B04/S/a

2013/14 NHS STANDARD CONTRACT
FOR HAEMATOPOIETIC STEM CELL TRANSPLANTATION (ADULT)

SECTION B PART 1 - SERVICE SPECIFICATIONS

Service Specification No.	B04/S/a
Service	Haematopoietic Stem Cell Transplantation (Adult)
Commissioner Lead	
Provider Lead	
Period	12 months
Date of Review	

1. Population Needs

1.1 National/local context and evidence base

The number of stem cell transplants in the UK has risen steadily since 1990, with increases seen in both allogeneic and autologous transplantation. In recent years, year on year increases in allogeneic transplants have been around 4% for the adult population (data source: British Society of Bone and Marrow Transplant (BSBMT) registry).

Nearly two thirds of all allogeneic transplants in the UK are performed to treat leukaemias with nearly 9 out of 10 used in the treatment of a haematological malignancy. The rate of allogeneic stem cell transplant varies across Europe. UK data (including Ireland) suggests an allogeneic transplant rate of 16.5 per million populations (2005-2008) BSBMT registry data. The median age of allogeneic transplant is 31 years with an age range of 0-72 (BSBMT data 1980-2010).

Changes in transplantation practices such as greater use of reduced conditioning regimes and more effective prevention of graft versus host disease (GvHD) are allowing patients of a more advanced aged to be considered for transplant (Popplewell 2002).

Allogeneic stem cell transplant has become a standard treatment in a number of conditions. Disease specific guidelines and consensus reports are available providing a distillation of the evidence base and expert opinion. The BSBMT have produced an indications table, based on literature, expert opinion and current practice. The table provides references for the evidence supporting its

recommendations, which generally consist of guidelines and observational studies. Randomized control trials of stem cell transplantation are rare (Burnett et al 2010). Most evidence is based on case series of registry data which relies on comparing outcomes with historical cases or other contemporary trails. Variation within and between trials in terms of patient selection, broader disease regimes etc. make comparison and collation of these studies very difficult.

National Guidance and European Guidance includes:

- Improving Outcomes in Haematological Cancer guidance.
- BSBMT.
- Joint Accreditation Committee EBMT – Euro ISHAGE (JACIE).
- London Thames Gateway Health Needs Assessment.
- National Institute of Clinical Excellence (NICE).
- National Registration requirements.
- Manual of quality measures for cancer.
- European Blood and Marrow Transplantation Group (EBMT).
- British Society for Medical Mycology standards of care for patients with invasive fungal infections.
- Stem Cell Strategic Forum Report on the future of unrelated stem cell transplantation (December 2010).

2. Scope

2.1 Aims and objectives of service

The aim of stem cell transplantation is to improve the chance of survival of patients through the implementation of a quality service as described in this service specification.

The objectives of the service are to deliver high quality care and improve outcomes in accordance with the NICE National Guidance for Improving Outcomes in Haematology Cancers and JACIE standards version 5 (Appendix 1).

This includes meeting the standards for:

- Treating patients in line with the agreed criteria for transplantation.
- Optimise patient outcome after autologous and allogeneic stem cell transplantation.
- Treating patients according to protocols as curative or life extending treatments.
- Reduction of morbidity and mortality associated with transplantation.
- Reduce unacceptable variation in clinical practice.
- Development and production of appropriate patient and carer information.
- Entry of patients to clinical trials and collection of national clinical trial data.

2.2 Service description/care pathway

Definition of Blood and Marrow Transplantation

Blood and marrow transplantation (BMT) is a term that encompasses a variety of procedures. Its essence is the ablation and replacement of the bone marrow in either an autologous fashion (i.e. patient has their own cells re-infused) or in an allogeneic procedure from either a family member or unrelated donor (matched or mismatched donor).

