
STANDARDS FOR HEMATOPOIETIC PROGENITOR CELL COLLECTION, PROCESSING & TRANSPLANTATION

**FROM THE JOINT ACCREDITATION COMMITTEE
OF ISCT-EUROPE AND EBMT**

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NOTICE

These Standards are designed to provide minimum guidelines for facilities and individuals performing hematopoietic 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 their practices and procedures to determine whether additional standards apply. The Joint Accreditation Committee of ISCT-Europe and EBMT disclaims any responsibility for setting maximum standards and expressly does 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 these Standards for Hematopoietic Progenitor Cell Collection, Processing and Transplantation is to promote quality medical and laboratory practice in hematopoietic progenitor cell transplantation. These Standards apply to hematopoietic progenitor cells isolated from bone marrow or peripheral blood and to all phases of collection, processing, and administration of these cells. This includes, but is not limited to, a variety of manipulations including removal or enrichment of various cell populations, expansion of hematopoietic cell populations, cryopreservation and infusion. For purposes of these Standards, the following definitions apply. Hematopoietic progenitor cells include primitive pluripotent hematopoietic cells capable of self-renewal as well as maturation into any of the hematopoietic lineages, including committed and lineage-restricted progenitor cells, unless otherwise specified, regardless of tissue source. Hematopoietic progenitor cells also include therapeutic cells as defined in this section. Hematopoietic progenitor cell therapy refers to the infusion of hematopoietic products with the intent of providing effector cells in the treatment of disease or support of other therapy.

These Standards also apply to the transplantation of umbilical cord blood cells under the clinical standards for transplantation of allogeneic or autologous hematopoietic progenitor cells, as appropriate. These Standards do not apply to the collection, processing or banking of cord blood cells. These Standards also do not address the collection, processing or administration of erythrocytes, mature granulocytes, platelets, plasma or plasma-derived products intended for transfusion support.

Additional JACIE publications will address the medical and laboratory practice of other cellular therapies such as genetic modification of hematopoietic and non-hematopoietic tissues intended to permanently or transiently engraft in the recipient and/or be used in the treatment of disease.

Every effort has been made in these Standards to incorporate sound recommendations fostering quality medical and laboratory practice in hematopoietic progenitor cell therapy. However, no Standards can guarantee the successful outcome of such therapies. JACIE Standards are minimal performance guidelines that may be exceeded as deemed appropriate by the responsible personnel in individual facilities. Clinical Programme Directors, Collection Facility and Laboratory Directors/Medical Directors assume responsibility for adopting JACIE Standards as appropriate to the facility, and for setting more rigorous internal requirements where appropriate. Attempts have been made to conform these Standards to existing European clinical practices; however, regulations are changed often and compliance with these Standards does not guarantee compliance with all regulations. In all cases, personnel must follow all applicable laws and regulations. These Standards will be reviewed and revised as appropriate based on developments in the field.

The current JACIE Standards for Hematopoietic Progenitor Cell Collection, Processing and Transplantation were developed after a review of the first edition of FACT Standards by the Foundation for the Accreditation of Hematopoietic Cell Therapy (FACT) Standards Committee. These draft Standards were submitted for comment from the public and from the membership of the parent organizations, International Society for Cellular Therapy (ISCT) and the American Society of Blood and Marrow Transplantation (ASBMT). Following a review of comments and legal review, this second edition was adopted by the FACT Board of Directors. These standards have been modified and adopted by JACIE.

The second edition of the JACIE Standards differs from the first in several ways. Section A now contains only terminology, definitions and abbreviations. Product names have been changed to be consistent with the International Council for Commonality in Blood Banking Automation nomenclature, in an effort to facilitate international cooperation and bar coding in the future. There are no specific standards in this section. The requirements for Policies and Procedures, Validation and Qualification, Quality Management and Safety previously found in section A have been customized and placed in the specific Clinical, Collection and/or Laboratory sections as appropriate.

In the Clinical Section B, data management standards now include the specific items required on the Transplant Essential Data (TED) forms of the International Bone Marrow Transplant Registry (IBMTR)/Autologous Blood and Marrow Transplant Registry (ABMTR) and MED A forms of the European Blood and Marrow group (EBMT). This does not mandate reporting to the IBMTR/ABMTR/EBMT. Specific standards have been added for Paediatric transplantation. Standards for hematopoietic progenitor cell donor evaluation and selection have been moved to the Clinical Section; and the therapy administration standards have been expanded.

In the Collection Section C, responsibilities for donor evaluation have been clarified. In the laboratory Section D, labelling standards have been consolidated into a single table; and packaging and transportation standards have been clarified.

Finally, the individual items in each section have been reorganized as applicable in a parallel fashion to facilitate ease of locating information. In addition, a comparison with the First Edition of JACIE Standards is provided in Appendix II.

These Standards are effective June 26, 2003.

JACIE ACCREDITATION

The basis for JACIE Accreditation is documented compliance with the current edition of these Standards. 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 hematopoietic cell therapy, who have attended inspector training and who have a working knowledge of JACIE Standards and of their application to various aspects of the hematopoietic progenitor cell facility.

Facilities performing hematopoietic progenitor cell collection, processing, storage and/or transplantation may apply for voluntary accreditation by JACIE as follows:

- 1) A clinical hematopoietic 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 JACIE Standards and have a clearly defined contractual or reporting relationship.
- 2) A hematopoietic 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 hematopoietic progenitor cell collection services for one or more clinical transplant programs, or in conjunction with a cell processing laboratory if the services of hematopoietic progenitor cell collection and processing/storage are functionally linked. An accredited hematopoietic progenitor cell collection facility may provide services for clinical transplant programs that are or are not JACIE accredited, but shall use a processing laboratory that meets JACIE Standards.
- 3) A hematopoietic 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 hematopoietic progenitor cell products for clinical programme(s) or collection facilities. A JACIE-accredited laboratory may provide services for clinical transplant programs and/or collection services that are or are not JACIE-accredited.

Accreditation of the clinical hematopoietic progenitor cell transplantation programme may be for allogeneic transplantation, autologous transplantation or both. The accreditation may cover hematopoietic progenitor cells derived from bone marrow and/or peripheral blood.

Accredited facilities will be re-inspected every three years or in response to complaints or information that a facility may be non-compliant with the Standards, or as determined by the JACIE Board of Directors. 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-JACIE International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release. There is a separate application and inspection process for NETCORD-FACT-JACIE accreditation. NETCORD-FACT-JACIE Standards for Cord Blood do not cover the clinical transplantation of cord blood cells. Cord Blood Bank accreditation is determined by evaluation of written information provided by the applicant facility and by on-site inspection. All inspections are conducted by persons qualified by training and experience in hematopoietic progenitor cell therapy and cord blood banking, who have attended cord blood bank inspector training, and who have a working knowledge of the NETCORD-FACT-JACIE Standards and of their application in the various cord blood banking activities.

PART A: TERMINOLOGY, ABBREVIATIONS AND DEFINITIONS

A1.000 TERMINOLOGY

A2.000 ABBREVIATIONS

A3.000 DEFINITIONS

PART A: TERMINOLOGY, ABBREVIATIONS AND DEFINITIONS

A1.000 TERMINOLOGY

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

A2.000 ABBREVIATIONS

The following abbreviations cover terms used in these Standards.

Abbreviations

<i>ABMTR</i>	Autologous Blood and Marrow Transplant Registry.
<i>ABO</i>	Human erythrocyte antigens, A, B, O.
<i>Ag</i>	Antigen.
<i>Anti-</i>	Antibody to the antigen designated.
<i>C</i>	Centigrade.
<i>CMV</i>	Cytomegalovirus.
<i>DNA</i>	Deoxyribonucleic acid.
<i>EBMT</i>	European Group for Blood and Marrow Transplantation
<i>EFI</i>	European Federation for Immunogenetics
<i>FACT</i>	Foundation for the Accreditation of Cellular Therapy
<i>GVHD</i>	Graft versus host disease.
<i>HLA</i>	Human Leukocyte Antigen.
<i>HBc</i>	Hepatitis B core.
<i>HBsAg</i>	Hepatitis B surface antigen.
<i>HCV</i>	Hepatitis C virus.
<i>HIV</i>	Human immunodeficiency virus.
<i>HPC</i>	Hematopoietic progenitor cells.
<i>HTLV</i>	Human T-lymphotropic virus.
<i>IBMTR</i>	International Bone Marrow Transplant Registry.
<i>IRB</i>	Institutional Review Board.
<i>ISCT</i>	International Society for Cellular Therapy
<i>JACIE</i>	Joint Accreditation Committee of ISCT-Europe (formally Euro-ISHAGE and EBMT.
<i>Rh</i>	Human erythrocytes antigen, Rhesus.

A3.000 DEFINITIONS

Allogeneic refers to cells obtained from a donor and intended for infusion into a genetically distinct recipient.

Autologous refers to cells obtained from a patient and intended for infusion into that patient.

Cellular therapy refers to the infusion of products with the intent of providing effector cells in the treatment of disease or support of other therapy.

Clinical Transplantation Programme (Programme) consists of an integrated medical team housed in geographically contiguous or proximate space with a single Programme Director, common staff, training programs, protocols, and quality assessment systems. The Programme shall use hematopoietic cell collection and processing facilities that meet JACIE Standards. Clinical programs that include non-contiguous institutions in the same metropolitan area shall demonstrate

common protocols, staff training procedures, quality assessment systems, 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 programme, do not fulfil the intent of these Standards. In contrast, collection facilities and/or processing laboratories serving one or more clinical programs are acceptable.

Collection includes any procedure for harvesting cells regardless of technique or source.

Competency is the adequate ability to perform a specific procedure according to direction.

Cord blood refers to hematopoietic progenitor cells collected from placental and umbilical cord blood vessels after the umbilical cord is clamped and/or severed.

Cord Blood Bank is a facility in which hematopoietic progenitor cells collected from the placental and umbilical cord blood vessels are processed, cryopreserved, and/or stored.

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

Collection Facility Director is an individual with a doctoral degree, qualified by postdoctoral training or experience for the scope of activities carried out in the collection facility. The Collection Facility Director is responsible for all technical procedures and administrative operations of the collection facility. The Collection Facility Director should participate regularly in educational activities related to the field of hematopoietic cell collection and/or transplantation. The Collection Facility Director may also serve as the Medical Director if appropriately credentialed.

Collection Facility Medical Director is a physician licensed in the jurisdiction in which the collection facility is located. This individual is directly responsible for the pre-collection evaluation of the donor, final approval of the prospective donor for the collection procedure, conduct of the collection procedure, care of any complications arising from collection and compliance of the collection facility with these Standards. The Collection Facility Medical Director should participate regularly in educational activities related to the field of hematopoietic cell collection and/or transplantation.

