to follow and complete the procedures successfully. Each individual procedure requires:

D5.3.1 A clearly written description of the objectives.

D5.3.2 A description of equipment and supplies used.

D5.3.3 Acceptable end-points and the range of expected results, where applicable.

D5.3.4 A stepwise description of the procedure, including diagrams and tables, as needed.

D5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

D5.3.6 A reference section listing appropriate literature.

D5.3.7 Documented approval of each procedure and procedural modification by the Processing Facility Director or Medical Director, as appropriate, prior to implementation and annually thereafter.

D5.3.8 Copies of current versions of orders, worksheets, reports, labels, and forms, where applicable.

D5.4 Copies of the Standard Operating Procedures Manual shall be readily available to the facility staff at all times.

D5.5 All personnel in the facility shall follow the Standard Operating Procedures detailed in the manual.

D5.6 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.

D5.7 Archived procedures, including inclusive dates of use and their historical sequence, shall be maintained for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

D5.8 Standard Operating Procedures for all procedures shall comply with these Standards and all applicable governmental regulations.

D6. PROCESS CONTROLS

D6.1 There shall be a written request from the recipient's physician before processing is initiated specifying the product type, recipient and donor identifier, the type of processing that is to be performed, and the anticipated date of processing.

D6.2 Information required by the Processing Facility prior to distribution of the cellular therapy product shall include:

D6.2.1 A statement of donor eligibility and suitability.

D6.2.2 For ineligible donors, the reason for their ineligibility.

D6.2.3 Documentation of urgent medical need and physician approval for use, if applicable.

D6.3 Processing procedures shall be validated in the Processing Facility and documented to result in acceptable target cell viability and recovery.

D6.3.1 Published validated processes shall be verified within the Processing Facility prior to implementation.

D6.4 Critical control points and associated assays shall be identified and performed on each product as defined in Standard Operating Procedures.

D6.5 Methods for processing shall employ aseptic technique and cellular therapy products shall be processed in a manner that minimizes the risk of cross contamination.

D6.5.1 Where processing of tissues and cells involves exposure to the environment, processing shall take place in an environment with specified air quality and cleanliness.

D6.5.2 The effectiveness of measures to avoid contamination and cross contamination shall be verified and monitored.

D6.6 The Processing Facility shall monitor and document microbial contamination of cellular therapy products after processing, as specified in Standard Operating Procedures.

D6.6.1 The results of microbial cultures shall be reviewed by the Processing Facility Director or designee in a timely manner.

D6.6.2 The recipient's physician shall be notified in a timely manner of any positive microbial cultures.

D6.7 Worksheets shall be completed concurrently with processing and shall be maintained for all procedures.

D6.7.1 The individual responsible for each significant step of processing shall be documented.

D6.7.2 Lot numbers, expiration dates, and manufacturer of critical reagents, supplies, and identification of key equipment used in each procedure shall be documented.

D6.8 The Processing Facility Director or designee shall review the processing record for each cellular therapy product prior to release.

D6.8.1 The recipient's physician and the Processing Facility Medical Director shall be notified when the clinically relevant processing end-points are not met.

D6.8.2 Notification and appropriate remedial actions, if taken, shall be documented in the processing record.

D6.9 Processing using more-than-minimal manipulation shall only be performed with Institutional Review Board or Ethics Committee approval, with the written informed consent of the recipient of the cellular therapy product and in compliance with applicable governmental laws and regulations.

D6.10 For allogeneic products, a test for the ABO group and Rh type shall be performed on each product or on blood obtained from the donor at the time of collection.

D6.10.1 If there are previous records, there shall be a comparison of ABO group and Rh type with the last available record. Any discrepancies shall be resolved and documented prior to issue of the product.

D6.11 For autologous products, a test for ABO group and Rh type shall be performed on the first product or on blood obtained from the donor at the time of first collection.

D6.12 For cryopreserved products, aliquot(s) shall be stored under conditions that ensure a valid representation of the clinical product and shall be available for testing, if required.

D6.13 Laboratory processes shall include:

D6.13.1 The establishment of appropriate and validated assays and test procedures for the evaluation of cellular therapy products.

D6.13.1.1 For all cellular therapy products, a total nucleated cell count and viability measurement shall be performed.

D6.13.1.2 HPC products, a CD-34 assay shall be performed.

D6.13.1.3 For products undergoing manipulation that alters the final cell population, a relevant and validated assay, where available, should be employed for evaluation of the target cell population before and after the processing procedures.

D6.13.2 Provisions for monitoring the reliability, accuracy, precision, and performance of laboratory test procedures and instruments.

D6.13.3 A documented system for the identification and handling of test samples so that they are accurately related to the corresponding product, donor, or recipient, as applicable.

D7. LABELS

D7.1 LABELLING OPERATIONS

D7.1.1 Labelling operations shall be conducted in a manner adequate to prevent mislabelling or misidentification of products and product samples.

D7.1.2 The labelling operation shall include, at a minimum, the following controls:

D7.1.2.1 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.

D7.1.2.2 Labels printed on demand at the Processing Facility shall be reviewed against a copy or template approved by the Processing Facility Director or designee to ensure accuracy regarding identity, content, and conformity.

D7.1.2.3 Stocks of unused labels for different cellular products shall be stored in a controlled manner to prevent errors.

D7.1.2.4 Stocks of obsolete labels shall be destroyed.

D7.1.2.5 A system for container label version control shall be employed.

D7.1.2.6 Representative obsolete labels shall be archived for ten (10) years with inclusive dates of use.

D7.1.2.7 A system of checks in labelling procedures shall be used to prevent errors in transferring information to labels.

D7.1.2.8 The information entered on a container label shall be verified by at least two (2) staff members prior to release of product.

D7.1.2.9 All labelling shall be clear, legible, and completed using indelible ink.

D7.1.2.10 The label shall be validated as reliable for storage under the conditions in use.

D7.1.3 Cellular products that are subsequently re-packaged into new containers shall be labelled with new labels, when appropriate.

D7.1.4 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.

D7.1.5 All data fields on labels shall be completed.

D7.1.6 Labelling elements required by applicable governmental regulations, if any, shall be observed.

D7.1.7 Records to allow tracking of products shall be maintained indefinitely, and include collection or processing facility identity, unique numeric or alphanumeric identifier, collection date and time, product identity, and donor and recipient information as found on the original container.

D7.2 PRODUCT IDENTIFICATION

D7.2.1 Each cellular therapy product shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any product to its donor, the donor's medical record, and to all records describing the handling and final disposition of the product.

D7.2.1.1 If a single cellular collection is stored in multiple containers, there shall be a system to identify each container.

D7.2.2 Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the cellular product.

D7.2.2.1 Supplementary identifiers shall not obscure the original identifier.

D7.2.2.2 The facility associated with each identifier shall be noted on the label.

D7.2.3 Cellular therapy products shipped by registries may obscure the donor name and collection facility identifiers to maintain confidentiality as long as there is sufficient documentation to allow tracking to the donor.

D7.2.4 Cellular products shall be identified according to the proper name of the product as defined in A3, including the appropriate product modifiers.

D7.2.4.1 Significant modifications made to the cellular product subsequent to collection and prior to cryopreservation shall be noted.

D7.3 LABEL CONTENT

D7.3.1 Each label shall include at least the elements detailed in the Cellular Therapy Product Labelling Table in Appendix I.

D7.4 PARTIAL LABEL

D7.4.1 If the product container is capable of bearing only a partial label, the container shall have affixed, at a minimum, the unique numeric or alphanumeric identifier of the product, the proper name of the product, the appropriate product modifiers[2], and, if known, the name and identifier of the intended recipient.

D7.4.2 Minimally, the information required in D7.4.1 shall be present on the product during all stages of processing.

D7.4.3 Any container bearing a partial label shall be accompanied by the information required in Appendix I. Such information shall be attached securely to the product on a tie tag or enclosed in a sealed package to accompany the product.

D7.5 BIOHAZARD LABEL

D7.5.1 Biohazard labels as required by applicable regulations, shall be affixed or attached to the product when the product is distributed. (See Appendices I & III)

D7.5.2 A biohazard label shall be used if there are reactive test results for relevant communicable disease agents as designated in B6.3.2 or if donor screening indicates the presence of a risk factor for relevant communicable disease or disease agents.

D7.6 WARNING LABELS

D7.6.1 Warning labels, as defined in Appendices I & III, shall be used, as applicable.

D7.6.2 Products collected for autologous use shall carry the label: “FOR AUTOLOGOUS USE ONLY”.

D7.7 LABELLING AT COMPLETION OF PROCESSING

D7.7.1 At the end of processing, the label on the product container shall bear the information in the Cellular Therapy Product Labelling Table in Appendix I.