The source of the marrow cells also varies. Currently stem cells obtained from peripheral blood are the most common source of cells for transplantation. Bone marrow itself or umbilical cord blood can also be used as sources for stem cells, but the volume of activity is much smaller. For unrelated transplants the Grafts will be purchased from approved donor centres within the UK and abroad.

There are several methods by which the marrow is ablated including large doses of chemo-radiotherapy (traditional transplants) or by using immunosuppressive strategies (reduced intensity transplants, mini transplants, micro transplants).

The procedure for transplantation can be divided into several phases:

- **Pre-transplant work-up:** Pre-transplant work-up includes assessment of eligibility for transplantation, tissue typing of donors if applicable and basic investigations for fitness of both donor and recipient.
- **Mobilisation:** Mobilisation involves collection of stem cells from either the donor or the patient and processing the cells in the laboratory.
- **Conditioning:** Conditioning prepares the marrow for transplantation by either myeloablation or immunosuppression.
- **Transplantation and engraftment:** The cells are transplanted in the form of an intravenous infusion and the patients are then kept in hospital until they have recovered enough neutrophil numbers to reduce the risk of infection (engraftment).
- **Post-transplant follow-up:** Post transplant follow-up varies according to the nature of the transplant itself and can take up to a year. Complications such as infection and graft versus host disease need to be managed by the transplant team.

Care Pathways

There are two referral routes:

- Referral from secondary care consultant clinicians including haematologists, oncologists and on occasion from other non-cancer specialists such as neurologists, immunologists and rheumatologists.
- In a small number of cases, from a GP referral.

Referrals should be made to the stem cell transplant centre.

A clearly defined after care programme shall be developed with the patient and the referring Provider unit. Communication with general practitioners and staff in primary care and the referring clinician shall be timely efficient and continuous. The GP shall

be informed at all stages of the patient's treatment and shall be informed on how to access advice.

2.3 Population covered

The service outlined in this specification is for patients ordinarily resident in England; or otherwise the commissioning responsibility of the NHS in England[1] (as defined in *Who Pays?, Establishing the responsible commissioner* and other Department of Health guidance relating to patients entitled to NHS care or exempt from charges).

Specifically, this service is for adults requiring a Bone Marrow Transplant (BMT). All patients aged 19 or above are covered by this specification. Patients 18 years and under with a malignancy must be referred to a designated Principal Treatment Centre for Children & Young People with Cancer as set out in the paediatric BMT service specification.

2.4 Any acceptance and exclusion criteria

This section should be read in conjunction with Section 4 of the NHS England HSCT / BMT Commissioning Policy (NHSCB/B04/P/a), which outlines which indications will be funded.

Acceptance Criteria

The service will accept inward referrals from secondary care clinicians as outlined in the commissioning policy section 4.

The classification of Indications may from time to time be revised by the Commissioner in accordance with national review processes. Any revision will be notified in writing within the agreed contract notice period.

Each Trust will work towards achieving at least 85% of their total volume of activity within the Standard of Care (S) category. For some centres with expertise in lymphoma, commissioners and providers may require review of the S/CO percentage split.

The Indications for Transplant table makes clear diseases for which transplantation is generally not recommended and these treatments will not be covered by the contract. The framework for agreeing and planning activity with provider units will be based on this classification table. It is expected that patients eligible for BSBMT

clinical trials will only be treated at Trusts participating in these trials. Proposals to enter patients into trials (where the category is D) will require prior agreement on service costs with the commissioner in advance of the treatment and preferably agreements must be made at an early stage when provider participation is being

planned.

Sub contract arrangements between transplant centres and a specified shared care unit may be agreed after approval by the Commissioners provided the JACIE standards are met in terms of protocols, audit, staff training, clinical responsibility and outcomes, that these are undertaken jointly and costs of care at local unit clearly identified and agreed between the parties. This agreement must be demonstrated in a formal Contract between the two parties. It should be noted JACIE has the right to inspect shared care services and the lead BMT Centre will need to work with the shared care service to ensure they are aware of the relevant standards and SOPs they should have in place as part of a linked service.