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

Laboratory Medical Director is a licensed physician with postdoctoral training in hematopoietic cell processing and/or transplantation. This individual is directly responsible for the medical aspects of the processing

procedures. The Medical Director should participate regularly in educational activities related to the field of hematopoietic cell processing and/or transplantation. The Medical Director may also serve as the Laboratory Director if appropriately credentialed.

Programme Director is the physician responsible for all administrative and medical operations of the clinical transplantation programme, including compliance with these Standards. The Programme Director shall be appropriately licensed to practice medicine in the European country where he/she works in one or more of the following specialties: Hematology, Medical Oncology, Immunology, and/or Paediatric Hematology/Oncology. Non-board certified physicians who completed medical training prior to 1985 may serve as Programme Director if they have documented experience and published contributions in the field of hematopoietic progenitor cell transplantation extending over ten years. The Programme Director should participate regularly in educational activities related to the field of hematopoietic stem cell transplantation.

Expansion refers to growth of one or more cell populations in an in vitro culture system.

Gene insertion refers to the introduction of one or more exogenous genes into one or more cell populations.

Hematopoietic progenitor cells include primitive pluripotent hematopoietic cells capable of self-renewal as well as maturation into any of the hematopoietic lineages, including committed and lineage-restricted progenitor cells, unless otherwise specified, regardless of tissue source.

For purposes of these Standards, hematopoietic progenitor cells also include therapeutic cells as defined in this section.

Hematopoietic progenitor cell therapy refers to the infusion of hematopoietic cell products with the intent of providing effector functions in the treatment of disease or support of other therapy.

Human tissue refers to cells obtained from any living or cadaveric human donor or organ.

Labelling process includes steps taken to identify the original hematopoietic progenitor cell collection, any products, and any product modifications; to complete the required reviews; and to attach the appropriate labels.

Manipulation refers to an ex vivo procedure(s) that functionally or genetically alters cell populations.

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

Manipulated cell products refers to cell products that have been functionally or genetically altered ex vivo, including ex vivo expanded cells.

Minimally manipulated cell products refers to cell products that have not been subjected to an ex vivo procedure that functionally or genetically alters specific nucleated cell populations.

Mid-Level Practitioners are Physician Assistants, Nurse Practitioners and other Advanced Practitioners who provide primary patient care.

New Patient: For purposes of these Standards, a new patient refers to a separate and distinct person, not necessarily a patient not previously treated by the Clinical Programme.

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

Processing includes all aspects of manipulation, labelling, and infusion of products, regardless of source.

Products

The proper name of each product is as follows:

Hematopoietic Progenitor Cells, Apheresis (HPC-A) - hematopoietic progenitor cells collected from the peripheral blood of a donor using an apheresis technique.

Hematopoietic Progenitor Cells, Marrow (HPC-M) - hematopoietic progenitor cells aspirated from the iliac crests, sternum or other bones of a human donor.

Hematopoietic Progenitor Cells, Cord Blood (HPC-C)

Therapeutic Cells (TC) - cell products harvested or manufactured for the purpose of providing therapeutic benefit.

Therapeutic Cells, T- cells (TC-T)

Therapeutic Cells, Dendritic (TC-D)

Therapeutic Cells, Natural Killer (TC-NK)

Therapeutic Cells, Cytotoxic Lymphocyte (TC-CTL)

Therapeutic Cells, other (such as tumour-derived cells) (TC-other)

Product modifications

Plasma Reduced - cells remaining after a portion of the plasma has been depleted by sedimentation or centrifugation using devices, supplies, and techniques validated for the procedure(s).

RBC Reduced - cells remaining after depletion of mature erythrocytes by sedimentation, centrifugation, or lysis using devices, supplies, and techniques validated for the procedure(s).

B-Cell-Depleted - cells processed by negative selection for B lymphocytes.

T-Cell-Depleted - cells processed by negative selection for T lymphocytes.

Buffy Coat Enriched - cells remaining after depletion of mature erythrocytes and plasma by sedimentation or centrifugation using devices, supplies, and

techniques validated for the procedure(s). Mononuclear cell (MNC) preparations made without density gradient medium are included in this category.

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

Other Target Cell Depletion or Enrichment:

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

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

Tumour Cell Depletion – cells processed by negative selection for tumour cells.

Cryopreserved - cells frozen using devices, supplies, and techniques validated to maintain viability.

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

Proficiency test refers to an evaluation of the ability to perform laboratory procedures within acceptable limits of accuracy, through the analysis of unknown specimens distributed at periodic intervals by a source outside the facility performing the proficiency test.

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

Quality refers to conformance of a product or process with pre-established specifications or standards.

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

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

Quality control refers to a product of a quality 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 hematopoietic progenitor cell products, including testing and product release.

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

Quality management refers to an integrated programme of quality assessment, assurance, control and improvement.

Safety refers to relative freedom from harmful effects to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time.

Standard Operating Procedures Manual refers to a compilation of written detailed instructions required to perform procedures.

Standards refers to the current North American edition of the *Standards for Hematopoietic Progenitor Cell Collection, Processing & Transplantation* published by FACT and adopted by JACIE.

Syngeneic refers to cells collected from the patient's genetically identical twin.

Time of collection refers to the end of the hematopoietic cell collection procedure.

Transplantation refers to the infusion of autologous, syngeneic or allogeneic hematopoietic progenitor cells with the intent of providing transient or permanent engraftment in support of therapy of disease.

Unmanipulated hematopoietic progenitor cells refers to hematopoietic progenitor cells as obtained at the time of collection and not subjected to any form of manipulation.

Validation refers to establishment of documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes. A process is validated to evaluate the performance of a system with regard to its effectiveness based on intended use.

PART B: CLINICAL PROGRAMME STANDARDS

- B1.000 GENERAL
- B2.000 CLINICAL UNIT
- B3.000 PERSONNEL
- B4.000 QUALITY MANAGEMENT
- B5.000 POLICIES AND PROCEDURES
- B6.000 DONOR EVALUATION, SELECTION AND MANAGEMENT
- B7.000 THERAPY ADMINISTRATION
- B8.000 CLINICAL RESEARCH
- B9.000 DATA MANAGEMENT
- B10.000 RECORDS

PART B: CLINICAL PROGRAMME STANDARDS

B1.000 GENERAL

B1.100 DEFINITION OF A CLINICAL TRANSPLANTATION PROGRAMME

The Clinical Transplantation Programme consists of an integrated medical team housed in geographically contiguous or proximate space with a single Programme Director and common staff training programs, protocols, and quality management systems. The Programme shall use hematopoietic cell collection and processing facilities that meet JACIE Standards with respect to their interactions with that clinical programme. 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 programme do not fulfil the intent of these Standards.

B1.200 The Clinical Programme shall abide by all applicable governmental laws and regulations.

B1.300 PROGRAMME SIZE

B1.310 A minimum of 10 new patients shall have been transplanted during the twelve-month period immediately preceding the application for programme accreditation and annually thereafter.

B1.320 If the Programme requests accreditation for both allogeneic and autologous transplantation, a minimum of 20 new patients, including at least 10 new allogeneic patients and at least 5 new autologous patients shall have been transplanted during the twelve-month period immediately preceding the application for programme accreditation and annually thereafter.

B1.330 If accreditation for only one type of transplant (allogeneic or autologous) is being requested, 10 new recipients of transplants of that type shall have been treated during the twelve-month period immediately preceding the application for programme accreditation and annually thereafter.

B1.340 For combined adult and paediatric programs, a minimum of four new adult patients and four new paediatric patients shall have been transplanted during the twelve-month period immediately preceding the application for each type of transplant (allogeneic or autologous) for which accreditation is requested and annually thereafter.

B1.350 For programs utilizing more than one clinical site for transplantation, a minimum of four new patients shall have been transplanted per site during the twelve-month period immediately preceding the application for accreditation and annually thereafter.

B2.000 CLINICAL UNIT

B2.100 The Programme shall have:

- B2.110 A designated inpatient unit that minimizes airborne microbial contamination.
- B2.120 A designated area for outpatient care that reasonably protects the patient from transmission of infectious agents and can provide, as necessary, appropriate patient isolation, administration of intravenous fluids, medications, and/or blood products.
- B2.130 Provisions for prompt evaluation and treatment by a transplant attending physician available on a 24-hour basis.
- B2.140 Nurses experienced in the care of transplant patients.
- B2.150 A nurse/patient ratio satisfactory to cover the severity of the patients' clinical status.
- B2.160 A Collection Facility and a Hematopoietic Progenitor Cell Processing Facility that meet these Standards with respect to their interaction with that Clinical Programme.
- B2.170 A transfusion service providing 24-hour availability of CMV appropriate and irradiated blood products needed for the care of transplant patients.
- B2.180 A pharmacy providing 24-hour availability of medications needed for the care of transplant patients.
- B2.181 If clinical research is performed, the pharmacy shall have a mechanism for tracking, inventory, and secured storage of investigational drugs.
- B2.190 Programs performing allogeneic hematopoietic cell transplants shall also use HLA testing laboratories accredited by the European Federation for Immunogenetics (EFI), with the capability of carrying out deoxyribonucleic acid (DNA) - based HLA-typing.

B2.200 SAFETY REQUIREMENTS

- B2.210 The Programme shall be operated in a manner to minimize risks to the health and safety of employees, donors, volunteers, and patients. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

B2.220 There shall be procedures for biological, chemical, and radiation safety, as appropriate, and a system for monitoring training and compliance.

B2.230 Hematopoietic progenitor cells shall be handled and discarded with precautions that recognize the potential for exposure to infectious agents.

B3.000 PERSONNEL

B3.100 TRANSPLANT TEAM

A dedicated transplant team including a Programme Director and at least one other physician trained or experienced in hematopoietic progenitor cell therapy shall have been in place for at least one year prior to being eligible for accreditation.

B3.110 Centres performing paediatric transplants shall have a transplant team trained in the management of paediatric patients.

B3.120 For programs performing paediatric transplantation, there shall be at least one attending physician who is board certified/eligible in Paediatric Hematology/Oncology or Paediatric Immunology.

B3.130 For programs performing adult transplantation, there shall be at least one attending physician who is board certified/eligible in Hematology, Medical Oncology or Immunology.

B3.140 The programme shall have access to a team of licensed physicians who are trained and competent in bone marrow harvesting.

B3.200 PROGRAMME DIRECTOR

B3.210 The Programme Director shall be appropriately licensed to practice medicine in the Europe in one or more of the following specialties: Hematology, Medical Oncology, Immunology, or Paediatric Hematology/Oncology. Non-board certified physicians who completed medical training prior to 1985 may serve as Programme Director if they have documented experience and published contributions in the field of hematopoietic progenitor cell transplantation extending over ten years.