D7.8 LABELLING PRIOR TO DISTRIBUTION

D7.8.1 D7.8.1 At the time of distribution, the label on the product container shall bear the information in the Cellular Therapy Product Labelling Table in Appendix I.

D7.8.2 Products distributed from donors for whom donor eligibility determination is incomplete shall bear the statement: “Not Evaluated For Infectious Substances”.

D7.8.2.1 Products from allogeneic donors shall also bear the statement: “Warning: Advise Patient of Communicable Disease Risks”.

[2] Standard D7.4.1 requires "appropriate product modifiers" to appear on the partial label but this is omitted in error from the table in Appendix I. For accreditation purposes, the text of the Standard supersedes the table.

D7.8.3 The name and address of the facility that determines that the product meets release criteria, and the name and address of the facility that makes the product available for distribution shall either appear on the product label or accompany the product at distribution.

D7.9 ACCOMPANYING DOCUMENTATION AT DISTRIBUTION

D7.9.1 According to FDA and non-U.S. regulations as applicable, the following shall accompany the cellular therapy product:

D7.9.1.1 A statement, based upon the results of donor screening and testing, that the donor has been determined to be either eligible or ineligible.

D7.9.1.2 A summary of records used to make the donor eligibility determination.

D7.9.1.3 The name and address of the establishment that made the donor-eligibility determination.

D7.9.1.4 A listing and interpretation of the results of all communicable disease screening and testing performed.

D7.9.1.5 A statement that the communicable disease testing was performed by a laboratory certified under CLIA of 1988, as amended from time to time, has met equivalent requirements as determined by the Centres for Medicare and Medicaid Services, or has met equivalent non-U.S. requirements.

D7.9.2 In the case of a donor who has been determined to be ineligible based upon screening or testing, and the cellular therapy product has been released by the Processing Facility Medical Director due to urgent medical need, there shall be:

D7.9.2.1 A statement noting the reason(s) for the determination of ineligibility.

D7.9.2.2 Documentation of notification of the physician using the product of the results of all testing and screening.

D7.9.3 Products distributed before completion of donor-eligibility determination shall be accompanied by:

D7.9.3.1 A statement that the donor-eligibility determination has not been completed.

D7.9.3.2 The results of required donor screening or testing that have been completed.

D7.9.3.3 A listing of any required screening or testing that has not yet been completed.

D7.9.3.4 Documentation that the physician using the cellular therapy product was notified that testing or screening was not complete.

D7.9.4 Instructions for use to prevent the introduction, transmission, or spread of communicable diseases shall accompany the product.

D7.10 ADDITIONAL DOCUMENTATION AT OR IMMEDIATELY AFTER DISTRIBUTION

D7.10.1 For products distributed before completion of donor eligibility determination, there shall be documentation that donor-eligibility determination was completed during or after the use of the product and that the physician using the product was informed of the results of that determination.

D7.10.2 If required by applicable regulations, the following shall accompany the product:

D7.10.2.1 The statement "Caution: New drug limited by federal law for investigational use only" for products under IND or IDE.

D7.10.2.2 The statement "Rx Only" for licensed products.

D8. DISTRIBUTION

D8.1 PROCESSING, TRACKING, AND RELEASE CRITERIA

D8.1.1 The processing and tracking records for each cellular therapy product shall be reviewed, prior to product release/distribution, by the Processing Facility Director or designee for compliance with Standard Operating Procedures and applicable regulations.

D8.1.1.1 Records shall demonstrate traceability from the donor to the recipient and from the recipient to the donor.

D8.1.2 Each cellular therapy product issued for infusion shall meet predetermined release criteria including donor eligibility prior to issue from the laboratory.

D8.1.2.1 The Processing Facility Medical Director or designee shall give specific authorization for exceptional release when the cellular therapy product does not meet release criteria.

D8.1.2.2 Documentation of agreement of the Processing Facility Medical Director and the recipient's physician consent to use any non-conforming product shall be retained in the processing record.

D8.1.3 Each cellular therapy product issued for infusion shall be visually inspected by two (2) trained personnel immediately before release to verify the integrity of the product container and appropriate labelling.

D8.1.3.1 A product shall not be released when the container is compromised and/or recipient or donor information is not verified unless the Processing Facility Director or designee gives specific authorization for the products release.

D8.2 DISTRIBUTION RECORDS

D8.2.1 The cellular therapy product processing records shall contain a written or printed record of product distribution including, at a minimum:

D8.2.1.1 The distribution date and time.

D8.2.1.2 Name and unique identifier of the intended recipient.

D8.2.1.3 The proper product name and identifier.

D8.2.1.4 Documentation of donor eligibility determination.

D8.2.1.5 Identification of the facility that supplied the product.

D8.2.2 The distribution record shall include documentation of:

D8.2.2.1 The date and time of receipt.

D8.2.2.2 The identity of the individual who accepted the cellular therapy product.

D8.3 CIRCULAR OF INFORMATION

D8.3.1 For each type of cellular therapy product, the laboratory shall maintain and distribute or make available to clinical staff a current document containing the following as appropriate:

D8.3.1.1 The use of the cellular therapy product, indications, contraindications, side effects and hazards, dosage, and administration recommendations.

D8.3.1.2 Instructions for handling the cellular therapy product to minimize the risk of contamination or cross-contamination.

D8.3.1.3 Appropriate warnings related to the prevention of the transmission or spread of communicable diseases.

D8.4 RETURN OF CELLULAR THERAPY PRODUCTS FROM ISSUE

D8.4.1 Cellular therapy products accepted for return shall meet the following criteria:

D8.4.1.1 The integrity of the primary container has not been compromised.

D8.4.1.2 The cellular therapy product has been maintained, subsequent to issue, at the specified temperature range during storage and transportation.

D8.4.2 If the criteria in Sections D8.4.1.1 and D8.4.1.2 have not been met, the Processing Facility shall not accept the product unless the Processing Facility Director or designee gives specific authorization to accept the product for return to inventory after determining the product is acceptable.

D8.4.3 The Processing Facility Director or designee shall consult with the recipient's physician regarding reissue or disposal of the returned product.

D8.4.4 Documentation of the events requiring return, the results of inspection upon return, and subsequent action taken to ensure product safety and viability shall be maintained in the Processing Facility records.

D9. STORAGE

D9.1 Facilities storing cellular therapy products shall control storage areas to prevent mix-ups, deterioration, contamination, cross-contamination and improper release of products.

D9.2 STORAGE DURATION

D9.2.1 Facilities storing cellular therapy products shall establish policies for the duration and conditions of storage and indications for disposal.

D9.2.1.1 Patients, donors, and associated cell therapy centres should be informed about these policies before the cellular therapy product collection.

D9.2.2 Facilities processing, storing, and/or releasing cellular therapy products for administration shall assign an expiration date and time, as appropriate, for fresh products and for products thawed after cryopreservation.

D9.3 TEMPERATURE

D9.3.1 Storage temperatures shall be defined in the Standard Operating Procedures Manual.

D9.3.2 Cellular therapy products stored in a liquid state shall be maintained within a specific temperature range to maintain viability and function, to inhibit infectious agents, and for a period of time not to exceed that specified in the Standard Operating Procedures Manual.

D9.3.3 Cryopreserved products shall be stored within a temperature range, as defined in the Standard Operating Procedures, that is appropriate for the cell product and cryoprotectant solution used.

D9.4 PRODUCT SAFETY

D9.4.1 Materials that may adversely affect cellular therapy products shall not be stored in the same refrigerators or freezers as the cellular products.

D9.4.2 For products immersed in liquid nitrogen, procedures to minimize the risk of cross-contamination of products shall be employed.

D9.4.3 Facilities storing cellular therapy products shall quarantine each product until completion of the donor eligibility determination, as required by governmental regulations.

D9.4.4 Quarantined cellular therapy products shall be easily distinguishable and stored in a manner that minimizes cross contamination and inappropriate release.

D9.5 MONITORING

D9.5.1 Refrigerators and freezers for cellular therapy product storage shall have a system to monitor the temperature continuously and to record the temperature at least every four (4) hours.

D9.5.1.1 For cellular therapy products fully immersed in liquid nitrogen, continuous temperature monitoring is not required.

D9.5.2 There shall be a mechanism to ensure that levels of liquid nitrogen in liquid nitrogen freezers are consistently maintained to assure that cellular therapy products remain within the specified temperature range.

D9.6 ALARM SYSTEMS

D9.6.1 Storage devices for cellular therapy products or reagents for product processing shall have alarm systems that are continuously active.

D9.6.2 Alarm systems shall have audible signals or other effective notification methods.