Post-transplant follow-up varies according to the nature of the transplant itself and can take up to a year. Complications such as infection and graft versus host disease need to be managed by the transplant team. For patients with invasive fungal infections, early accurate diagnosis and appropriate treatment have a major impact on survival. High quality care requires a multidisciplinary approach to diagnosis and management. The use of CT scans and the use of medical mycology tests shall be undertaken to ensure accurate prescribing.

Stem cell transplantation is divided into distinct phases of treatment. NHS England is responsible for 30 days before transplant and continues until 100 days post-transplant and will include critical care related to the transplant episodes. No further charges than those set out herein will be made or accepted.

The prices in the activity schedule are fully inclusive and therefore no further charges for drugs, consumables, pathology, or any other aspects of care will be made or accepted within the timescale defined for each transplant package by any commissioner.

For payment to be made, the complete dataset for each transplant patient must have been provided to the Commissioner. Furthermore, only completed transplants will be chargeable. Transplants that are in progress are at the Provider's own financial risk until completed.

Exclusion Criteria

This service specification does not cover BMT for children and young people up to the age of 19 or above. In addition, this section should be read in conjunction with the commissioning policy section 4.

In addition:

- **Repeat** allogeneic transplants for relapsed disease will not be commissioned routinely commissioner agreement must in all cases be sought for such procedures. Repeat autologous transplants will not be commissioned routinely other than for the clinical indications explicitly listed in section 4 of the commissioning policy.
- Transplants for indications within categories D and GNR will not be

commissioned routinely, and commissioner agreement will need to be sought for transplantation of all cases falling within these categories as detailed in the commissioning policy for BMT.

- Cord transplants will be undertaken in centres agreed with the commissioner.
- Antifungals post 100 days are excluded.
- Should the patient die before infusion incomplete transplants will not be funded.
- Extracorporeal photopheresis (ECP) for acute GVHD will require commissioner agreement.

For those transplants/drugs listed above, written approval to fund is required before proceeding and these are defined in the prior approval form in the contract (Section B, Part 5). Where approval for these transplants is not provided in writing, no charges will be made to NHS England or the Clinical Commissioning Groups for any treatment supplied.

2.5 Interdependencies with other services

Whole System Relationships

- Donor Registries
- Histocompatibility & Immunogentics (H&I) laboratories
- Haematology and Cancer Services

Co-located Services

- Haematology
- Immunology
- Cardiology
- Critical care
- Interventional radiology
- Renal
- Medical Oncology (Please read in with the JACIE Standards version 5.)

Interdependent service

- Gastroenterology
- Respiratory medicine
- Dermatology

- Endocrinology
- Genetics
- Occupational Therapy
- Physiotherapy
- Dietetics
- Pharmacy

Related services:

- Psychology
- Social Workers
- Palliative Care Team

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

Standards

The following core standards apply:

All transplants shall take place in JACIE accredited centres and BMT centres need to adhere to JACIE standards V5.

As such a minimum of five (5) new allogeneic patients shall have been transplanted during the twelve (12) month period immediately preceding program accreditation and a minimum average of five (5) new autologous patients shall be transplanted per year within the accreditation. This standard shall also apply to Umbilical cord transplants. Centres which undertake umbilical cord transplants must be part of a provider network with a combined catchment population of at least 4 million people.

In addition all centres shall adhere to the key IOG recommendation that all patients be managed by a multidisciplinary haemato-oncology team.

Transplant Centres must meet the standards for specialist units by undertaking transplants in accordance with the extant guidance as recommended from JACIE. The commissioner will monitor against these standards and expect providers to provide evidence in support.

Centres shall meet the requirements defined as level 3 and /or 4 in accordance with previous BCSH extant Guidelines. (Level 4 if Matched Unrelated Donor (MUD) transplants are undertaken).