B3.220 The Programme Director shall have at least one year of specific clinical training in hematopoietic progenitor cell transplantation as defined in B3.400, or two years experience as an attending physician responsible for the clinical management of hematopoietic progenitor cell transplant patients in the inpatient and outpatient settings. The Programme Director shall have written confirmation of his/her training or experience from the Director of the programme, department, or institution in which that training or experience was obtained. The Programme Director should

participate regularly in educational activities related to the field of hematopoietic stem cell transplantation.

B3.230 The Programme Director is responsible for the administrative and clinical operations including compliance with these Standards. The Programme Director shall have oversight of all elements of the programme including the selection of patients and donors, collection of cells, and processing of cells whether internal or contracted services.

B3.231 The Programme Director shall be responsible for the quality management of the entire programme.

B3.232 The Programme Director shall be responsible for the policies and procedures for donor evaluation, selection, and pre- and post- donation care and compliance with these Standards as listed in Section B6.000.

B3.240 The Programme Director shall have oversight of the medical care provided by the Programme including medical care provided by the physicians on the transplant team. The Programme Director is responsible to verify 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 B3.300.

B3.300 OTHER ATTENDING PHYSICIANS

B3.310 Transplant Programme attending physicians shall be appropriately licensed to practice medicine in Europe, and should be board certified or eligible in one of the specialties listed in B3.210.

B3.320 Transplant Programme attending physicians should have specific clinical training in hematopoietic progenitor cell transplant medicine as defined in B3.400, and should participate regularly in educational activities related to the field of hematopoietic stem cell transplantation.

B3.400 PHYSICIAN TRAINING FOR TRANSPLANT PROGRAMME DIRECTORS AND ATTENDING PHYSICIANS

B3.410 Method of Training

B3.411 Adequate specific clinical training in hematopoietic progenitor cell transplant medicine shall be defined as a minimum of a one year experience in the management of transplant patients in both the inpatient and outpatient settings.

B3.412 Clinical training and competency shall include the management of:

- a) Autologous transplant patients for physicians in Programs requesting JACIE accreditation for autologous transplantation.
- b) Allogeneic transplant patients for physicians in Programs requesting JACIE accreditation for allogeneic transplantation.
- c) Both autologous and allogeneic transplant patients for physicians in Programs requesting JACIE accreditation for autologous and allogeneic transplantation.

B3.413 Programs transplanting paediatric patients shall have physicians experienced in treating paediatric patients.

B3.420 Cognitive Skills

B3.421 Specific training and competency in each of the following areas required for physicians in Programs requesting JACIE accreditation for autologous and/or allogeneic transplantation shall include:

- a) Indications for hematopoietic progenitor cell transplantation.
- b) Selection of appropriate patients and preparative high dose therapy regimens.
- c) Pre-transplant patient evaluation, including assessment of appropriate patient eligibility and hematopoietic progenitor cell adequacy with respect to collection.
- d) Administration of high-dose therapy.
- e) Administration of growth factors for hematopoietic progenitor cell mobilization and for post-transplant hematopoietic cell reconstitution.
- f) Management of neutropenic fever.
- g) Diagnosis and management of infectious and non-infectious pulmonary complications of transplantation.
- h) Diagnosis and management of fungal disease.
- i) Diagnosis and management of veno-occlusive disease of the liver.
- j) Management of thrombocytopenia and bleeding.
- k) Management of hemorrhagic cystitis.
- l) Management of nausea and vomiting.

- m) Management of pain.
- n) Management of terminal care patients.
- o) Documentation and reporting for patients on investigational protocols.
- p) Diagnosis and management of hematopoietic progenitor cell graft failure.

B3.422 Specific clinical training and competency in each of the following additional areas required for physicians in Programs requesting JACIE accreditation for allogeneic hematopoietic cell transplantation shall include:

- a) Identification and selection of hematopoietic progenitor cell source, including use of donor registries.
- b) Methodology and implications of human leukocyte antigen (HLA) typing.
- c) Management of patients receiving ABO incompatible hematopoietic progenitor cell products.
- d) Diagnosis and management of cytomegalovirus (CMV) infection and disease.
- e) Diagnosis and management of other viral infections in immunocompromised hosts.
- f) Diagnosis and management of acute and chronic graft versus host disease (GVHD).
- g) Diagnosis and management of post-transplant immunodeficiencies.
- h) Evaluation of chimerism.

B3.430 Procedural Skills

B3.431 The hematopoietic progenitor cell transplant physician shall be proficient in the following procedures:

- a) Hematopoietic progenitor cell product infusion.

B3.432 The hematopoietic progenitor cell transplant physician shall be knowledgeable in the following procedures:

- a) Hematopoietic progenitor cell processing.

- b) Hematopoietic progenitor cell cryopreservation.
- c) Bone marrow harvest procedures.
- d) Apheresis procedures.

B3.500 MID-LEVEL PRACTITIONERS

- B3.510 Mid-level practitioners shall be licensed to practice in the jurisdiction of the Transplant Programme.
- B3.520 Mid-level practitioners shall be trained and competent specifically in the transplant-related cognitive and procedural skills that they routinely practice. These skills include but may not be limited to those listed in B3.420 and B3.430. Mid-level practitioners should participate regularly in educational activities related to the field of hematopoietic stem cell transplantation.

B3.600 CONSULTING PHYSICIANS

- B3.610 The Transplant Programme shall have access to board eligible or certified consulting physicians from key disciplines who are capable of assisting in the management of patients requiring medical care, including but not limited to: surgery, pulmonary medicine, intensive care, gastroenterology, nephrology, infectious disease, cardiology, pathology, psychiatry and, if radiation therapy is administered, radiation oncology with experience in large-field (e.g., total body or total lymphoid) irradiation treatment protocols.
- B3.620 Programs treating paediatric patients shall have consultants, as defined in B3.610, qualified to manage paediatric patients.

B3.700 NURSES

- B3.710 Programs shall have nurses and nurse supervisors formally trained and experienced in the management of patients receiving hematopoietic progenitor cell transplants.
- B3.720 Programs treating paediatric patients shall have nurses formally trained and experienced in the management of paediatric patients.
- B3.730 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.
- B3.740 There shall be written policies for all relevant nursing procedures, including infection prevention and control, administration of the preparative regimen, transplantation of hematopoietic progenitor cells, use of immunosuppressive agents, and blood product transfusion.

B3.800 OTHER STAFF

The Programme shall have appropriate staff available to maintain support services, as follows:

- B3.810 One or more designated staff to assist in the provision of appropriate pre-transplant patient evaluation, treatment and post-transplant follow-up and care.
- B3.820 Pharmacy staff knowledgeable in the use and monitoring of pharmaceuticals used by the Transplant Programme.
- B3.830 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.
- B3.840 Social Services staff.
- B3.850 Physical Therapy staff.
- B3.860 Data Management staff sufficient to comply with Section B9.000.

B4.000 QUALITY MANAGEMENT

- B4.100 The Programme shall have a written Quality Management Plan that describes, at a minimum, the methods for oversight of patient care (including detection of errors, accidents and adverse reactions), significant outcome parameters, the means for review of aggregate data on a regular basis (audits), and requirements for meetings, review, documentation, corrective actions and reporting.
- B4.110 The Programme Director is responsible for the Quality Management Plan as it pertains to the clinical programme. The performance of this activity may be delegated to an individual within the programme with sufficient expertise.

B4.200 AUDITS

- B4.210 The programme shall develop and identify performance measures and shall establish processes for collection and analysis of data related to performance.
- B4.220 The results of such performance audits shall be used to identify improvement opportunities and strategies to achieve improvement. Audit results and improvement strategies shall be reviewed with documentation in accordance with the quality management plan.

B4.300 ERRORS, ACCIDENTS AND ADVERSE REACTIONS

- B4.310 The programme shall have a system for detecting, evaluating, documenting and reporting errors, accidents, suspected adverse

reactions and biological product deviations. Corrective actions shall be documented and reviewed by the Programme Director.

- B4.320 All suspected adverse reactions shall be evaluated promptly according to Standard Operating Procedures and reviewed by the Programme Director.
- B4.330 Documentation of adverse reactions in the Programme shall comply with institutional requirements and applicable governmental laws and regulations.
- B4.340 Where applicable, the event shall also be reported to the appropriate regulatory agency and as indicated, to the appropriate collection facility and/or processing laboratory.

B5.000 POLICIES AND PROCEDURES

- B5.100 The Programme shall have written policies and procedures addressing all appropriate aspects of the operation including, but not limited to, donor and patient evaluation, selection and treatment; consent; emergency and safety procedures; donor and patient confidentiality; quality management and improvement; errors, accidents and adverse reactions; biological product deviations; corrective actions; personnel training; competency assessment; outcome analysis; audits; facility maintenance and monitoring; disposal of medical and biohazard waste; and disaster response.
- B5.200 The Programme shall maintain a detailed Standard Operating Procedures (SOP) Manual.
 - B5.210 The Standard Operating Procedures Manual shall include:
 - B5.211 A procedure for preparing, implementing and reviewing all procedures.
 - B5.212 A standardized format for procedures, including worksheets, reports and forms.
 - B5.213 A system of numbering and/or titling of individual procedures.
 - B5.220 Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual procedure shall include:
 - B5.221 A clearly written description of the purpose.
 - B5.222 A clear description of equipment and supplies used.
 - B5.223 The objectives of the procedure, and acceptable end-points and the range of expected results where applicable.
 - B5.224 A reference section listing appropriate literature.

- B5.225 Documented approval of procedure and each procedural modification by the Programme Director or designee prior to implementation and annually thereafter.
- B5.226 Examples of correctly completed orders, worksheets, reports, labels and forms, where applicable.
- B5.300 Copies of the Standard Operating Procedures Manual shall be available in the immediate area to the facility staff at all times.
- B5.400 All personnel in the facility shall follow the Standard Operating Procedures detailed in the manual.
- B5.500 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.
- B5.600 Archived procedures and their historical sequence shall be maintained indefinitely, including the inclusive dates of use.
- B5.700 Deviations from Standard Operating Procedures shall be documented and approved, if appropriate, by the Programme Director or designee.
- B5.800 Standard Operating Procedures for all procedures shall comply with these Standards.
- B6.000 DONOR EVALUATION, SELECTION AND MANAGEMENT
- B6.100 There shall be donor evaluation procedures in place to protect the safety of the hematopoietic progenitor cell donor and recipient. Both the potentials for disease transmission from the donor to the recipient and the risks to the donor from the collection procedure shall be assessed. Donor evaluation and selection test results shall be documented.
- B6.110 There shall be written criteria for donor evaluation and selection.
- B6.120 Any abnormal findings shall be reported to the prospective donor with documentation in the donor record of recommendations made for follow-up care.
- B6.130 The use of a donor not meeting the criteria shall require documentation of the rationale for his/her selection by the transplant physician and the informed consent of the donor and the recipient.
- B6.131 Procedures shall be in place to ensure both confidentiality of donor and patient health information.
- B6.140 Issues of donor health that pertain to the safety of the collection procedure shall be communicated in writing to the collection facility staff.