D9.6.3 If laboratory personnel are not always present in the immediate area of the storage device, a system shall be in place that alerts responsible personnel of alarm conditions on a 24-hour basis.

D9.6.4 Alarms shall be set to activate at a temperature or level of liquid nitrogen that will allow time to salvage products.

D9.6.5 There shall be written instructions to be followed if the storage device fails. These instructions shall be displayed in the immediate area of the storage device.

D9.6.5.1 A procedure for notifying laboratory personnel shall be placed at each remote alarm location and in the immediate area of the storage device.

D9.6.5.2 In the event of storage device failure, the written instructions shall outline procedures that ensure that cellular therapy products are maintained at safe temperatures. Any corrective actions in order to maintain integrity of the cellular therapy product shall be documented.

D9.6.6 Alarm systems shall be checked periodically for function.

D9.6.7 Additional storage devices of appropriate temperature shall be available for product storage if the primary storage device fails.

D9.7 SECURITY

D9.7.1 The storage device shall be located in a secure area and accessible only to authorized personnel.

D9.8 INVENTORY CONTROL

D9.8.1 An inventory control system to identify the location of each product and associated sample aliquots shall be in use.

D9.8.2 The inventory control system records shall include:

D9.8.2.1 Donor name or unique identifier

D9.8.2.2 Recipient name or unique identifier (if known)

D9.8.2.3 Product unique identifier

D9.8.2.4 Product or specimen proper name

D9.8.2.5 Date and time (including time zone if appropriate)of collection

D9.8.2.6 Storage device identifier

D9.8.2.7 Location within the storage device

D9.8.2.8 Date of issue

D9.8.2.9 Disposition

D10. RECEIPT AND TRANSPORTATION

D10.1 Procedures shall be established, maintained, and documented for acceptance, rejection, or quarantine, and transportation of cellular therapy products.

D10.1.1 Each cellular therapy product shall be inspected at receipt to verify the integrity of the container and appropriate labelling, and to evaluate for evidence of microbial contamination.

D10.1.2 There shall be procedures to verify that the cellular therapy product was appropriately transported and that it is accompanied by appropriate documentation and samples.

D10.1.3 There shall be procedures to maintain cellular therapy products in quarantine until they have been determined to meet criteria for release from quarantine.

D10.2 Procedures for transportation of non-frozen and/or cryopreserved products shall be designed to protect the integrity of the product and the health and safety of individuals in the immediate area.

D10.2.1 The primary product container for non-frozen products shall be placed in a secondary plastic bag and sealed to prevent leakage.

D10.3 All cryopreserved or non-frozen products that require a temperature-controlled environment and that are transported within a facility over an extended time shall be transported in a container validated to maintain the appropriate temperature range.

D10.4 All products that leave the facility shall be transported in an outer shipping container.

D10.4.1 Shipping conditions shall be established and maintained to preserve the integrity and safety of cellular therapy products during transport.

D10.4.2 The outer shipping container shall conform to the applicable regulations regarding the mode of transport.

D10.4.3 The outer shipping container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.

D10.4.4 The shipping container shall be validated to be of appropriate design and construction to preserve the integrity of the cellular therapy product and to protect it from contamination during transport.

D10.4.5 During transport, the product temperature shall be maintained at the storage temperature specified by the Processing Facility.

D10.4.5.1 The shipping facility shall transport products in a shipper validated to maintain appropriate temperature.

D10.4.5.2 The temperature of shippers containing cryopreserved products shall be continuously monitored during transportation.

D10.4.5.3 The shipping facility shall maintain a record of the temperature during transport.

D10.4.5.4 The receiving facility shall verify and record the acceptability (i.e. integrity, appearance, etc.) of the product.

D10.4.5.5 The receiving facility shall document the temperature of the shipper upon arrival. For cryopreserved products, processing records shall include documentation of the container temperature during transport.

D10.4.6 The outer shipping container shall be labelled as defined in the Cellular Therapy Product Shipping Labels Table in Appendix II.

D10.4.7 There shall also be a label inside the shipping container that includes all the information required on the outer shipping container, in conformity with the Cellular Therapy Product Labelling Table in Appendix I and the Cellular Therapy Product Shipping Labels Table in Appendix II.

D10.4.8 The shipping container shall be labelled in accordance with applicable regulations regarding the cryogenic material used and the transportation of biologic materials.

D10.5 Method of Transport

D10.5.1 The transit time should be minimized.

D10.5.2 If the intended recipient has received high-dose therapy, the cellular therapy product shall be transported by a qualified courier.

D10.5.3 There shall be plans for alternative transport in an emergency.

D10.5.4 The products should not be passed through X-Ray irradiation devices designed to detect metal objects. If inspection is necessary, the contents of the container should be inspected manually.

D10.6 Transport Records

D10.6.1 Transport records shall permit tracing of the cellular therapy product from one facility to another.

D10.6.2 Transport records shall include:

D10.6.2.1 Date and time product was shipped

D10.6.2.2 Date and time product was received

D10.6.2.3 Shipping facility

D10.6.2.4 Receiving facility

D10.6.2.5 Personnel responsible for shipping and receiving product

D10.6.2.6 Identity of courier

D10.6.2.7 Any delay or problems incurred during transport

D11. DISPOSAL

D11.1 There shall be written policies for disposal of cellular therapy products.

D11.2 There shall be written documentation of patient death or no further need for the product before any product is discarded.

D11.3 Prior to collection, there should be a written agreement between the storage facility and the donor or donor's legal representative, or the patient or designated recipient, as appropriate, defining the length of storage and the circumstances for disposal or transfer of cellular therapy products.

D11.3.1 If the patient or designated recipient is still alive at the time of disposal specified by the written agreement, the patient shall be offered the opportunity to transfer the product to another facility.

D11.3.2 If there is no pre-existing agreement describing conditions for product storage and/or discard, the storage facility shall:

D11.3.2.1 Communicate with the designated recipient's physician about continuing need for storage of the product.

D11.3.2.2 Make a documented effort to notify the patient or designated recipient about product disposition or disposal.

D11.3.3 Disposal of cellular therapy products obtained through donor registries shall adhere to conditions mutually agreed upon by the storing facility and the donor registry.

D11.4 The Processing Facility Medical Director, in consultation with the recipient's physician, shall approve of the product discard, disposition, or method of disposal.

D11.5 The method of disposal and decontamination shall meet governmental regulations for disposal of biohazardous materials and/or medical waste.

D11.6 The records for discarded products shall indicate the product was discarded, date of discard, and disposition of product or method of disposal.

D12. RECORDS

D12.1 GENERAL REQUIREMENTS

D12.1.1 A records management system shall be established and maintained to facilitate the review of records pertaining to a particular product prior to distribution and for follow-up evaluation or investigation.

D12.1.1.1 The records management system shall facilitate tracking of the product from the donor to the recipient or final disposition and from the recipient, or final disposition, to the donor.

D12.1.1.2 For cellular therapy products that are to be shipped for use at another institution, the consignee shall be informed in writing, at or before the time of distribution of the product, of the tracking system and of the requirement for tracking the product.

D12.1.2 Records shall be maintained in such a way as to ensure their integrity and preservation.

D12.1.2.1 If records are maintained in more than one location there shall be a system to ensure prompt identification, location, and retrieval of all records.

D12.1.2.2 Records shall be accurate, legible, and indelible.

D12.1.3 All records and communications among the collection, processing, and transplant facilities, and their patients and donors shall be regarded as privileged and confidential.

D12.1.3.1 Safeguards to assure this confidentiality shall be established and followed in compliance with applicable governmental laws and regulations.

D12.1.4 Records shall be made concurrently with each step of the processing, testing, cryopreservation, storage, and infusion or disposal/ disposition/distribution of each product in such a way that all steps may be accurately traced.

D12.1.4.1 Records shall identify the person immediately responsible for each significant step, including dates and times of various steps, where appropriate.

D12.1.4.2 Records shall show the test results and the interpretation of each result, where appropriate.

D12.1.5 Records shall be maintained in one or more of the following ways: electronically, as original paper records, or as true copies.

D12.1.5.1 Equipment to make the records available and legible shall be readily available.

D12.1.5.2 For electronic records Section D12.2 applies.

D12.2 ELECTRONIC RECORDS

D12.2.1 If a computer record-keeping system is used, there shall be a system to ensure the authenticity, integrity, and confidentiality of all records.

D12.2.2 There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.

D12.2.3 There shall be a back-up or alternative system for all electronic records that ensures continuous operation in the event that primary electronic data are not available. The alternative system shall be tested periodically.

D12.2.4 There shall be written procedures for record entry, verification, and revision. A system shall be established for review of data before final acceptance.