Each transplant centre shall have a named designated person acting as a Blood and Marrow Transplant co-ordinator.

There shall be a full range of support staff including social workers, psychological support, physiotherapy, pharmacy and radiology support.

There shall be close co-operation with the Palliative Care Service.

The transplant centre shall have a full range of back up services on a 24-hour basis including Intenive therapy Unit (ITU), specialist respiratory, renal, cardiac, gastroenterological and microbiological expertise on site.

Strategies for prevention, control and treatment of infections and other complications shall be defined and updated.

Clinical nurse specialist shall be available to provide support. Clinical nurse specialists shall have specific training in communication, counselling and ethics and shall be members of the multidisciplinary team.

Days/Hours of Operation

Transplant centres must be staffed on a 24-hour basis. There shall be appropriately trained specialised nursing staff. The nurse to patient ratio shall be at 1:2 or better.

Each BMT Unit must provide 24 hour inpatient care and appropriate access to day care and outpatient services.

The commissioner will monitor length of stay and trends towards early transfer back to secondary care, including cost implications for district general hospitals of shared care.

The BMT consultants must report back to the referring consultants on the progress of the patient. The quality of communication between BMT providers and referring consultants will be monitored as appropriate to the treatment plan.

There shall be arrangements for direct 24-hour emergency access after discharge.

Referral Criteria and Sources

The Commissioner will expect and encourage local consultants to refer to those provider units, which the Commissioner has contracted with. The contract does not stipulate approved providers for specific disease types but agreement on this will be discussed and agreed in Contract with each Provider unit.

The Commissioner reserves the right to designate providers for certain services with 6 months' notice. Such designation process will apply equally to all relevant providers but the outcome may differentiate between providers where there are differences in quality, service, value, sub- specialty or patient experience.

Consultants shall refer patients already registered in BSBMT/National Cancer research Network (NCRN) trials to the contracted provider units taking part in these trials.

The network shall facilitate rapid referral and admission through the use of agreed protocols and funding of the network should be sufficient to ensure that providers are capable of meeting the national minimum datasets.

Discharge Process and after care

Discharge paperwork shall be sent to the relevant health care professionals on the day of the patient's discharge in accordance with National Guidelines. Discharge meetings with other care providers are also arranged as required.

A clearly defined after care programme should be developed with the patient and the referring Provider unit. Communication with general practitioners and staff in primary care and the referring clinician shall be timely efficient and continuous.

The general practitioner shall be informed at all stages of the patient's treatment and shall be informed on how to access advice.

The BMT consultants must report back to the referring consultants on the progress of the patient. The quality of communication between BMT providers and referring consultants will be monitored as appropriate to the treatment plan.

The follow up process must run for the period of time agreed with the referring clinicians. A clinical review will be required for 3 months after transplant between referring and providing clinicians to enhance communication, to plan further treatment and to agree on transfer arrangement.

Delays in planned or agreed transfers will be audited. The clinical quality, timing and effect in terms of cost to secondary care hospitals of these transfer arrangements will be monitored.

Response Times and Prioritisation

Providers will respond to the referral and initiate the admission process or put in train any other clinical actions required in line with protocol for that cancer type.

If providers do not have capacity to accept patients the service must liaise with other providers to arrange an alternative admission to specialist services.

Tissue typing turnaround times are agreed as follows:

- 96 hour turnaround for extremely urgent patients.
- 5 -10 working days for all other patients according to clinical need.

Informed Participation

The transplant centre must enable the informed participation of the patient, donor, carer and advocate, and be able to demonstrate this. Provision shall be made for patients with communication difficulties and those whose first language is not English. Patients and carers shall be given details of the names and responsibilities of the multidisciplinary team.

A dedicated counselling service shall be available to the patient at all stages of treatment, from point of referral onwards. Counselling shall be accessible, at least during working hours, either personally or via telephone. Uptake of counselling shall be monitored routinely and the service evaluated by patients periodically.