- B6.150 Prospective donors shall be evaluated by medical history, physical examination and laboratory testing for the risks of the collection procedure including the possible need for central venous access and/or mobilization therapy for collection of blood cells and anaesthesia for collection of marrow. This evaluation shall be documented.
- B6.160 The medical history shall include at least the following:
- B6.161 Vaccination history.
 - B6.162 Travel history.
 - B6.163 Blood transfusion history.
 - B6.164 Questions to identify persons at high risk for significant transmissible infections as defined by the applicable governmental laws or regulations for donors of cellular and tissue-based products.
- B6.170 Within 30 days prior to collection, each donor shall be tested for evidence of infection by the following communicable disease agents:
- B6.171 Human immunodeficiency virus, type 1
 - B6.172 Human immunodeficiency virus, type 2
 - B6.173 Hepatitis B virus
 - B6.174 Hepatitis C virus
 - B6.175 Human T-lymphotropic virus, type I
 - B6.176 Human T-lymphotropic virus, type II
 - B6.177 *Treponema pallidum* (syphilis)
 - B6.178 Cytomegalovirus (unless previously documented to be positive)
- B6.200 ALLOGENEIC DONORS
- B6.210 A transplant physician shall document in the recipient's medical record the prospective donor's suitability before the recipient's high dose therapy is initiated.
 - B6.220 Laboratory tests required for donor selection shall be performed by a laboratory accredited or licensed in accordance with applicable governmental laws and regulations and shall include at least the following:
 - B6.221 HLA-A, B, DR typing by an EFI-accredited laboratory.
 - B6.222 ABO group and Rh type and appropriate red cell compatibility with the recipient.

B6.223 Pregnancy assessment for all female donors of childbearing potential.

B6.300 AUTOLOGOUS DONORS

B6.310 Laboratory tests required for donor selection shall be performed by a laboratory accredited or licensed in accordance with applicable governmental laws and regulations using one or more tests approved by the applicable governmental laws or regulations for that purpose and shall include at least the following:

B6.311 ABO group and Rh type.

B6.312 Pregnancy assessment for all female donors of childbearing potential.

B6.400 DONOR CONSENTS

B6.410 ALLOGENEIC DONORS

B6.411 Informed consent from the donor shall be obtained and documented by a licensed physician or other health care provider familiar with the collection procedure before the high dose therapy of the recipient is initiated.

B6.412 The procedure shall be explained in terms the donor can understand, and shall include information about the significant risks and benefits of the procedure and tests performed to protect the health of the donor and recipient and the rights of the donor to review the results of such tests.

B6.413 The donor shall have an opportunity to ask questions and the right to refuse to donate.

B6.414 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.

B6.415 If the donor's name is to be added to a hematopoietic progenitor cell donor registry, specific informed consent and authorization to release the donor's health information as appropriate shall be obtained and documented in advance.

B6.420 AUTOLOGOUS DONORS

B6.421 Informed consent from the patient shall be obtained and documented by a licensed physician or other health care provider familiar with the collection procedure.

B6.422 The procedure shall be explained in terms the patient can understand, and shall include information about the significant risks and benefits of the procedure and tests

performed to protect the health of the patient and the rights of the patient to review the results of such tests.

B6.423 The patient shall have an opportunity to ask questions and the right to refuse to donate.

B6.424 In the case of a minor patient, informed consent shall be obtained from the patient's parents or legal guardian in accord with applicable law and shall be documented.

B7.000 THERAPY ADMINISTRATION

- B7.100 There shall be a written policy to ensure that the preparative regimen is administered safely.
- B7.110 The treatment orders shall include the patient height and weight, specific dates, daily doses (if appropriate) and route of each agent. Pre-printed orders should be used for protocols and standardized regimens.
- B7.120 The pharmacist preparing the chemotherapy shall verify the doses against the protocol or standardized regimen listed on the orders.
- B7.130 Prior to administration of chemotherapy, two 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.
- B7.200 There shall be a written policy to ensure safe administration of hematopoietic cell products.
- B7.210 Two qualified persons shall verify the identity of the recipient and the product prior to the infusion of the product.
- B7.220 There shall be documentation in the patient's medical record of the unit identifier for all infused products.

B8.000 CLINICAL RESEARCH

- B8.100 If required by applicable regulations, Programs shall have formal review of investigational treatment protocols and patient consent forms by a mechanism that is approved by the local ethics committee and governmental institutions in each country as applicable.
- B8.200 Documentation for all research protocols performed by the Programme, including all audits, documentation of Institutional Review Board approval, correspondence with regulatory agencies, and any adverse outcomes, shall be maintained in accordance with institutional policies and applicable laws and regulations.
- B8.300 For clinical research, informed consent shall be obtained from each research subject, or his/her legally authorized representative, in language he or she can understand and under circumstances that minimize the possibility of coercion or undue influence. The research subject shall be given the opportunity to ask questions and to have these answered to his/her satisfaction, and to withdraw from the research without prejudice. Informed consent for a research subject shall contain at least the following elements and comply with applicable laws and regulations:

- B8.310 An explanation of the research purposes, a description of the procedures to be followed and the identification of experimental procedures.
- B8.320 The expected duration of the subject's participation.
- B8.330 A description of the reasonably expected risks, discomforts, benefits to the subject or others, and alternative procedures.
- B8.340 A statement of the extent to which confidentiality will be maintained.
- B8.350 An explanation of the extent of compensation for injury.
- B8.400 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.
- B9.000 DATA MANAGEMENT
- B9.100 The Programme shall keep complete and accurate patient records.
- B9.200 The Programme shall collect all the data contained in the Transplant Essential Data Forms of the EBMT or IBMTR (See Appendix I).
- B9.300 Each transplant programme shall use its data to periodically audit patient outcomes.
- B10.000 RECORDS
- B10.100 Clinical Unit Records
- Records related to quality control, personnel training or competency, facility maintenance, facility management, or other general facility issues shall be retained for 10 years by the clinical transplant programme, although not all need be immediately available.
- B10.200 Patient Care Records
- Patient care records including consents shall be maintained in a confidential manner as required by applicable governmental laws and regulations.
- B10.300 Research Records
- Research records shall be maintained in a confidential manner as required by applicable governmental laws and regulations.
- B10.400 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

- B10.410 If two or more facilities participate in the collection, processing or transplantation of the product, the records of each facility must show plainly the extent of its responsibility.
- B10.420 The Programme shall furnish to other facilities involved in the collection or processing of the product, transplant outcome data in so far as they concern the safety, purity and potency of the product involved.

PART C: HEMATOPOIETIC PROGENITOR CELL COLLECTION STANDARDS

C1.000	GENERAL
C2.000	HEMATOPOIETIC PROGENITOR CELL COLLECTION FACILITY
C3.000	PERSONNEL
C4.000	QUALITY MANAGEMENT
C5.000	POLICIES AND PROCEDURES
C6.000	DONOR EVALUATION AND MANAGEMENT
C7.000	HEMATOPOIETIC PROGENITOR CELL COLLECTION
C8.000	LABELS
C9.000	RECORDS

PART C: HEMATOPOIETIC PROGENITOR CELL COLLECTION STANDARDS

C1.000 GENERAL

- C1.100 These Standards apply to marrow and peripheral blood progenitor cells and therapeutic cell collection activities.
- C1.200 The Collection Facility shall abide by all applicable governmental laws and regulations.

C2.000 HEMATOPOIETIC PROGENITOR CELL COLLECTION FACILITY

- C2.100 There shall be adequate and confidential space for donor examination and evaluation.
- C2.200 There shall be emergency medical care available for the donor, including:
 - C2.210 A transfusion facility or blood bank providing 24-hour blood product support including irradiated blood products and products suitable for CMV-negative recipients.
 - C2.220 An intensive care unit and emergency services.
- C2.300 There shall be a designated area for appropriate preparation and storage of the reagents and equipment needed and for the performance of the collection procedure.
- C2.400 Procedures that will require general or regional anaesthesia shall be performed by a licensed, board-certified, or board-eligible anaesthesiologist.
- C2.500 Central venous catheters shall be placed by a licensed physician qualified to perform the procedure.
 - C2.510 Adequacy of line placement shall be documented.
- C2.600 Hematopoietic growth factor administration shall be under the supervision of a physician experienced in the management of persons receiving these agents.
- C2.700 SAFETY
 - C2.710 Each collection facility shall be operated in a manner to minimize risks to the health and safety of employees, donors, volunteers, and patients. Suitable quarters, environment, and equipment shall be available to maintain safe operations.
 - C2.720 There shall be procedures for biological, chemical, and radiation safety, as appropriate, and a system for monitoring training and compliance.
 - C2.730 Hematopoietic progenitor cell collections shall be handled and discarded with precautions that recognize the potential for transmission of infectious agents.

C3.000 PERSONNEL

- C3.100 There shall be a Collection Facility Director who is an individual with a relevant doctoral degree, qualified by postdoctoral training or experience for the scope of activities carried out in the collection facility. The Collection Facility Director is responsible for all technical procedures and administrative operations of the collection facility. The Collection Facility Director should participate regularly in educational activities related to the field of hematopoietic cell collection and/or transplantation. The Collection Facility Director may also serve as the Medical Director if appropriately credentialed.
- C3.110 The Collection Facility Director shall have at least one year's experience in the collection procedure, and shall have performed or supervised at least 10 collection procedures of each type (marrow and/or peripheral blood hematopoietic progenitor cells) for which the collection facility is requesting accreditation.
- C3.200 There shall be a Collection Facility Medical Director who is a licensed physician with postdoctoral training in hematopoietic cell collection and/or transplantation. This individual is directly responsible for the medical care of patients undergoing the apheresis procedure. The Medical Director should participate regularly in educational activities related to the field of hematopoietic cell collection and/or transplantation. The Medical Director may also serve as the Collection Facility Director if appropriately credentialed.
- C3.210 The Collection Facility Medical Director or designee is responsible for the pre-collection evaluation of the prospective donor at the time of donation, performance of the collection procedure and supervision of assistants for the procedure, care of any complications resulting from the collection procedure, and compliance with these Standards.
- C3.220 The Collection Facility Medical Director shall have at least one year's experience in the collection procedure, and shall have performed or supervised at least 10 collection procedures of each type (marrow and/or peripheral blood hematopoietic progenitor cells) for which the collection facility is requesting accreditation.
- C3.300 There shall be adequate numbers of trained support personnel available at the facility where the collection is performed.
- C3.310 The training, continued education and continued competency for the performance of operations shall be documented.