D12.2.4.1 The Quality Management Programme shall include an assessment of electronic functions to ensure that errors and problems are reported and resolved.

D12.2.5 There shall be a system whereby access to the electronic records is limited to authorized individuals.

D12.2.6 There shall be the ability to generate true copies of the records, in both paper and computer format, suitable for inspection and review.

D12.2.7 When an electronic system is used, there shall be validated procedures for and documentation of:

D12.2.7.1 Systems development

D12.2.7.2 Numerical designation of system versions, if applicable

D12.2.7.3 Prospective validation of system, including hardware, software, and databases

D12.2.7.4 Installation of the system

D12.2.7.5 Training and continuing competency of personnel in systems use

D12.2.7.6 Monitoring of data integrity

D12.2.7.7 Back-up of the electronic records system on a regular schedule

D12.2.7.8 System maintenance and operations

D12.2.8 All system modifications shall be authorized, documented, and validated prior to implementation.

D12.2.9 The electronic system shall ensure that all donor, product, and patient identifiers are unique.

D12.3 RECORDS TO BE MAINTAINED

D12.3.1 Processing Facility records related to quality control, personnel training or competency, facility maintenance, facility management, or other general facility issues shall be retained for at least ten (10) years by the Processing Facility, or longer in accordance with applicable laws or regulations, or with a defined programme or institution policy, unless otherwise specified in these standards. Not all records need be immediately available.

D12.3.2 All records related directly to the processing, testing, storage, or release of cellular products shall be maintained for ten (10) years after their creation. The records pertaining to a cellular product shall be maintained at least ten (10) years after the date of its administration, or if the date of administration is not known, then at least ten (10) years after the date of the cellular product's distribution, disposition, or expiration, whichever is latest, or according to applicable laws and regulations or institutional policy, whichever requires the longest maintenance period. The following records shall be maintained:

D12.3.2.1 Processing records

D12.3.2.2 Compatibility test records

D12.3.2.3 Cryopreservation records

D12.3.2.4 Distribution records

D12.3.2.5 Records of errors, accidents, adverse events, adverse reactions, and complaints.

D12.3.2.6 All quality management records.

D12.4 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

D12.4.1 If two (2) or more facilities participate in the collection, processing, or distribution of the product, the records of the Processing Facility shall show plainly the extent of its responsibility.

D12.4.2 The Processing Facility shall maintain a listing of the names, addresses, and responsibilities of other facilities that perform manufacturing steps on a product.

D12.4.3 There shall be a system to allow the Processing Facility access to information that tracks all manufacturing steps performed by other facilities. This tracking system shall comply with D4.12.

D12.4.4 The Processing Facility shall furnish to the facility of final disposition a copy of all records relating to the collection and processing procedures performed in so far as they concern the safety, purity, and potency of the product involved.

APPENDICES

APPENDIX I

CELLULAR THERAPY PRODUCT LABELLING

Table version 3.1 incorporating minor changes from original table. Changes marked in yellow.

Each label shall include at least the elements detailed in the following table:

Element	Partial label	Label at completion of collection	Label at completion of processing	Label at distribution	Inner shipping container label
Unique numeric or alphanumeric identifier	AF	AF	AF	AF	
Proper name of product	AF	AF	AF	AF	
Product modifiers	AF		AF	AF	
Recipient name and identifier	AF (if applicable)	AT (if applicable)	AT (if applicable)	AT	
Identity and address of collection facility or donor registry		AT	AT	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		AT	AT	AT	
Biohazard and/or Warning Labels (as applicable) see D7.5 and Appendix III		AT	AT	AT	AF
If applicable: Statement “Not evaluated For Infectious Substances”		AT	AT	AT	AF
Statement “Warning: Advise Patient of Communicable Disease Risks”		AT	AT	AT	AF
Statement “Warning: Reactive Test Results for [name of disease agent or disease]”		AT	AT	AT	AF
Identity and address of processing and distribution facility(s)			AT	AT	
Statement “Do Not Irradiate”			AT	AF	
Expiration Date (if applicable)			AC	AT	
Expiration Time (if applicable)			AC	AT	
ABO and Rh of donor (if applicable)			AC	AT	
RBC compatibility testing results (if applicable)				AT	
Statement "Properly Identify Intended Recipient and Product"				AT	
Statement indicating that leukoreduction filters should not be used.				AF	
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	

AF=Affix, AT=Attach or Affix, AC=Accompany, Attach or Affix

APPENDIX II

CELLULAR THERAPY PRODUCT SHIPPING LABELS

Each label shall include at least the elements detailed in the following table:

Element	Inner & outer shipping container label
Date of distribution	AF
Statement “Do Not X-Ray”	AF
Statements "Medical Specimen", “Handle with Care”	AF
Shipper handling instructions	AF
Shipping facility name, street address and phone number	AF
Receiving facility name, street address and phone number	AF
Identity of person or position responsible for receipt of the shipment	AF

AF=Affix

Modified Circular of Information Biohazard and Warning Labels

		Title 21 CFR Citation [F]	Status					Product Labels					
			All Screening and Testing Completed	Abnormal Results of Donor Screening	Abnormal Results of Donor Testing	Donor is resident in country on USDA[E] BSE list OR Testing performed in non-CLIA-certified laboratory	Urgent Medical Need	Biohazard Legend [per 21 CFR 1271.3(b)]	For Autologous Use Only	Not Evaluated for Infectious Substances	WARNING Advise patient of communicable disease risks	WARNING Reactive test results for (name of disease agent or disease)
Donor Eligibility Determination Required [21 CFR 1271.45(b)]												
1	Allogeneic donors with incomplete donor eligibility determination [A,B]	1271.60	No	No	No		yes			X	X	
2	Allogeneic donors found ineligible											
	A first-degree or second-degree blood relative [C]	1271.65(b)(1)(i)	Yes	No/Yes	Yes		N/A	X			X	X
	A first-degree or second-degree blood relative [C]	1271.65(b)(1)(i)	Yes	Yes	No		N/A	X			X	
	Unrelated donor	1271.65(b)(1)(iii)	Yes	No/Yes	Yes		Yes	X			X	X
	Unrelated donor	1271.65(b)(1)(iii)	Yes	Yes	No		Yes	X			X	
	Unrelated donor (U.S. Regulation [G])		Yes	No	No	Yes	Yes	X			X	
Donor Eligibility Determination Not Required [21 CFR 1271.90(a)]												
3	Autologous donors [D]	1271.90(a)(b)										
	Autologous donor	1271.90(a)(1)(2)	No	No	No				X	X		
	Autologous donor	1271.90(b)(1)(3)	Yes	No/Yes	Yes			X	X			X
	Autologous donor	1271.90(b)(1)(3)	Yes	Yes	No			X	X			

A. The donor eligibility must be finalized during or after the use of the cellular therapy product. The results must be communicated to the treating physician [21 CFR 1271.60 (b)4]
B. Abnormal results of any screening or testing requires labeling as in item 2 in this table (21 CFR 1271.65 applies)
C. Notification of the recipient's and donor's physicians of abnormal screening and/or testing results is required
D. Any abnormal donor screening or testing results (even though neither screening nor testing is mandated for this group of donors) require appropriate labeling [21 CFR 1271.90 (b)]
E. USDA – United States Department of Agriculture
F. USA Federal Register, Code of Federal Regulations, Part 1271, Human Cells, Tissues, and Cellular Based Products, Revised January 1, 2004.
G. Applies to any cord blood unit collected, processed, stored, transported or transplanted in the US.

Modified table from the *Circular of Information for the Use of Cellular Therapy Products*, AABB et al. July 2005

B9.1 DATA MANAGEMENT

Instructions to the Applicant Facility:

1. Select the applicable consecutive records from the complete patient log for the most recent year (B1 .3) for audit, and list these patients by unique patient identifier below. Use additional pages if necessary.

    a. For programs applying for allogeneic accreditation, submit ten consecutive allogeneic records, and five consecutive autologous records.
    b. For programs applying for autologous accreditation only, submit five consecutive autologous records.
    c. For programs with more than 1 clinical site, include at least five patients from each site.
    d. If both paediatric and adult patients are treated in a combined program at the same clinical site include at least five patients in each population.

2. For each of these patient records, complete and submit the applicable Transplant Essential Data (TED) forms or the Minimum Essential Data-A (MED-A) forms.

3. Mark or flag the source documents in the primary patient record for each data point on the TED or MED-A form to facilitate verification by the on-site inspector.