Unless the urgent need for treatment precludes the possibility, all patients of reproductive age shall be offered a review by a reproductive medicine physician prior to starting treatment.

Good quality information shall be made available to patients. Written information (which has been evaluated by patients) shall be available at the point of referral and shall be used to reinforce clinical communication and to inform patients about all aspects of the condition and treatment and its effects on daily living. This shall include balanced information about the probability of improved survival and/or symptom reduction, together with risks and potential short and long-term adverse effects. Where appropriate, patients shall be given information on the reasons anticipated treatments/interventions are not being offered to them. A review of information shall be carried out annually.

Surveys of patients' experience shall be carried out covering patients' views of the information they were given and its sufficiency in enabling them to make informed consent about each intervention, quality of care and pain control.

The patient's contact with the unit in terms of attendance for day care and local shared care shall be planned in consultation with the patient. The care plan shall include the likely time scale for treatment.

The existence of a patient run support group is desirable.

Facilities

- The transplant centre shall have a designated transplant unit with four or more designated beds. This could be part of a larger facility for the treatment of patients with haematological and/or other malignancies. This unit shall have facilities, which minimise airborne microbial contamination.
- All patients receiving induction therapy - single rooms.
- Designated outpatient area that reasonably protects the patient from transmission of infectious agents.
- The transplant centre shall be able to perform on site all procedures connected to the harvesting and manipulation storage of bone marrow and/or PBSCs or confirm to the lead Commissioner that alternative appropriate arrangements have been made with another centre or Blood Authority.
- The centre shall have facilities for the reverse barrier nursing of patients.
- Adequate access to CT and MRI is essential, and access to CT/PET scanning is desirable.
- Reports shall be provided by Radiologists experienced in the use of these techniques for Haematological malignancies.
- There shall be easy access to the Radiotherapy Service with at least two Radiotherapists with a Special interest in Haematological malignancy and expertise in specialised techniques e.g. total body irradiation.

4. Key Service Outcomes

Expected Outcomes

Mortality rates shall be recorded at one and five years.

- Autologous day 100 treatment mortality should be less than 5%
- Allogeneic day 100 treatment mortality should be less than 30%

The level of progression free survival and overall survival will depend on a number of factors, including the disease group, the condition of the patient, the type of transplant offered and the degree of stem cell match. The service shall demonstrate survival rates equivalent to reported trial data.

The service shall demonstrate their processes to minimise the risk of and the management of treatment related complications, such as infections and graft versus host disease.

The service shall provide long term quality of life monitoring and allogeneic transplant services shall aim to provide a late effects service.

Transplant centres shall inform the lead commissioner of patients being entered into clinical trials.

The provider will agree with the Commissioner on how outcomes of care will be assessed by the provider. There will be an agreed basis for monitoring and sharing patient specific outcomes, both long term and short term with all providers.

Regular and documented clinical audit shall be carried out. A planned programme for future clinical audits shall be made available to the Commissioner on an annual basis.

Each provider must share the results of the BMT programme with all referring clinicians with education and audit reviews (with emphasis on improving communication and collaboration between cancer centres and units).

All transplants shall be registered with the BSBMT and the European Bone Marrow Transplant Register via the BSBMT Data Office.

There shall also be arrangements in place for selective call back of patients by the provider on a long-term basis.

As a minimum commissioners will want to monitor by each provider separately for:

- 100 day survival post-transplant
- Overall survival rates

Providers will be expected to provide full data to populate the national BMT dashboard, either directly or via the BSBMT registry as agreed with commissioners.

Additional relevant information will be agreed and may be a by-product of major trials of e.g. leukaemia, myeloma and lymphoma treatments.

Appendix 1

JACIE FACT-JACIE International Standards (Fifth Edition)
PART B: CLINICAL PROGRAM STANDARDS

B1 General

B1.1: The Clinical Program consists of an integrated medical team housed in geographically contiguous or proximate space with a Clinical Program Director(s) and common staff training, programs, protocols and quality management systems.