C4.000 QUALITY MANAGEMENT

- C4.100 The Collection Facility shall have a written Quality Management Plan that describes, at a minimum, the methods for oversight of donor care (including detection of errors, accidents and adverse reactions), significant

outcome parameters, the means for review of aggregate data on a regular basis (audits), validation of significant processes of the Collection Programme and requirements for meetings, review, documentation, corrective actions and reporting.

C4.110 The Collection Facility Director is responsible for the Quality Management Plan as it pertains to the Collection Facility.

C4.120 The Collection Facility shall establish and maintain a programme of quality management, under the supervision of a designated person. The individual shall review and approve policies and procedures that document compliance with regulatory requirements and standards, and the performance of quality audits.

C4.130 Protocols shall be developed, implemented, and documented for the validation or qualification of significant products of facilities, processes, equipment, reagents, labels, containers, packaging materials, and computer systems. Determination of which elements are to be validated or qualified shall be made by the Collection Facility Director.

C4.140 Evaluation of validation studies and audits shall be reviewed with documentation of approval by the appropriate individual from the quality management programme.

C4.200 LABORATORY TESTING

C4.210 Tests required by these Standards shall be performed in a laboratory accredited or licensed in accordance with applicable governmental laws and regulations.

C4.300 SUPPLIES AND REAGENTS

C4.310 Reagents used in collection of products shall be of appropriate grade for the intended use and shall be sterile.

C4.320 Procedures for production of in-house reagents shall be validated.

C4.330 Each supply and reagent used in the collection of the product shall be examined visually for damage or evidence of contamination as it comes into inventory. Such examination shall include inspection for breakage of seals, abnormal colour and expiration date.

C4.340 All supplies and reagents used in the collection of products shall be stored in a safe, sanitary, and orderly manner.

C4.350 Lot numbers and expiration dates of reagents and disposables shall be recorded.

C4.400 EQUIPMENT

C4.410 Equipment used in the collection of products shall be maintained in a clean and orderly manner and located so as to facilitate cleaning, calibration and maintenance.

- C4.420 The equipment shall be observed, standardized and calibrated on a regularly scheduled basis as described in the Standard Operating Procedures Manual and according to the Manufacturer's recommendations.
- C4.500 REVIEW OF COLLECTION RECORDS
- C4.510 Records pertinent to the product collected shall be regularly reviewed by the Collection Facility Director or designee.
- C4.520 A thorough investigation, including resolution and outcome of any adverse event or the failure of a product to meet any of its specifications shall be made and documented.
- C4.600 ERRORS, ACCIDENTS AND ADVERSE REACTIONS
- C4.610 Each Collection Facility shall have a system for detecting, evaluating, documenting and reporting errors, accidents, suspected adverse reactions, biological product deviations and complaints. Corrective actions shall be documented and reviewed by the Collection Facility Director.
- C4.620 All suspected clinical adverse reactions to the collection of cells shall be evaluated promptly according to Standard Operating Procedures, and reviewed by the Collection Facility Medical Director.
- C4.630 A written evaluation of reported adverse reactions to the collection of cells shall be included as part of the hematopoietic progenitor cell collection record and made available to the donor's physician.
- C4.640 Where applicable, the event shall also be reported to the appropriate regulatory agency, clinical programme and cell processing laboratory as appropriate.
- C4.700 OUTCOME ANALYSIS
- C4.710 Documentation and review of product quality shall be part of the ongoing quality programme.
- C4.720 There shall be ongoing review of the products collected.
- C4.730 All suspected adverse reactions to the collection of a product shall be evaluated promptly and reviewed by the Collection Facility Medical Director.

C4.740 Documentation and review of time to engraftment after hematopoietic progenitor cell infusion shall be part of the on-going quality management programme.

C5.000 POLICIES AND PROCEDURES

- C5.100 The Collection Programme shall have written policies and procedures addressing all aspects of the operation including, but not limited to, screening, consent, collection, treatment, emergency and safety procedures, donor and patient confidentiality, quality management and improvement, errors, accidents and adverse reactions; biological product deviations, corrective actions, personnel training, competency assessment, outcome analysis, audits, labelling, storage, transportation, expiration dates, release and exceptional release, disposal of medical and biohazard waste, equipment and supplies, maintenance and monitoring, cleaning and sanitation procedures, and a disaster plan.
- C5.200 The Collection Programme shall maintain a detailed Standard Operating Procedures (SOP) Manual.
- C5.210 The Standard Operating Procedures Manual shall include:
- C5.211 A procedure for preparing, implementing and reviewing all procedures.
- C5.212 A standardized format for procedures, including worksheets, reports and forms.
- C5.213 A system of numbering and/or titling of individual procedures.
- C5.220 Procedures shall be sufficiently detailed and unambiguous to allow qualified technical staff to follow and complete the procedures successfully. Each individual procedure requires:
- C5.221 A clearly written description of the purpose.
- C5.222 A clear description of equipment and supplies used.
- C5.223 The objectives of the procedure, and acceptable end-points and the range of expected results where applicable.
- C5.224 A reference section listing appropriate literature.
- C5.225 Documented approval of procedure and each procedural modification by the Collection Facility Director or designee prior to implementation and annually thereafter.
- C5.226 Examples of correctly completed orders, worksheets, reports, labels and forms, where applicable.
- C5.300 Copies of the Standard Operating Procedures Manual shall be available in the immediate area to the facility staff at all times.
- C5.400 All personnel in the facility shall follow the Standard Operating Procedures detailed in the manual.

- C5.500 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.
- C5.600 Archived procedures and their historical sequence shall be maintained indefinitely, including the inclusive dates of use.
- C5.700 Deviations from Standard Operating Procedures shall be documented and approved, if appropriate, by the Collection Facility Director or designee.
- C5.800 Standard Operating Procedures for all procedures shall comply with these Standards.
- C6.000 DONOR EVALUATION AND MANAGEMENT
- C6.100 In the case of more than one collection from the same donor, the tests in B6.170 as appropriate, shall have been performed within 30 days prior to each collection.
- C6.200 There shall be written documentation of an interim assessment of donor suitability for the collection procedure by a qualified person immediately prior to each collection procedure.
- C6.300 For donors of peripheral blood products, a complete blood count, including platelet count, shall be performed within 72 hours prior to the first collection and within 24 hours before each subsequent apheresis.
- C7.000 HEMATOPOIETIC PROGENITOR CELL COLLECTION
- C7.100 Collection of hematopoietic progenitor cells shall be performed according to written procedures in the facility's Standard Operating Procedures manual.
- C7.200 Before collection of marrow or peripheral blood progenitor cells is undertaken, there must be a written order for the collection from a physician regarding timing and procedural details of collection and goals of collection.
- C7.300 Methods for collection shall employ aseptic technique and shall use procedures validated to result in acceptable progenitor cell viability and recovery.
- C7.400 The collected cells shall be packaged in a closed sterile container and labelled.
- C7.410 For marrow and peripheral blood cells, the hematopoietic progenitor cells shall be packaged in transfer packs approved for human cells.

- C7.420 Marrow cells shall be filtered to remove particulate material prior to final packaging, distribution or transplantation using sterile filters that are non-reactive with blood.
- C7.500 Procedures for transportation of the collected product shall be designed to protect the integrity of the product being shipped and the health and safety of facility personnel. Frozen or non-frozen products that leave the facility or are transported on public roads shall be shipped in an outer shipping container.
- C7.510 The primary product container shall be placed in a secondary container and sealed to prevent leakage.
- C7.520 The outer shipping container should be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.
- C7.530 The product shall be shipped to the processing laboratory at a temperature defined in the Standard Operating Procedure Manual.
- C8.000 LABELS
- C8.100 LABELING OPERATIONS
- C8.110 Labelling operations shall be conducted in a manner adequate to prevent mislabelling of products.
- C8.120 The labelling operation shall include the following quality management elements:
- C8.121 Container labels shall be held upon receipt from the manufacturer pending review and proofing against a copy approved by the Collection Facility Director or designee to ensure accuracy regarding identity, content, and conformity.
- C8.122 Stocks of unused labels representing different products shall be stored in an orderly manner to prevent errors. Stocks of obsolete labels shall be destroyed.
- C8.123 A system of checks in labelling procedures shall be used to prevent errors in translating information to container labels.
- C8.124 All labelling shall be clear and legible and printed using moisture-proof ink.
- C8.130 Labels shall be affixed or attached firmly to the container.
- C8.140 The proper name and significant modification(s) shall be noted on the label.

- C8.150 Products that are subsequently re-packaged into new containers shall be labelled with new labels as appropriate. Records to allow tracking of products including collection or processing facility identity, unique numeric or alphanumeric identifier, collection date and time, product identity, donor and recipient information on the original container shall be maintained.
- C8.160 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.
- C8.170 The product label shall be complete. Not applicable (NA) may be used when appropriate.
- C8.180 Labelling requirements, if any, required by applicable governmental laws or regulations shall be observed.
- C8.200 PRODUCT IDENTIFICATION
- C8.210 Each product shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to relate any product to its donor, the donor's medical record, and to all records describing the handling and final disposition of the product. If a single product is divided in multiple containers, there shall be a system of identifying each container.
- C8.220 Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the product. Supplementary identifiers shall not obscure the original identifier. The facility associated with each identifier shall be designated.
- C8.221 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 original donor.
- C8.230 Products shall be identified according to the proper name of the product as defined in A3.000, including the appropriate modifiers.
- C8.300 LABEL CONTENT
- C8.310 PARTIAL LABEL
- C8.311 If the container is capable of bearing only a partial label, the container shall show as a minimum the unique identifier of the product, proper name of the product as well as the name and identifier of the intended recipient, if known.
- C8.312 Additional information, as required in Section D8.300, shall be provided with the product when the product is distributed.

C8.320 LABELING AT THE END OF COLLECTION

C8.321 Labelling at the end of collection shall occur before the container is removed from the proximity of the donor.

C8.322 At the end of collection in the operating room or apheresis unit, the label on the primary container shall bear the information in the Table D8.310.

C8.330 BIOHAZARD LABEL

C8.331 A biohazard label shall be applied to each product prior to release from the Collection Facility if any test shows evidence of infection due to communicable disease agent(s) as designated in B6.171 – B6.177.

C8.332 A biohazard label shall be applied to each product if testing was not performed or final results are not available.

C9.000 RECORDS

C9.100 Collection Facility Records

Records related to quality control, personnel training or competency, facility maintenance, facility management, or other general facility issues shall be retained for 10 years by the collection facility, although not all need be immediately available.