ALLOGENEIC TRANSPLANT RECIPIENTS			
Unique Pt. ID	**Transplant Date**	**Paediatric or Adult?**	**Clinical Site of Transplant**
1			
2			
3			
4			
5			
6			
7			
8			
9			
1			
AUTOLOGOUS TRANSPLANT RECIPIENTS			
Unique Pt. ID	**Transplant Date**	**Paediatric or Adult?**	**Clinical Site of Transplant**
1			
2			
3			
4			
5.			
Additional AUTOLOGOUS TRANSPLANT RECIPIENTS for multiple sites or populations:			
1			
2			
3			
4			

5.			

B9.1 DATA MANAGEMENT (continued)

INSTRUCTIONS TO THE INSPECTOR:

1. The Clinical Program has selected a list of ten (10) consecutive allogeneic and/or five (5) consecutive autologous transplant patient records, as applicable, for audit.

2. Verify by using the patient log submitted that these are consecutive patients.

3. Verify that a minimum of 5 patients from each age group (paediatric and adult) and a minimum of 5 patients from each clinical site have been included.

4. You must audit a minimum of thirty (30) data points for each type of transplant performed. You may audit as many items and as many records as are needed to determine if there are data management deficiencies in evidence.

5. Select the data points that you audit from any of the Transplant Essential Data (TED) or Minimum Essential Data-A (MED-A) forms submitted by the applicant program. You should audit at least some data points for some patients from the one year or later follow up forms, if possible.

6. You may select at random the specific patient records you will audit.

7. If you are inspecting a COMBINED PROGRAM (either a program that transplants both adults and children or a program with more that one clinical site utilizing the same data management system and personnel), you must include a representative number of records of paediatric and adult transplant patients or a representative number of records from each clinical site.

8. For each type of transplant performed, five data points have been selected. There are listed on the INSPECTOR REPORT FORMS which follow these instructions. You must audit these five items on at least three patients records.

9. Chose the remainder of the data points at random on the same three patient records or from different records.

10. NOTE: If you notice a pattern of errors, audit additional charts for the items where errors have occurred to determine if this is a random transcriptional error, or if there is a systemic problem in data management that results in the same errors being made repeatedly.

11. Record your audit results on the report forms that follow these instructions. Be certain to record the unique patient identifier for each of the charts audited. Verify the items that are listed, and list the additional items that you audited.

12. During the chart audit, a knowledgeable member or members of the Data Management Team of the applicant Program should be present to assist you. Ask these personnel if you have any questions, any difficulty finding the source data or in verifying accuracy.

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

PRIMARY DISEASE DIAGNOSIS: .....

TYPE OF TRANSPLANT: ☐ Auto ☐ Allo ☐ Syngeneic

DATE OF TRANSPLANT: ..... - ..... - ..... (yyyy mm dd)

CENTRE IDENTIFICATION

EBMT Code (CIC): ....

CIBMTR/ABMTR Code .....

Hospital: ..... Unit: .....

Contact person.....

Phone:.....

Fax:.....

e-mail: .....

REPORT INFORMATION

Date of this Report: ..... - ..... - ..... (yyyy mm dd)

Patient asked to consent to data submission? ☐ Yes ☐ No

Is this a non-transplant registration? ☐ Yes ☐ No

Is registration to be sent to CIBMTR ☐ Yes ☐ No

IUBMID *(only if data is to be sent to CIBMTR)*:_____

Patient following national / international study / trial:
☐ Yes ☐ No ☐ Unknown

Name of study / trial .... Num Pat.....

PATIENT IDENTIFICATION

Unique Patient Number or Code: .....

Compulsory, registrations will not be accepted without this item

Initials: ....._..... (first name(s) _surname(s))

Date of Birth: ..... - ..... - ..... (yyyy mm dd)

Sex: ☐ Male ☐ Female

DISEASE

Date of initial diagnosis: ..... - ..... - ..... (yyyy mm dd)

Disease classification sheet: **Complete and attach only the relevant page with date and status at transplantation**

Performance score:
☐ Good (Karn≥80; ECOG 0-1; Lansky≥80)
☐ Poor (Karn<80; ECOG 2-3; Lansky<80)
☐ Unknown

Type of Transplant:
☐ AUTOlogous *(self)*
☐ ALLOgeneic
☐ Syngeneic *(monozygotic twin)*
☐ HLA-identical sibling *(may include non monozygotic twin)*
☐ HLA-matched other relative
☐ HLA-mismatched relative
☐ HLA-matched unrelated donor
☐ HLA-mismatched unrelated donor

Donor Sex *(for allografts)*: ☐ Male ☐ Female

Multiple donors *(check all relevant HLA types above)*
☐ Yes ☐ No

Source of Stem Cells *(check all that apply)*:
☐ Bone Marrow ☐ Peripheral Blood
☐ Cord Blood ☐ Other: .....

Chronological no. of transplant for this patient .....

Date of previous transplant: ..... - ..... - ..... (yyyy mm dd)

Type of previous transplant:_____ ☐ N/A

Was the current transplant part of a planned multiple graft protocol? ☐ Yes ☐ No ☐ Unknown

Graft manipulation ex-vivo (including T-cell depletion) *(other than for RBC removal or volume reduction)*
☐ Yes ☐ No ☐ Unknown

TRANSPLANTATION (cont.)

Conditioning regimen:

Non myeloablative/Reduced intensity ☐ Yes ☐ No

Total Body Irradiation ☐ Yes ☐ No

AFTER TRANSPLANTATION

Engraftment *(Neutrophils ≥0.5X10⁹ /L)*:

☐ Yes: Date of engraftment : ..... - ..... - ..... (yyyy mm dd)

☐ No: Date of last assessment : ..... - ..... - ..... (yyyy mm dd)

☐ Never below

Acute Graft Versus Host Disease:

Maximum Grade: ☐ Absent ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ Unknown ☐ Not applicable

Additional cell therapy given *(not for relapse or progression)*
(if additional transplant given, submit separate registration)

☐ Yes ☐ No ☐ Unknown

Date of first infusion: .... *(may be the same as transplant date)* (yyyy mm dd)

Type of cell(s): *(check all that apply)*
☐ Lymphocytes ☐ Fibroblasts
☐ Dendritic cells ☐ Other .....

Best disease status (response) after transplant

☐ Continued complete remission (CR)

☐ CR achieved: Date achieved : ..... - ..... - ..... (yyyy mm dd)

☐ Never in CR: Date assessed: ..... - ..... - .....☐ Unknown (yyyy mm dd)

DATE OF LAST CONTACT

Date of last follow up or death: ..... - ..... - ..... (yyyy mm dd)

PATIENT AND DISEASE STATUS AT FOLLOW UP

First Relapse or Progression after transplant:
☐ Yes ☐ No ☐ Continuous progression ☐ Unknown

Tick all methods used for the assessment with the dates on which they were used, adding whether relapse/progression was first detected for that method on the date indicated *(complete only for relapse)*

Molecular: Date ..... - ..... - ..... (yyyy mm dd)
☐ Done ☐ Not done
Relapse/progression first detected with this method: ☐ Yes ☐ No

Cytogenetic: Date ..... - ..... - ..... (yyyy mm dd)
☐ Done ☐ Not done
Relapse/progression first detected with this method: ☐ Yes ☐ No

Haematological/clinical: Date ..... - ..... - ..... (yyyy mm dd)
☐ Done ☐ Not done
Relapse/progression first detected with this method: ☐ Yes ☐ No

Survival Status:
☐ Alive ☐ Dead ☐ Died before transplant
Check here if patient lost to follow up ☐

Main Cause of Death *(check only one main cause)*:
☐ Relapse or Progression
☐ Transplantation Related Cause
(check as many as appropriate):
☐ Acute GVHD ☐ Cardiac Toxicity
☐ Rejection/Poor graft function ☐ Infection
☐ Pulmonary toxicity ☐ Veno occlusive disorder
☐ Post transplant lymphoproliferative disorder
☐ Other:.....
☐ Unknown
☐ Other: .....

EBMT MED-A 2003 – *reformatted for Promise 2, modified 11 Oct 2006 - p. 1*

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

Follow up report: 1 year post transplant and annually thereafter

PRIMARY DISEASE DIAGNOSIS: .....

TYPE OF TRANSPLANT: ☐ Auto ☐ Allo ☐ Syngeneic

CENTRE IDENTIFICATION

EBMT Code (CIC): ....
CIBMTR/ABMTR Code .....
Hospital: .....
Unit: .....
Contact person.....
Phone:.....
Fax:.....
e-mail: .....