B1.2 The Clinical Program shall use cell collection and processing facilities that meet FACT-JACIE Standards with respect to their interactions with the Clinical Program.

B1.3 The Clinical Program shall abide by all applicable laws and regulations.

B1.3.1 The Clinical Program shall be licensed, registered, and/or accredited as required by the appropriate governmental authorities for the activities performed.

B1.4 For initial accreditation, a dedicated transplant team including a Clinical Program Director(s) and at least one other physician trained and/or experienced in cellular therapy and/or HPC transplantation shall have been in place for at least twelve (12) Months preceding accreditation.

B1.5 If the Clinical Program requests accreditation for allogeneic HPC transplantation, a minimum of ten (10) new allogeneic patients shall have been transplanted during the twelve (12) month period immediately preceding program accreditation and a minimum average of ten (10) new allogeneic patients shall be transplanted per year within the accreditation cycle. A Clinical Program that is accredited for allogeneic transplantation will be considered to have met the numeric requirement for autologous transplantation.

B1.5.1 For Clinical Programs utilising more than one clinical site and requesting accreditation for allogeneic HPC transplantation, a minimum of five (5) new allogeneic patients shall have been transplanted at each site performing allogeneic transplants during the twelve (12) month period. Immediately preceding accreditation, a minimum average of five (5) new allogeneic patients shall be transplanted at each site, performing allogeneic transplants per year within the accreditation cycle. A site that is accredited for allogeneic transplantation will be

considered to have met the numeric requirement for autologous transplantation.

B1.5.1.1 For clinical sites performing only autologous transplants, a minimum of five (5) new autologous patients shall have been transplanted at each site during the twelve (12) month period Immediately preceding accreditation, a minimum average of five (5) new autologous patients shall be transplanted at each site per year within the accreditation cycle.

B1.5.2 A combined Clinical Program caring for paediatric and adult patients at the same site shall perform a minimum average of five (5) allogeneic HPC transplants for each population per year within the accreditation cycle.

B1.6 If the Clinical Program requests accreditation for only autologous HPC transplantation, minimum of five (5) new recipients of autologous transplantation shall have been transplanted during the twelve (12) month period immediately preceding accreditation and a minimum average of five (5) new recipients of autologous transplantation shall be transplanted per year within the accreditation cycle.

B1.6.1 For Clinical Programs utilising more than one clinical site and requesting accreditation for autologous HPC transplantation only, a minimum of five (5) new patients shall have been transplanted at each site during the twelve (12) month period immediately preceding accreditation and a minimum average of five (5) new patients shall be transplanted at each site per year within the accreditation cycle.

B1.6.2 A combined Clinical Program requesting accreditation for autologous HPC transplantation only and caring for paediatric and adult patients at the same site shall perform a minimum average of five (5) transplants for each population per year within the accreditation cycle.

B2 Clinical unit

B2.1 There shall be a designated inpatient unit of adequate space, design, and location that minimizes airborne microbial contamination.

B2.1.1 The inpatient program shall have an intensive care unit or equivalent coverage available. B2.1.1.1 There shall be written guidelines for clear communication and prompt transfer during and ongoing monitoring of the transfer of patients to an intensive care unit or equivalent coverage.

B2.2 There shall be a designated area for outpatient care that protects the patient from transmission of infectious agents and allows, as necessary, for appropriate patient isolation; administration of intravenous fluids, medications, and/or blood products; and confidential donor examination and evaluation.

B2.2.1 Outpatient facilities shall have a plan for providing access to an intensive care unit or equivalent coverage for patients who may become critically ill.

B2.3 Facilities used by the Clinical Program shall be maintained in a clean, sanitary, and orderly manner.

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

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

B2.4.1.1 If general medical physicians provide inpatient-based care to transplant patients, there shall be a policy for their scope of care and afterhours coverage.