C9.200 Patient Care Records

Patient care records including consents shall be maintained in a confidential manner as required by applicable governmental laws and regulations.

C9.300 Research Records

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

C9.400 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

C9.410 If two or more facilities participate in the collection, processing or transplantation of the product, the records of each facility must show plainly the extent of its responsibility.

C9.420 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.

PART D: HEMATOPOIETIC PROGENITOR CELL PROCESSING STANDARDS

D1.000	GENERAL
D2.000	LABORATORY FACILITIES
D3.000	PERSONNEL
D4.000	QUALITY MANAGEMENT
D5.000	POLICIES AND PROCEDURES
D6.000	HEMATOPOIETIC PROGENITOR CELL PROCESSING
D7.000	CRYOPRESERVATION
D8.000	LABELS
D9.000	ISSUE OF PRODUCTS FOR INFUSION
D10.000	CONDITIONS FOR STORAGE
D11.000	TRANSPORTATION
D12.000	DISPOSAL
D13.000	RECORDS

PART D: HEMATOPOIETIC PROGENITOR CELL PROCESSING STANDARDS

D1.000 GENERAL

- D1.100 These Standards apply to the processing of marrow and/or peripheral blood cells by the collection facility and/or laboratory.
- D1.200 The Processing Facility shall abide by all applicable governmental laws and regulations.

D2.000 LABORATORY FACILITIES

- D2.100 The facility responsible for processing hematopoietic progenitor cells shall be of adequate space and design for the intended procedures.
- D2.200 The operation of the facility shall be divided into defined areas of adequate size for each operation to prevent improper labelling and/or contamination of the product.
- D2.300 The facility shall be operated in a manner to minimize risks to the health and safety of employees, patients, donors and visitors.
 - D2.310 The facility shall have written policies and procedures for infection control, biosafety, chemical and radiological safety, emergency response to worksite accidents, and waste disposal.
 - D2.311 Instructions for action in case of exposure to communicable disease, or to chemical, biologic and radiological hazards shall be included in the safety manual.
 - D2.320 Decontamination and disposal techniques for medical waste shall be described. Human tissue shall be disposed in such a manner as to minimize any hazard to facility personnel or the environment in accordance with applicable governmental laws and regulations.
 - D2.330 Eating, drinking, smoking, the application of cosmetics or the insertion or removal of contact lenses shall not be permitted in work areas.
 - D2.340 Gloves and protective clothing shall be worn while handling human tissue specimens. Such protective clothing shall not be worn outside the work area.
- D2.400 There shall be adequate equipment for the procedures performed at the facility.
- D2.500 The facility shall be maintained in a clean and orderly manner as established in Standard Operating Procedures.
- D2.600 The facility shall be secure to prevent the admittance of unauthorized personnel.

D3.000 PERSONNEL

- D3.100 There shall be a Laboratory Director who is an individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the cell processing facility. The Laboratory Director is responsible for all procedures and administrative operations of the processing facility, including compliance with these Standards. The Laboratory Director should participate regularly in educational activities related to the field of hematopoietic cell processing and/or transplantation. The Laboratory Director may also serve as the Medical Director if appropriately credentialed.
- D3.200 There shall be a Medical Director who is a licensed physician with postdoctoral training in hematopoietic cell processing and/or transplantation. This individual is directly responsible for the medical aspects of the processing procedures. The Medical Director should participate regularly in educational activities related to the field of hematopoietic cell processing and/or transplantation. The Medical Director may also serve as the Laboratory Director if appropriately credentialed.
- D3.300 There shall be a Laboratory Quality Management Supervisor designated by the Laboratory Director to establish and maintain systems to review, modify as necessary, and approve all procedures intended to monitor compliance with these Standards and/or the performance of the facility. The Laboratory Quality Management Supervisor should participate regularly in educational activities related to the field of hematopoietic cell processing, transplantation and quality management.
- D3.400 The Cell Processing Laboratory shall have adequate staff whose training, continuing education, and continued competency for the performance of all operations shall be documented.

D4.000 QUALITY MANAGEMENT

- D4.100 The Cell Processing Laboratory shall establish and maintain a programme of quality management as it pertains to the laboratory, under the supervision of a designated person. The individual shall review and approve policies and procedures that document compliance with regulatory requirements and standards, and the performance of quality audits.
- D4.110 Protocols shall be developed, implemented and documented for the validation or qualification of significant procedures of facilities, processes, equipment, reagents, labels, containers, packaging materials, and computer systems. Determination of which elements are to be validated or qualified shall be made by the Laboratory Director.
- D4.120 Evaluation of validation studies and audits shall be reviewed with documentation of approval by the appropriate individual from the Quality Management Programme.

D4.130 Outcome Analysis

Documentation and review of time to engraftment after hematopoietic progenitor cell infusion shall be part of the on-going quality management programme.

D4.200 TESTING OF PRODUCTS

D4.210 The Laboratory Director shall prescribe tests and procedures for measuring, assaying, or monitoring properties of the cell products essential to the evaluation of their safety and usefulness. Results of all such tests and procedures shall become part of the permanent record of the product processed.

D4.220 There shall be documentation of on-going proficiency testing for tests performed within the cell processing laboratory as designated by the Laboratory Director.

D4.230 Tests required by these Standards, not performed by the hematopoietic progenitor cell collection or laboratory facility, shall be performed in a laboratory accredited or licensed in accordance with applicable governmental laws and regulations.

D4.240 A nucleated cell count shall be performed for any product after collection and as specified in Standard Operating Procedures.

D4.250 The processing facility shall monitor and document microbial contamination of hematopoietic progenitor cells after processing and as specified in Standard Operating Procedures.

D4.251 The results of microbial cultures shall be reviewed by the Laboratory Director or designee in a timely manner.

D4.252 The recipient's transplant physician shall be notified in a timely manner of any positive microbial cultures.

D4.260 A test for the ABO group and Rh type shall be performed on each product or on blood obtained from the donor at collection. 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.

D4.261 A test for red cell compatibility shall be performed if indicated.

D4.270 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 procedure(s).

D4.300 SUPPLIES AND REAGENTS

- D4.310 Protocols shall be developed, implemented, and documented for the validation or qualification of significant products of facilities, processes, equipment, reagents, labels, containers, packaging materials, and computer systems. Determination of which elements are to be validated or qualified shall be made by the Laboratory Director.
- D4.320 Reagents used in processing and preservation of products shall be of appropriate grade for the intended use and shall be sterile.
- D4.330 Procedures for production of in-house reagents shall be validated.
- D4.340 Each supply and reagent used in the processing and infusion of the product shall be examined visually for damage or evidence of contamination as it comes into inventory. Such examination shall include inspection for breakage of seals, abnormal colour and expiration date.
- D4.350 All supplies and reagents used in the processing, testing, freezing, storage, and transplantation of products shall be stored in a safe, sanitary, and orderly manner.
- D4.360 All supplies and reagents coming into contact with products during processing, storage, and transplantation shall be sterile.
- D4.370 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

D4.400 EQUIPMENT

- D4.410 Equipment used in the processing, testing, freezing, storage, transportation, and transplantation of products shall be maintained in a clean and orderly manner and located so as to facilitate cleaning, calibration and maintenance.
- D4.420 The equipment shall be observed, standardized and calibrated on a regularly scheduled basis as described in the Standard Operating Procedures Manual and according to the Manufacturer's recommendations.
- D4.430 Sterilization equipment shall be designed, maintained and used to ensure the destruction of contaminating microorganisms.
- D4.440 Refrigerators and freezers used for the storage of specimens, hematopoietic progenitor cell products, blood products, human tissues, or reagents shall not be used for any other purpose.

D4.500 REVIEW OF PROCESSING RECORDS

- D4.510 Records pertinent to the product shall be regularly reviewed by the Laboratory Director or designee.
- D4.520 The review may be performed at appropriate periods during or after product processing, testing, freezing, and storing.
- D4.530 A thorough investigation, including resolution and outcome of any unexplained discrepancy or the failure of a product to meet any of its specifications shall be made and documented.

D4.600 ERRORS, ACCIDENTS AND ADVERSE REACTIONS

- D4.610 Each cell processing facility shall have a system for detecting, evaluating, documenting and reporting errors, accidents, suspected adverse reactions, biological product deviations and complaints. Corrective actions shall be documented and reviewed by the Laboratory Director.
- D4.620 All suspected clinical adverse reactions shall be evaluated promptly according to Standard Operating Procedures, and reviewed by the Laboratory Medical Director.
- D4.630 A written evaluation of reported adverse reactions shall be included as part of the processing record and made available to the patient's physician.
- D4.640 Where applicable, the event shall also be reported to the clinical programme, the collection facility and appropriate regulatory agency.

D5.000 POLICIES AND PROCEDURES

- D5.100 The Cell Processing Facility shall have written policies and procedures addressing all appropriate aspects of the operation including processing; emergency and safety procedures; donor and patient confidentiality; quality management and improvement; errors, accidents and adverse reactions; biological product deviations; corrective actions; personnel training; competency assessment; outcome analysis; audits; labelling; storage, including alternative storage if the primary storage device fails; transportation; expiration dates; release and exceptional release; disposal of medical and biohazard waste; equipment and supplies; maintenance and monitoring; cleaning and sanitation procedures; and a disaster plan.
- D5.200 The Cell Processing Laboratory shall maintain a detailed Standard Operating Procedures (SOP) Manual.
- D5.210 The Standard Operating Procedures Manual shall include:

- D5.211 A procedure for preparing, implementing and reviewing all procedures.
- D5.212 A standardized format for procedures, including worksheets, reports and forms.
- D5.213 A system of numbering and/or titling of individual procedures.
- D5.220 Procedures shall be sufficiently detailed and unambiguous to allow qualified technical staff to follow and complete the procedures successfully. Each individual procedure requires:
 - D5.221 A clearly written description of the purpose.
 - D5.222 A clear description of equipment and supplies used.
 - D5.223 The objectives of the procedure, and acceptable end-points and the range of expected results where applicable.
 - D5.224 A reference section listing appropriate literature.
 - D5.225 Documented approval of procedure and each procedural modification by the Laboratory Director or Medical Director as appropriate prior to implementation and annually thereafter, including the associated validation studies.
 - D5.226 Examples of correctly completed orders, worksheets, reports, labels and forms, where applicable.
- D5.300 Copies of the Standard Operating Procedures Manual shall be available in the immediate area to the facility staff at all times.
- D5.400 All personnel in the facility shall follow the Standard Operating Procedures detailed in the manual.
- D5.500 New and revised policies and procedures shall be reviewed by the staff prior to implementation. This review and associated training shall be documented.
- D5.600 Archived procedures and their historical sequence shall be maintained indefinitely, including the inclusive dates of use.
- D5.700 Deviations from Standard Operating Procedures shall be documented and approved, if appropriate, by the Laboratory Director or designee.
- D5.800 Standard Operating Procedures for all procedures shall comply with these Standards.
- D6.000 HEMATOPOIETIC PROGENITOR CELL PROCESSING
 - D6.100 Laboratory control procedures shall include:

- D6.110 The establishment of validated and appropriate assays, standards and test procedures for the evaluation of products.
- D6.120 Provisions for monitoring the reliability, accuracy, precision and performance of laboratory test procedures and instruments.
- D6.130 Identification and handling of all test samples so that they are accurately related to the corresponding product being tested, or to its donor, or to the corresponding recipient, where applicable.