REPORT INFORMATION

Date of this Report: ..... - ..... - .....
yyyy mm dd
Patient asked to consent to data submission? ☐
(if not consented before, i.e. pre-2003 registrations)

Check here if follow up is to be passed on to the CIBMTR☐

Patient following national / international study / trial:
☐ Yes ☐ No ☐ Unknown
Name of study / trial .... Num Pat …

PATIENT AND TRANSPLANT IDENTIFICATION

Unique Patient Number or Code: .....
(Compulsory, registrations will not be accepted without this item)
Initials: ....._..... (first name(s) _surname(s))

Date of Birth: ..... - ..... - .....
yyyy mm dd
Sex: ☐ Male ☐ Female
Date of the transplant to which this follow up refers to:
..... - ..... - .....
yyyy mm dd

AFTER TRANSPLANTATION

(if information not submitted with first report)

Engraftment *(Neutrophils >0.5X10⁹ /L)*:
☐ Previously reported
☐ Yes: Date of engraftment : ..... - ..... - .....
yyyy mm dd
☐ No: Date of last assessment : ..... - ..... - .....
yyyy mm dd
☐ Unknown

Acute Graft Versus Host Disease:
Maximum Grade:
☐ Previously reported
☐ Absent ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ Unknown

Best disease status after transplant:
☐ Previously reported
☐ Continued complete remission (CR)
☐ CR achieved: Date CR: ..... - ..... - .....
☐ Never in CR *yyyy mm dd*
☐ Unknown
Date response assessed: ..... - ..... - .....
yyyy mm dd

DATE OF LAST CONTACT

Date of last follow up or death: ..... - ..... - .....
yyyy mm dd

LATE COMPLICATIONS OF TRANSPLANT

Late graft failure
Did late graft failure occur? ☐ Yes ☐ No
Chronic Graft Versus Host Disease *(allografts only)*
☐ Yes ☐ No ☐ Unknown
If yes: Date first evidence of cGvHD: ..... - ..... -.....
yyyy mm dd
Maximum extent up to date of this follow up
☐ Limited ☐ Extensive ☐ Unknown

LATE COMPLICATIONS (cont.)

Secondary disease or lymphoproliferative disease?
☐ Yes: Diagnosis: .....
Date of diagnosis: ..... - ..... - .....
yyyy mm dd
☐ No: Date assessed : ..... - ..... - .....
yyyy mm dd
☐ Unknown

ADDITIONAL TREATMENT

Additional cell therapy given since last report:
(can be for relapse or progression; if additional transplant given, submit separate registration)
☐ Yes ☐ No ☐ Unknown
Date of first infusion: ....
yyyy mm dd
Type of cell: *(check all that apply)*
☐ Lymphocytes ☐ Fibroblasts
☐ Dendritic cells ☐ Other .....

DISEASE STATUS

First Relapse or Progression after transplant:
☐ Yes ☐ No ☐ Continuous progression ☐ Unknown
☐ Previously reported
Tick all methods used for the assessment with the dates on which they were used, adding whether relapse/progression was first detected for that method on the date indicated *(complete only for relapse)*

Molecular: Date ..... - ..... - .....
☐ Done ☐ Not done *yyyy mm dd*
Relapse/progression first detected with this method: ☐ Yes ☐ No

Cytogenetic: Date ..... - ..... - .....
☐ Done ☐ Not done *yyyy mm dd*
Relapse/progression first detected with this method: ☐ Yes ☐ No

Haematological/clinical: Date ..... - ..... - .....
☐ Done ☐ Not done *yyyy mm dd*
Relapse/progression first detected with this method: ☐ Yes ☐ No

CONCEPTION

Has patient or partner become pregnant after this transplant?
☐ Yes ☐ No ☐ Unknown

PATIENT STATUS

Survival Status:
☐ Alive ☐ Dead

Check here if patient lost to follow up ☐

Current disease status
☐ Complete remission (CR)
☐ Not in remission

Last date disease assessed: ..... - ..... - .....
yyyy mm dd

Main Cause of Death *(check only one main cause)*:
☐ Relapse or Progression
☐ Secondary malignancy
☐ Transplantation Related Cause
(check as many as appropriate):
☐ Chronic GVHD ☐ Cardiac Toxicity
☐ Rejection/Poor graft function ☐ Infection
☐ Pulmonary toxicity ☐ Veno occlusive disorder
☐ Post transplant lymphoproliferative disorder
☐ Other:.....
☐ Unknown
☐ Other: .....

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 1

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

ACUTE LEUKEMIAS

Classification:

Acute Myelogenous Leukemia (AML)
- ☐ M0
- ☐ M1
- ☐ M2
- ☐ M3
- ☐ M4
- ☐ M5
- ☐ M6
- ☐ M7
- ☐ Other AML, specify:_____
- ☐ AML unspecified
- ☐ Transformed from MDS → *Complete MDS section on DiseaseClassification Sheet 2. Do not complete the remainder of AML*

Acute Lymphoblastic Leukemia (ALL)
- ☐ ALL B-lineage
- ☐ ALL T-lineage
- ☐ Mature B cell (L3)
- ☐ ALL unspecified
- ☐ T-cell granular lymphocytic leukaemia
- ☐ Aggressive NK-cell leukaemia
- ☐ Adult T-cell lymphoma/leukaemia (HTLV1+)
- ☐ Other ALL, specify:_____

Other Acute Leukemias
- ☐ Acute undifferentiated
- ☐ Acute biphenotypic
- ☐ Acute mast cell leukemia
- ☐ Other, specify: _____

Secondary origin?:
- ☐ Yes: Disease related to prior exposure to therapeutic drugs or radiation
- ☐ No
- ☐ Unknown

Date of this transplant: ..... - ..... - .....
yyyy mm dd

Status at Transplantation:

STATUS	NUMBER	FOR COMPLETE REMISSION ONLY	Yes	No	Not evaluated	Unknown
☐ Untreated	*(complete only for CR or relapse)*					
☐ Primary induction failure	☐ 1st	Cytogenetic	☐	☐	☐	☐
☐ Complete remission (CR)	☐ 2nd	Molecular	☐	☐	☐	☐
☐ Relapse	☐ 3rd or higher					

CHRONIC MYELOGENOUS LEUKEMIA (CML)

Classification:
- ☐ CML, Translocation (9;22) negative
- ☐ CML, Translocation (9;22) positive
- ☐ CML, not otherwise specified

Date of this transplant: ..... - ..... - .....
yyyy mm dd

Status at Transplantation:

PHASE	NUMBER	FOR CHRONIC PHASE ONLY, TYPE OF REMISSION *(check all that apply)*				
☐ Chronic phase (CP)	☐ 1st	Haematological:	☐ Yes	☐ No, stable phase		
☐ Accelerated phase	☐ 2nd	Cytogenetic:	☐ Complete	☐ No	☐ Not eval.	☐ Unknown
☐ Blast crisis	☐ 3rd or higher	Molecular (bcr/abl):	☐ Yes	☐ No	☐ Not eval.	☐ Unknown
		Other:.....				

OTHER LEUKEMIAS

Classification:
- ☐ Chronic lymphocytic leukemia (CLL), B-cell/ small lymphocytic lymphoma
- ☐ CLL, T-cell
- ☐ CLL, not otherwise specified
- ☐ Prolymphocytic Leukemia
  - ☐ B-cell
  - ☐ T-cell
- ☐ Hairy Cell Leukemia
- ☐ Other leukemia, specify:_____

Date of this transplant: ..... - ..... - .....
yyyy mm dd

Status at Transplantation:
- ☐ Untreated
- ☐ Complete remission (CR)
- ☐ Partial remission (PR)
- ☐ No response/stable
- ☐ Progression

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 2

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

MYELODYSPLASTIC and MYELOPROLIFERATIVE SYNDROMES

Classification:

Myelodysplastic Syndromes (MDS)

At diagnosis	At transplantation
☐	☐ RA
☐	☐ RARS
☐	☐ RAEB
☐	☐ RAEB-t
	☐ Transformed to AML
☐	☐ MDS not otherwise specified
☐	☐ Other, specify:_____

Myeloproliferative Syndromes (MPS)

At diagnosis	At transplantation
☐	☐ Polycythemia vera
☐	☐ Essential or primary thrombocythemia
☐	☐ Myelofibrosis with myeloid metaplasia
☐	☐ Acute myelofibrosis or myelosclerosis
☐	☐ MPS not otherwise specified
☐	☐ Other, specify:_____

Myelodysplastic and Myeloproliferative Syndrome (MDS/MPS)

At diagnosis	At transplantation
☐	☐ Chronic myelomonocytic leukaemia (CMMoL, CMML)
☐	☐ Juvenile myelomonocytic leukaemia (JMML, JCML, JCMML)
☐	☐ Other, specify _____

Date of this transplant: ..... - ..... - .....