B2.4.2 There shall be a pharmacy providing 24-hour availability of medications needed for the care of transplant patients.

B2.4.3 There shall be access to renal support under the direction of nephrologists and trained personnel.

B2.4.4 There shall be 24-hour availability of autologous and/or CMV-appropriate and irradiated blood products needed for the care of transplant patients.

B2.4.5 The Clinical Program shall refer planned discharges to facilities and health care professionals adequate for post-transplant care.

B2.4.5.1 The Clinical Program shall provide or secure oversight of care that meets applicable standards

B2.4.6 Clinical Programs performing allogeneic cell transplants shall use HLA testing laboratories appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or equivalent, with the capability of carrying out deoxyribonucleic acid (DNA)–based HLA-typing.

B2.5 Safety requirements

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

B2.5.2 The Clinical Program shall have a written safety manual that includes instructions for action in case of exposure to communicable disease or to chemical, biological, or radiological hazards, where applicable.

B3 Personnel

B3.1 Clinical Program Director

B3.1.1 The Clinical Program Director shall be a physician appropriately licensed or certified to practice medicine in the jurisdiction in which the program is located who has achieved specialist certification in one or more of the following specialties: Haematology, Medical Oncology, Paediatric, Immunology, or Paediatric Haematology/Oncology. Physicians trained prior to requirements for specialty training may serve as Clinical Program Director if they have documented experience in the field of HPC transplantation extending over ten (10) years.

B3.1.2 The Clinical Program Director shall have two (2) years of experience as an attending physician responsible for the direct clinical management of HPC transplant patients in the inpatient and outpatient settings.

B3.1.3 The Clinical Program Director shall be responsible for administrative and clinical operations, including compliance with these Standards and applicable laws and regulations.

B3.1.4 The Clinical Program Director shall be responsible for all elements of the design of the Clinical Program including quality management, the selection and care of patients and donors, cell collection, and processing, whether internal or contracted services.

B3.1.5 The Clinical Program Director shall have oversight of the medical care provided by all members of the Clinical Program including medical care provided by the physicians on the transplant team.

B3.1.5.1 The Clinical Program Director shall be responsible for verifying the knowledge and skills of the physicians and mid-level practitioners of the transplant team.

B3.1.6 The Clinical Program Director shall participate regularly in educational activities related to the field of HPC transplantation.

B3.2 Attending physicians

B3.2.1 Clinical Program attending physicians shall be appropriately licensed to practice medicine in the jurisdiction of the Clinical Program and should be specialist certified or trained in one of the following specialties: Haematology, Medical Oncology, Adult or Paediatric Immunology, or Paediatric Haematology/Oncology.

B3.2.2 Clinical Program attending physicians shall participate regularly in educational activities related to the field of HPC transplantation.

B3.3 Clinical transplant team

B3.3.1 Clinical Programs performing paediatric transplantation shall have a transplant team trained in the management of paediatric patients.

B3.3.2 Clinical Programs performing paediatric transplantation shall have at least one attending physician who has achieved specialist certification in Paediatric Haematology or Oncology or Paediatric Immunology. An attending physician may also serve as the Clinical Program Director, if appropriately credentialed.

B3.3.3 For Clinical Programs performing adult transplantation, there shall be at least one attending physician who has achieved specialist certification in Haematology, Medical Oncology, or Immunology. An attending physician may also serve as the Clinical Program Director, if appropriately credentialed.

B3.3.4 The Clinical Program shall have access to licensed physicians who are trained and competent in marrow collection and a marrow collection facility that

meets these Standards.

B3.3.5 The Clinical Program shall have access to personnel who are trained and competent in cellular therapy product collection by apheresis and an apheresis collection facility that meets these Standards.

B3.4 Training for Clinical Program Directors and attending physicians

B3.4.1 Attending physicians shall each have a total of one year of supervised training in the management of transplant patients in both inpatient and outpatient settings.