D6.200 CELL PROCESSING

- D6.210 There shall be a written request from the recipient's physician before processing is initiated.
- D6.220 Processing of hematopoietic progenitor cells shall be performed according to protocols defined in the facility's Standard Operating Procedures.
- D6.230 Methods for processing shall employ aseptic technique and be validated to result in acceptable hematopoietic progenitor cell viability and recovery.
- D6.240 The objectives and acceptable end-points for each procedure shall be specified.
- D6.250 Worksheets shall be maintained for all procedures.
 - D6.251 The individual responsible for each significant step of processing shall be documented.
 - D6.252 Lot numbers and expiration dates of reagents and disposables and a record of key equipment used in processing shall be documented.
- D6.260 The Laboratory Director or designee shall review the processing record for every product.
 - D6.261 The appropriate transplant physician shall be notified when the clinically relevant processing end-points are not met.
 - D6.262 Notification and appropriate remedial actions, if taken, shall be documented in the processing record.
- D6.270 Processing using more than minimal manipulation shall only be performed with Institutional Review Board approval and with the written informed consent of the recipient of the product, or in compliance with applicable governmental laws and regulations.
- D6.280 There shall be a policy and procedure to cover the processing of ABO incompatible products.

D7.000 CRYOPRESERVATION

- D7.100 SAMPLES
- D7.110 Sample aliquots of the product, cryopreserved and stored under the same conditions as the product, should be available for testing as necessary.
- D7.200 PROCEDURES
- D7.210 Cryopreservation procedures shall be included in the cell processing facility's Standard Operating Procedures and shall describe:
- D7.211 The name and freezing criteria of the hematopoietic progenitor cell product or aliquot.
- D7.212 The cryoprotectant solution and its final concentration.
- D7.213 Cryopreservation container.
- D7.214 Acceptable range of product volume for reproducible cryopreservation.
- D7.215 Acceptable range of nucleated cell concentration of the final product after cryopreservation.
- D7.216 Cooling rate.
- D7.217 Product temperature at endpoint of controlled cooling.
- D7.218 Acceptable temperature range for storage.
- D7.300 COOLING RATE:
- D7.310 The cryopreservation procedure shall be validated.
- D7.320 The cooling rate achieved shall be recorded if a rate-controlling device is used.
- D8.000 LABELS
- D8.100 LABELING OPERATIONS
- D8.110 Labelling operations shall be conducted in a manner adequate to prevent mislabelling of products.
- D8.120 The labelling operation shall include the following quality management elements:
- D8.121 Container labels shall be held upon receipt from the manufacturer pending review and proofing against a copy approved by the Laboratory Director or designee to ensure accuracy regarding identity, content, and conformity.

- D8.122 Stocks of unused labels representing different products shall be stored in an orderly manner to prevent errors. Stocks of obsolete labels shall be destroyed.
- D8.123 A system of checks in labelling procedures shall be used to prevent errors in translating information to container labels.
- D8.124 All labelling shall be clear and legible and printed using moisture-proof ink.
- D8.130 Labels shall be affixed or attached firmly to the container.
- D8.140 The proper name and significant product modification(s) shall be noted on the label.
- D8.150 Products that are subsequently re-packaged into new containers shall be labelled with new labels as appropriate. Records to allow tracking of products including collection or processing facility identity, unique numeric or alphanumeric identifier, collection date and time, product identity, donor and recipient information on the original container shall be maintained.
- D8.160 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.
- D8.170 The product label shall be complete. Not applicable (NA) may be used when appropriate.
- D8.180 Labelling requirements, if any, required by applicable governmental laws or regulations shall be observed.
- D8.200 **PRODUCT IDENTIFICATION**
- D8.210 Each product shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to relate any product to its donor, the donor's medical record, and to all records describing the handling and final disposition of the product. If a single product is stored in multiple containers, there shall be a system of identifying each container.
- D8.220 Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the product. Supplementary identifiers shall not obscure the original identifier. The facility associated with each identifier shall be designated.
- D8.221 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 original donor.
- D8.230 Products shall be identified according to the proper name of the product as defined in A3.000, including the appropriate modifiers.

D8.231 Significant modifications made to the product subsequent to collection and prior to cryopreservation shall be noted.

D8.300 LABEL CONTENT

D8.310 Each label shall include at least the elements detailed in the following table:

Element	Partial label	Label at completion of collection	Label during processing	Label at completion of processing	Label at distribution	Inner & outer shipping container label
Unique identifier of product	X	X	X	X	X	
Proper name of product	X	X	X	X	X	
Recipient name and identifier	X (If applicable)	X (If applicable)	X (If applicable)	X (If applicable)	X	
Date, time collection ends and (if applicable) time zone		X		X	X	
Approximate volume		X		X	X	
Name and volume or concentration of anticoagulant and other additives		X		X	X	
Donor identifier and (if applicable) name		X		X	X	
Identity and address of collection facility or donor registry		X		X	X	
Recommended storage temperature		X		X	X	
Biohazard Label		X (if applicable)		X (if applicable)	X (if applicable)	X (if applicable)
Identity and address of processing facility				X	X	
ABO and Rh of donor				X	X	
RBC compatibility testing results					X (if applicable)	
Statement "Properly Identify Intended Recipient and Product"				X	X	
Statement "Warning: This Product May Transmit Infectious Agents"				X	X	
Expiration Date				X (if applicable)	X (if applicable)	
Expiration Time				X (if applicable)	X (if applicable)	
Statement "For Autologous Use Only" OR Statement "For Use By Intended Recipient Only"				X (if applicable) X (if for allogeneic recipient)	X (if applicable) X (if for allogeneic recipient)	
Statement "Do Not Irradiate"				X	X	
Statement "Not for Infusion" including reason				X (if applicable)	X (if applicable)	
Name and street address of receiving institution						X

Name and phone number of contact person at receiving institution						X
Statement "Medical Specimen"						X
Statement "Do Not X-Ray"						X
Name, street address and phone number of shipping facility						X

D8.320 PARTIAL LABEL

D8.321 If the container is capable of bearing only a partial label, the container shall show as a minimum the unique identifier of the product, proper name of the product as well as the name and identifier of the intended recipient, if known.

D8.322 Additional information, as required in Section D8.300, shall be provided with the product when the product is distributed.

D8.330 BIOHAZARD LABEL

D8.331 A biohazard label shall be applied to each product if any test shows evidence of infection due to communicable disease agent(s) as designated in B6.171 – B6.177.

D8.332 A biohazard label shall be applied to each product if testing was not performed or final results are not available.

D8.340 LABEL DURING PROCESSING

D8.341 Any container used during processing shall contain at a minimum the information required in the Table D8.310.

D8.350 LABELING AT COMPLETION OF PROCESSING

D8.351 At the end of processing, the label on the product container shall bear the information in the Table D8.310.

D8.360 LABELING PRIOR TO DISTRIBUTION

D8.361 At the time of distribution the name and unique patient identifier of the intended recipient shall be attached to the product container if this information is not already on the primary container label.

D9.000 ISSUE OF PRODUCTS PRIOR TO DISTRIBUTION

D9.100 INSPECTION OF PRODUCTS PRIOR TO DISTRIBUTION

- D9.110 Each product issued for infusion shall be inspected by two trained personnel immediately before release to verify appropriate labelling and integrity of the product container.
- D9.120 The Laboratory Director or designee shall give specific authorization for use when the container is compromised and/or recipient information is not verified.
- D9.200 RETURN OF PRODUCTS FROM ISSUE
- D9.210 Products accepted for return shall meet the following conditions:
- D9.211 The integrity of the primary container has not been compromised subsequent to issue from the laboratory.
- D9.212 The product has been maintained subsequent to issue at the specified temperature range during storage and transportation.
- D9.220 If the conditions in Sections D9.211 and D9.212 have not been met, the Laboratory Director or designee shall give specific authorization to accept the products for return.
- D9.230 The Laboratory Director or designee shall consult with the patient's transplant physician regarding reissue or discard of the returned product.
- D9.240 Documentation of the events requiring return, the results of inspection upon return, and subsequent action taken to insure product safety and viability shall be maintained in the laboratory record.
- D9.300 INSTRUCTIONS FOR ADMINISTRATION
- D9.310 For each type of product, the laboratory shall maintain a current document containing the following as appropriate:
- D9.311 The use of the hematopoietic progenitor cell product, indications, contraindications, side effects and hazards, dosage and administration recommendations.
- D9.320 The instructions for administration shall be available to the clinical staff caring for the recipient.
- D9.400 INFUSION FORMS
- D9.410 The laboratory shall provide a written form to be completed for products issued containing at a minimum the name and unique identifier of the intended recipient, the proper product name and product identifier, and the initials of the medical staff receiving the product.
- D10.000 CONDITIONS FOR STORAGE

D10.100 STORAGE DURATION

D10.110 Facilities storing hematopoietic progenitor cell products shall establish policies for the duration and conditions of storage and indications for discard. Patients, donors, and associated transplant centres should be informed about these policies before hematopoietic progenitor cell collection.

D10.200 TEMPERATURE

D10.210 Storage temperatures shall be defined in the Standard Operating Procedures Manual.

D10.220 Hematopoietic progenitor cells stored in a liquid state shall be maintained within a specific temperature range and for a period of time specified in a Standard Operating Procedure.

D10.230 Cryopreserved products shall be stored within a temperature range appropriate for the cell product and cryoprotectant solution used and as defined in the Standard Operating Procedures.

D10.300 PRODUCT SAFETY

D10.310 Materials that may adversely affect hematopoietic progenitor cell products shall not be stored in the same refrigerators or freezers.

D10.320 For products immersed in liquid nitrogen, procedures to minimize the risk of microbial cross-contamination of products shall be employed.

D10.400 MONITORING

D10.410 Refrigerators and freezers for product storage shall have a system to monitor the temperature continuously and to record the temperature at least every 4 hours.

D10.411 For products fully immersed in liquid nitrogen continuous temperature monitoring is not required.