Status at Transplantation:

☐ Untreated (Supportive care only)
☐ Treatment without intent to achieve complete remission (CR)
☐ Treatment with intent to achieve a CR – CR not achieved
☐ Treatment with intent to achieve a CR – CR achieved and sustained
☐ Relapse after CR

NUMBER *(complete for CR or relapse)*
☐ 1st
☐ 2nd
☐ 3rd or higher

ANAEMIA

Classification:

☐ Acquired Severe Aplastic Anaemia (SAA), not otherwise specified
- ☐ Acquired SAA, secondary to hepatitis
- ☐ Acquired SAA, secondary to toxin/other drug
- ☐ Amegakaryocytosis acquired (not congenital)
- ☐ Acquired Pure Red Cell Aplasia (PRCA) (not congenital)
- ☐ Other acquired cytopenic syndrome, specify: _____

☐ Fanconi anaemia
☐ Diamond-Blackfan anaemia (congenital PRCA)
☐ Schwachman-Diamond
☐ Other constitutional anaemia, specify: _____
☐ Paroxysmal nocturnal hemoglobinuria (PNH)

Date of this transplant: ..... - ..... - .....

HEMOGLOBINOPATHY

Classification:

☐ Thalassemia
☐ Sickle cell disease
☐ Other hemoglobinopathy, specify: _____

Date of this transplant: ..... - ..... - .....

PLATELET DISORDERS

Classification:

☐ Congenital amegakaryocytosis / congenital thrombocytopenia
☐ Glanzmann thrombasthenia
☐ Other inherited platelet abnormalities, specify: _____

Date of this transplant: ..... - ..... - .....

HISTIOCYTIC DISORDERS

Classification:

☐ Histiocytic disorders, not otherwise specified
☐ Langerhans Cell Histiocytosis (Histiocytosis-X)
☐ Malignant histiocytosis
☐ Familial erythro/hemophagocytic lymphohistiocytosis (FELH)
☐ Hemophagocytosis (reactive or viral associated)
☐ Other, specify:_____

Date of this transplant: ..... - ..... - .....

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 3

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

LYMPHOMAS

Classification:

☐ **Non-Hodgkin's lymphoma (NHL)**

B-cell Neoplasms

- ☐ Follicular lymphoma
  - ☐ Grade I ☐ Grade II ☐ Grade III ☐ Unknown
- ☐ Mantle cell lymphoma
- ☐ Extranodal marginal zone of MALT type
- ☐ Diffuse large B-cell lymphoma
- ☐ Mediastinal large cell lymphoma
- ☐ Burkitt's lymphoma/Burkitt cell leukemia
- ☐ Precursor B-lymphoblastic leukemia/lymphoma
- ☐ Lymphoplasmacytic lymphoma *(including Waldenstrom)*
- ☐ Splenic marginal zone B-cell lymphoma
- ☐ Nodal marginal zone B-cell lymphoma
- ☐ Other, specify:_____

T-cell & NK-cell Neoplasms

- ☐ Angioimmunoblastic (AILD)
- ☐ Peripheral (all variants)
- ☐ Anaplastic large-cell, T/null cell, primary cutaneous
- ☐ Anaplastic large-cell, T/null cell, primary systemic
- ☐ Precursor T-lymphoblastic lymphoma/leukemia
- ☐ Extranodal NK/T-cell lymphoma, nasal type
- ☐ Enteropathy-type T-cell lymphoma
- ☐ Hepatosplenic gamma-delta T-cell lymphoma
- ☐ Subcutaneous panniculitis-like T-cell lymphoma
- ☐ Mycosis fungoides
- ☐ Sezary syndrome
- ☐ Other, specify:_____

☐ **Hodgkin**
☐ **Other** _____

Date of this transplant: ..... - ..... - .....
yyyy mm dd

Status at Transplantation:

STATUS	NUMBER *(complete only for CR or relapse)*	SENSITIVITY TO CHEMOTHERAPY *(complete only for relapse)*
☐ Untreated	☐ 1st	☐ Sensitive
☐ Primary refractory	☐ 2nd	☐ Resistant
☐ Complete remission (CR) ☐ Confirmed ☐ Unconfirmed (CRU*)	☐ 3rd or higher	☐ Untreated
☐ 1st Partial response (PR1)		☐ unknown
☐ 1st Very good partial response (VGPR1)		
☐ Relapse		
☐ Progression		

*CRU – complete response with persistent scan abnormalities of unknown significance

PLASMA CELL DISORDERS including MULTIPLE MYELOMA

Classification

- ☐ Multiple myeloma - IgG
- ☐ Multiple myeloma - IgA
- ☐ Multiple myeloma – IgD
- ☐ Multiple myeloma – IgE
- ☐ Multiple myeloma-light chain
- ☐ Multiple myeloma-non-secretory

LIGHT CHAIN TYPE

- ☐ Kappa
- ☐ Lambda

SALMON & DURIE

STAGE AT DIAGNOSIS *(Multiple Myeloma only)*

- ☐ I and ☐ A
- ☐ II ☐ B
- ☐ III

- ☐ Plasma cell leukemia
- ☐ Solitary plasmacytoma
- ☐ Primary amyloidosis
- ☐ Other, specify:_____

Date of this transplant: ..... - ..... - .....
yyyy mm dd

Status at Transplantation:

	NUMBER *(complete for CR, PR or relapse)*
☐ Untreated	☐ 1st
☐ Complete remission (CR)	☐ 2nd
☐ Partial remission (PR)	☐ 3rd or higher
☐ Minimal response (MR)	
☐ Relapse / Progression	
☐ No change / stable disease	

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 4

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

BREAST CANCER

Staging at Diagnosis

METASTASES
- ☐ No distant metastases
- ☐ Metastatic

STAGE
- ☐ 0
- ☐ I
- ☐ II
- ☐ III

CLASSIFICATION:
- ☐ Inflammatory
- ☐ Non-inflammatory

Date of this transplant: ..... - ..... - .....

Status at Transplantation:
- ☐ Adjuvant (Stage II, III only)
- ☐ Untreated (upfront)
- ☐ Primary refractory
- ☐ Complete remission (CR)
  - ☐ Confirmed ☐ Unconfirmed (CRU*)
- ☐ 1st Very good partial response (VGPR1)
- ☐ 1st Partial response (PR1)
- ☐ Relapse
  - ☐ Local ☐ Metastatic

NUMBER *(complete only for CR or relapse)*
- ☐ 1st
- ☐ 2nd
- ☐ 3rd or higher

SENSITIVITY TO CHEMOTHERAPY *(complete only for relapse)*
- ☐ Sensitive
- ☐ Resistant
- ☐ Untreated
- ☐ Unknown

*CRU – complete response with persistent scan abnormalities of unknown significance

OTHER MALIGNANCIES

Classification:
- ☐ Bone sarcoma (excluding Ewing sarcoma)(include sarcoma PNET)
- ☐ Central nervous system tumors (include CNS PNET)
- ☐ Cervical
- ☐ Colorectal
- ☐ Ewing sarcoma
- ☐ External genitalia
- ☐ Fibrosarcoma
- ☐ Gastric
- ☐ Germ cell tumour, extragonadal only
- ☐ Head and neck
- ☐ Hemangiosarcoma
- ☐ Hepatobiliary
- ☐ Kidney and urinary tract
- ☐ Leiomyosarcoma
- ☐ Liposarcoma
- ☐ Lung cancer, non-small cell
- ☐ Lung cancer, small cell
- ☐ Lung cancer, not otherwise specified
- ☐ Lymphangiosarcoma
- ☐ Mediastinal neoplasm
- ☐ Medulloblastoma
- ☐ Melanoma
- ☐ Neuroblastoma
- ☐ Neurogenic sarcoma
- ☐ Other
- ☐ Ovarian
- ☐ Pancreas
- ☐ Prostate
- ☐ Retinoblastoma
- ☐ Rhabdomyosarcoma
- ☐ Sarcoma not otherwise specified
- ☐ Soft tissue sarcoma (include sarcoma PNET)
- ☐ Synovial sarcoma
- ☐ Testicular
- ☐ Thymoma
- ☐ Uterus
- ☐ Vagina
- ☐ Wilm tumour
- ☐ Other, specify .....