D10.420 There shall be a mechanism to ensure that levels of liquid nitrogen in liquid nitrogen freezers are maintained.

D10.500 ALARM SYSTEMS

D10.510 Storage devices for products or reagents for product processing shall have alarm systems that are continuously active.

D10.520 Alarm systems shall have audible signals.

D10.530 If laboratory personnel are not always present in the immediate area of the storage device, a remote alarm device shall be required at a location staffed 24 hours a day.

D10.540 Alarms shall be set to activate at temperatures or an unsafe level of liquid nitrogen to allow time to salvage products.

D10.550 There shall be written instructions to be followed if the storage device fails. These instructions shall be displayed in the immediate area containing the storage device.

D10.551 A procedure for notifying laboratory personnel shall be placed at each remote alarm location and in the immediate area of the storage device.

D10.560 Alarm systems shall be checked periodically for function.

D10.570 Additional storage devices of appropriate temperature shall be available for product storage if the primary storage device fails.

D10.600 SECURITY

D10.610 The storage device shall be located in a secure area. Locking capability for the device or the storage location should be used when the area is unattended.

D10.700 INVENTORY CONTROL

D10.710 An inventory control system to identify the location of each product and associated sample aliquots shall be in use.

D10.720 The inventory control system records shall include:

D10.721 Donor name or identifier

D10.722 Patient name or identifier (if known)

D10.723 Product unique identifier

D10.724 Product or specimen proper name

D10.725 Date of collection

D10.726 Storage device identifier

D10.727 Location within the storage device

D10.728 Dates of issue

D10.729 Disposition

D11.000 TRANSPORTATION

D11.100 Procedures for transportation of non-frozen and/or cryopreserved products shall be designed to protect the integrity of the product being shipped and the health and safety of facility personnel.

D11.200 The primary product container for non-frozen products shall be placed in a secondary plastic bag and sealed to prevent leakage.

- D11.300 Frozen or non-frozen products that leave the facility or are transported on public roads shall be shipped in an outer shipping container.
- D11.310 The outer shipping container shall be thermally insulated and shall conform to the regulations regarding the mode of transport.
- D11.320 The outer shipping container should be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.
- D11.330 The shipping container shall be of appropriate design and construction for transportation of the cryogenic material used.
- D11.340 Cryopreserved products with an indicated storage temperature below -80°C shall be shipped in a liquid nitrogen "dry shipper" that contains adequate absorbed liquid nitrogen to maintain temperature at least 48 hours beyond the expected time of arrival at the receiving facility.
- D11.350 During transport, the product temperature shall be maintained at the storage temperature specified by the Processing Laboratory.
- D11.360 The sending facility shall include a temperature monitor in the shipper.
- D11.370 Outer shipping container shall be labelled as defined in D8.300.
- D11.380 There shall also be a label inside the shipping container that includes all the information required on the outer shipping container as defined in D8.300.
- D11.390 The shipping container shall be labelled in accordance with applicable regulations regarding the cryogenic material used and the transportation of biologic materials.
- D11.400 The receiving facility shall verify the presence of cryogenic material (absorbed liquid nitrogen or dry ice as applicable) in the shipper and the status of the temperature monitor shall be recorded upon arrival.
- D11.500 Method of Transport
- D11.510 The transit time should be minimized.
- D11.520 If the intended recipient has received high-dose therapy, the product shall be hand-carried by a suitably informed courier in the passenger compartment.
- D11.530 There shall be plans for alternative transport in an emergency.
- D11.540 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 shall be inspected by hand.
- D11.600 Transport Records

- D11.610 Transport records shall permit tracing of the product from one facility to another.
- D11.620 Transport records shall identify the date and time product is shipped and received.
- D11.630 Transport records shall identify the source facility, the receiving facility, and the personnel responsible for shipping and receiving the product.
- D11.640 Transport records shall document the identity of the courier and any delays or problems occurring during transportation of the product.

D12.000 DISPOSAL

- D12.100 There shall be a written policy for disposal of hematopoietic progenitor cell products.
- D12.200 There shall be a written agreement between the patient or designated recipient and the storage facility defining the circumstances for disposal or transfer of cells.
 - D12.210 If the patient or designated recipient is still alive his/her written consent for disposal or transfer of the products shall be obtained. If consent is denied the patient shall be offered the opportunity to ship the product to another facility.
- D12.300 There shall be written documentation of patient death or no further need for the product before any product is discarded.
- D12.400 The records for discarded products shall indicate the product discarded, date of discard, and method of disposal.
- D12.500 The Laboratory Medical Director of the processing facility, in consultation with the patient's transplant physician, shall approve of product discard and method of disposal.
- D12.600 The method of disposal and decontamination shall meet the federal, state and provincial laws, current codes, rules and regulations for disposal of biohazardous materials.

D13.000 RECORDS

D13.100 GENERAL REQUIREMENTS

- D13.110 All records and communications among the collection, processing and transplant facilities and their patients shall be regarded as privileged and confidential. Safeguards to assure this

confidentiality shall be established and followed in compliance with applicable governmental laws and regulations.

- D13.120 Records shall be made concurrently with each step of the processing, testing, cryopreservation, storage, and infusion or disposal of each product in such a way that all steps may be accurately traced.
- D13.130 Records shall be legible and indelible, shall identify the person immediately responsible for each significant step, and shall include dates (and times where appropriate) of various steps and shall show the test results as well as the interpretation of each result where appropriate.
- D13.140 Records of each step shall be as detailed as necessary for a clear understanding of each step by a person experienced in hematopoietic progenitor cell processing and transplantation, and shall be available for inspection by authorized individuals.
- D13.150 Appropriate records shall be available from which to determine the lot numbers and manufacturer of supplies and reagents used for the processing of specific products.
- D13.160 Records shall be maintained in such a way as to assure their integrity and preservation.

D13.200 RECORDS TO BE MAINTAINED INDEFINITELY

Records related directly to the processing, testing, storage or release of hematopoietic progenitor cells shall be maintained indefinitely.

- D13.210 Processing records:
- D13.211 Identity of any facility involved in the collection, processing, storage or transplantation of the product.
- D13.212 Product processing, including lot numbers and expiration dates of reagents and disposables and a record of key equipment used in processing shall be documented.
- D13.213 Authorization by the transplant physician for the processing of products.
- D13.214 Results and interpretation of all tests and re-tests.
- D13.215 Information on characterization of materials and devices used in the manipulation of products including but not limited to antibodies, serum, cytokines, toxins, antibiotics, pharmacologic agents, other chemicals or solid supports. Records shall include the manufacturer's name and lot numbers of all reagents used.
- D13.216 Records of laboratory personnel involved in the labelling, processing, storage or distribution of the product, including

their name, signature, initials, identification and inclusive dates of employment.

D13.217 Documentation of donor's infectious disease testing results.

D13.218 Signature of the Laboratory Medical Director authorizing the release of products in cases where there is a nonconforming product.

D13.220 Storage and distribution records:

D13.221 Distribution or disposition, as appropriate, of products.

D13.222 Visual inspection of liquid products immediately before distribution.

D13.223 Product storage temperature, including initialled temperature recorder charts.

D13.224 Reissue, including records of proper temperature maintenance, documentation of events requiring return, results of inspection upon return and actions taken to insure product safety and viability prior to reissue.

D13.230 Compatibility test records:

D13.231 Results of all compatibility tests, including red cell compatibility testing of patient samples, antibody screening and identification as specified in the facility SOP.

D13.240 Errors, accidents, adverse reactions and complaints:

D13.241 Records of errors, accidents and corrective action regarding processing, storage or infusion occurring within the facility.

D13.250 All superseded procedures and policies.

D13.300 RECORDS TO BE MAINTAINED FOR 10 YEARS

Records related to quality control, personnel training or competency, equipment maintenance, sterilization of supplies and reagents, disposition of rejected supplies and reagents, management, or other general facility issues shall be retained for 10 years by the processing facility, although not all need be immediately available. If governmental laws or regulations require a longer retention period, records shall be retained for the period required by such laws or regulations.

D13.310 Temperature charts and records for storage of reagents.

- D13.320 Calibration and standardization of equipment including initial installation.
- D13.330 Performance checks of equipment and reagents.
- D13.340 Periodic tests of capacity and integrity of shipping containers to maintain proper temperature in transit.
- D13.350 Periodic check on aseptic technique and competency.
- D13.360 Proficiency test results.
- D13.370 Results of inspection and accreditation visits.
- D13.380 General facility records.
 - D13.381 Sterilization records of supplies and reagents prepared within the facility, including date, time interval, temperature and mode.
 - D13.382 Technical personnel training, continuing education, and periodic competency testing.
 - D13.383 Maintenance records for equipment including preventive maintenance and general physical plant.
 - D13.384 Documentation of acceptance for supplies and reagents, including name of manufacturer or supplier, lot numbers, date of receipt and expiration date as established in the facility SOP.
 - D13.385 Disposition of rejected supplies and reagents used in the collection, processing, testing, freezing and storage of products.

D13.400 ELECTRONIC RECORDS

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

- D13.410 If a computer record-keeping system is used, there shall be a system to ensure the authenticity, integrity and confidentiality of all records.
- D13.420 There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.
- D13.430 The facility shall have an alternative system that ensures continuous operation in the event that computerized data are not available. The alternative system shall be tested periodically.

- D13.440 There shall be established written procedures for record entry, verification and revision. A system shall be established for display of data before final acceptance.
- D13.441 The quality assurance system shall include an assessment of computer functions to ensure that errors and problems are reported and resolved.
- D13.450 There shall be a system whereby access is limited to authorized individuals.
- D13.460 There shall be the ability to generate true copies of the records in both paper and computer form suitable for inspection and review.
- D13.470 When a computer system is used, there must be validated procedures for and documentation of:
- D13.471 Systems development, if carried out internally.
- D13.472 Numerical designation of system versions if applicable.
- D13.473 Prospective validation of system, including hardware, software, and database.
- D13.474 Installation of the system.
- D13.475 Training and continuing competency of personnel in systems use.
- D13.476 Validation and monitoring of data integrity.
- D13.477 Policies and procedures for system maintenance and operations. Documentation shall be complete, in language understandable by users.
- D13.480 All system modifications must be authorized, documented, and validated prior to implementation.
- D13.490 The computer system shall ensure that all donor, product and patient identifiers are unique.
- D13.500 **RECORDS IN CASE OF DIVIDED RESPONSIBILITY**
- D13.510 If two or more facilities participate in the collection, processing or transplantation of the product, the records of the Cell Processing Laboratory must show plainly the extent of its responsibility.
- D13.520 The Cell Processing Laboratory 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
APPENDIX II

IBMTR/EBMT TRANSPLANT ESSENTIAL DATA FORMS
COMPARISON OF FACT STANDARDS

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