Date of this transplant: ..... - ..... - .....
Yyyy mm dd

Status at Transplantation:
- ☐ Adjuvant
- ☐ Untreated (upfront)
- ☐ Primary refractory
- ☐ Complete remission (CR)
- ☐ 1st Very good partial response (VGPR1)
- ☐ 1st Partial response (PR1)
- ☐ Relapse

NUMBER *(complete only for CR or relapse)*
- ☐ 1st
- ☐ 2nd
- ☐ 3rd or higher

SENSITIVITY TO CHEMOTHERAPY *(complete only for relapse)*
- ☐ Sensitive
- ☐ Resistant
- ☐ Untreated

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CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 5

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

INHERITED DISORDERS OF METABOLISM

Classification:

- ☐ Adrenoleukodystrophy
- ☐ Aspartyl glucosaminuria
- ☐ B-glucuronidase deficiency (VII)
- ☐ Fucosidosis
- ☐ Gaucher disease
- ☐ Glucose storage disease
- ☐ Hunter syndrome (II)
- ☐ Hurler syndrome (IH)
- ☐ I-cell disease
- ☐ Krabbe disease (globoid leukodystrophy)
- ☐ Lesch-Nyhan (HGPRT deficiency)
- ☐ Mannosidosis
- ☐ Maroteaux-Lamy (VI)
- ☐ Metachromatic leukodystrophy
- ☐ Morquio (IV)
- ☐ Mucolipidoses, not otherwise specified
- ☐ Mucopolysaccharidosis (V)
- ☐ Mucopolysaccharidosis, not otherwise specified
- ☐ Niemann-Pick disease
- ☐ Neuronal ceriod – lipofuscinosis (Batten disease)
- ☐ Osteopetrosis (malignant infantile osteopetrosis)
- ☐ Polysaccharide hydrolase abnormalities, unspecified
- ☐ Sanfilippo (III)
- ☐ Scheie syndrome (IS)
- ☐ Wolman disease
- ☐ Other, specify: .....
- ☐ Unspecified

Date of this transplant: ..... - ..... - .....
yyyy mm dd

IMMUNE DEFICIENCIES

Classification:

- ☐ Absence of T and B cells SCID
- ☐ Absence of T, normal B cell SCID
- ☐ ADA deficiency severe combined immune deficiency (SCID)
- ☐ Ataxia telangiectasia
- ☐ Bare lymphocyte syndrome
- ☐ Cartilage hair hypoplasia
- ☐ CD 40 Ligand deficiency
- ☐ Chediak-Higashi syndrome
- ☐ Chronic granulomatous disease
- ☐ Common variable immunodeficiency
- ☐ DiGeorge anomaly
- ☐ HIV infection
- ☐ Kostmann syndrome-congenital neutropenia
- ☐ Leukocyte adhesion deficiencies
- ☐ Neutrophil actin deficiency
- ☐ Omenn syndrome
- ☐ Reticular dysgenesis
- ☐ SCID other, specify: .....
- ☐ SCID, not otherwise specified
- ☐ Wiskott Aldrich syndrome
- ☐ X-linked lymphoproliferative syndrome
- ☐ Other, specify: .....
- ☐ Immune Deficiencies, not otherwise specified

Date of this transplant: ..... - ..... - .....
yyyy mm dd

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 6

NOTE: The MED-A First Report should be submitted at time of mobilisation for all patients with autoimmune diseases

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

Neurologist Name_____
Address_____
Fax_____ Email_____

AUTOIMMUNE DISORDERS – I

Classification	Involved Organs/Clinical Problem	Reason for Transplant	Miscellaneous
CONNECTIVE TISSUE DISEASE			
☐ Systemic sclerosis	☐ diffuse cutaneous	☐	☐ Scl 70 positive
	☐ limited cutaneous	☐	☐ ACA positive
	☐ lung parenchyma	☐	
	☐ pulmonary hypertension	☐	
	☐ systemic hypertension	☐	
	☐ renal (biopsy type:_____)	☐	
	☐ oesophagus	☐	
	☐ other GI tract		
	☐ Raynaud	☐	
	☐ CREST	☐	
	☐ other, specify:_____	☐	
☐ Systemic lupus erythematosus	☐ renal (biopsy type:_____)	☐	☐ ds DNA (_____)
	☐ CNS (type:_____)	☐	☐ complement (_____)
	☐ PNS (type:_____)	☐	☐ other (_____)
	☐ lung	☐	
	☐ serositis	☐	
	☐ arthritis	☐	
	☐ skin (type:_____)	☐	
	☐ haematological (type:_____)	☐	
	☐ vasculitis (type:_____)	☐	
	☐ other, specify:_____	☐	
☐ Sjögren syndrome	☐ SICCA	☐	
	☐ exocrine gland swelling	☐	
	☐ other organ lymphocytic infiltration	☐	
	☐ lymphoma, paraproteinemia	☐	
	☐ other, specify:_____	☐	
☐ Polymyositis-dermatomyositis	☐ proximal weakness	☐	☐ CPK
	☐ generalized weakness (including bulbar)	☐	☐ typical biopsy
	☐ pulmonary fibrosis	☐	☐ typical EMG
	☐ vasculitis (type:_____)	☐	☐ typical rash (DM)
	☐ malignancy (type:_____)	☐	
	☐ other, specify:_____	☐	
☐ Antiphospholipid syndrome	☐ thrombosis (type:_____)	☐	☐ anticardiolipin IgG
	☐ CNS (type:_____)	☐	☐ anticardiolipin IgM
	☐ abortion	☐	
	☐ skin (livido, vasculitis)	☐	
	☐ hematological (type:_____)	☐	
	☐ other, specify:_____	☐	
☐ other, specify:_____			

Date of this transplant: ..... - ..... - ..... (*yyyy - mm - dd*)

CIC: Unique Patient Number (UPN): .....

Minimum Essential Data - A

First report - 100 days after transplant

DISEASE CLASSIFICATION SHEET 7

NOTE: The MED-A First Report should be submitted at time of mobilisation for all patients with autoimmune diseases

EBMT Centre Identification Code (CIC) ..... Hospital Unique Patient Number .....
CIBMTR/ABMTR Code .....

AUTOIMMUNE DISORDERS – II

Classification	Involved Organs/Clinical Problem	Reason for Transplant	Miscellaneous

Neurologist Name_____
Address_____
Fax_____ Email_____

VASCULITIS

☐ Wegener granulomatosis	☐ upper respiratory tract	☐	☐ c-ANCA positive
	☐ pulmonary	☐	
	☐ renal (biopsy type:_____)	☐	
	☐ skin	☐	
	☐ other, specify:_____	☐	
☐ Classical polyarteritis nodosa			
	☐ renal (type:_____)	☐	
☐ Classical	☐ mononeuritis multiplex	☐	☐ p-ANCA positive
☐ Microscopic	☐ pulmonary haemorrhage	☐	☐ c-ANCA positive
	☐ skin	☐	☐ hepatitis serology
	☐ GI tract	☐	
	☐ other, specify:_____	☐	

Other vasculitis:
☐ Churg-Strauss
☐ Giant cell arteritis
☐ Takayasu
☐ Behçet's syndrome
☐ overlap necrotising arteritis
☐ other, specify:_____

ARTHRITIS

☐ Rheumatoid arthritis	☐ destructive arthritis	☐
	☐ necrotising vasculitis	☐
	☐ eye (type:_____)	☐
	☐ pulmonary	☐
	☐ extra articular (specify:_____)	☐
	☐ other, specify:_____	☐
☐ Psoriatic arthritis/psoriasis	☐ destructive arthritis	☐
	☐ psoriasis	☐
	☐ other, specify:_____	☐

☐ Juvenile idiopathic arthritis (JIA): systemic (Stills disease)
☐ Juvenile idiopathic arthritis: Oligoarticular
☐ Juvenile idiopathic arthritis: Polyarticular
☐ Juvenile idiopathic arthritis: other, specify:_____
☐ Other arthritis: .....

MULTIPLE SCLEROSIS

☐ Multiple sclerosis	☐ primary progressive	☐
	☐ secondary progresive	☐
	☐ relapsing/remitting	☐
	☐ other:_____	☐

OTHER NEUROLOGICAL AUTOIMMUNE DISEASE
☐ Myasthenia gravis
☐ Other autoimmune neurological disorder, specify:_____

HAEMATOLOGICAL AUTOIMMUNE DISEASES
☐ Idiopathic thrombocytopenic purpura (ITP)
☐ Hemolytic anemia
☐ Evan syndrome
☐ other autoimmune cytopenia, specify:_____

BOWEL DISEASE
☐ Crohn's disease
☐ Ulcerative colitis
☐ Other autoimmune bowel disease, specify:_____

Date of this transplant: ..... - ..... - ..... (*yyyy - mm - dd*)

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CONTACT

JACIE Accreditation Office
EBMT Secretariat
Dept. of Haematology
Esc 4, 3º
Villarroel 170
08036 Barcelona
SPAIN

Tel.: +34 93 454 9543
Fax: +34 93 453 1263
Skype: jacie-office
email: jacie@ebmt.org
Website: www.jacie.org