B3.4.2 Clinical training and competency shall include the management of:

B3.4.2.1 Autologous transplant patients for physicians in Clinical Programs requesting accreditation for autologous transplantation.

B3.4.2.2 Allogeneic transplant patients for physicians in Clinical Programs requesting accreditation for allogeneic transplantation.

B3.4.2.3 Both allogeneic and autologous transplant patients for physicians in Clinical Programs requesting accreditation for allogeneic and autologous transplantation.

B3.4.3 Clinical Program Directors and attending physicians in all Clinical Programs shall have received specific training and maintain competency in each of the following areas:

B3.4.3.1 Indications for HPC transplantation.

B3.4.3.2 Selection of appropriate patients and preparative regimens.

B3.4.3.3 Pre-transplant patient evaluation, including assessment of appropriate patient eligibility and HPC adequacy with respect to collection.

B3.4.3.4 Donor and recipient informed consent.

B3.4.3.5 Administration of preparative regimens.

B3.4.3.6 Donor evaluation and management.

B3.4.3.7 Administration of growth factors for HPC mobilization and for post-transplant hematopoietic cell reconstitution.

B3.4.3.8 HPC product infusion and patient management. B3.4.3.9 Management of neutropenic fever.

B3.4.3.10 Diagnosis and management of infectious and non-infectious pulmonary complications of transplantation.

B3.4.3.11 Diagnosis and management of fungal disease.

B3.4.3.12 Diagnosis and management of veno-occlusive disease of the liver.

B3.4.3.13 Management of thrombocytopenia and bleeding.

B3.4.3.14 Management of hemorrhagic cystitis.

B3.4.3.15 Management of mucositis, nausea, and vomiting.

B3.4.3.16 Management of pain.

B3.4.3.17 Palliative and end of life care.

B3.4.3.18 Diagnosis and management of HPC graft failure.

B3.4.3.19 Evaluation of post-transplant cellular therapy outcomes.

B3.4.3.20 Evaluation of late effects of allogeneic and autologous transplants, including cellular, pharmacologic, and radiation therapy.

B3.4.3.21 Documentation and reporting for patients on investigational protocols.

B3.4.3.22 Applicable regulations and reporting responsibilities for adverse events.

B3.4.4 Additional specific clinical training and competency required for physicians in Clinical Programs requesting accreditation for allogeneic HPC transplantation shall include:

B3.4.4.1 Identification, evaluation, and selection of HPC source, including use of donor registries.

B3.4.4.2 Donor eligibility determination.

B3.4.4.3 Methodology and implications of human leukocyte antigen (HLA) typing.

B3.4.4.4 Management of patients receiving ABO incompatible HPC products.

B3.4.4.5 Diagnosis and management of cytomegalovirus (CMV) infection and disease.

B3.4.4.6 Diagnosis and management of other viral infections in immunocompromised hosts.

B3.4.4.7 Diagnosis and management of acute and chronic graft versus host disease.

B3.4.4.8 Diagnosis and management of post-transplant immunodeficiencies.

B3.4.5 The attending physicians shall be knowledgeable in the following

procedures:

B3.4.5.1 HPC processing.

B3.4.5.2 HPC cryopreservation.

B3.4.5.3 Marrow collection procedures.

B3.4.5.4 Apheresis collection procedures.

B3.4.5.5 Extracorporeal photopheresis for allogeneic transplants, if applicable.

B3.5 Mid-level Practitioners
(Physician Assistants, Nurse Practitioners, Advanced Practitioners)

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

B3.5.2 Mid-level practitioners shall have received specific training and maintain competency in the transplant-related cognitive and procedural skills that they routinely practice. These skills shall be documented and may include but are not limited to those listed in B3.4.3.

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

B3.6 Nurses

B3.6.1 The Clinical Program shall have nurses formally trained and experienced in the management of patients receiving cellular therapy.

B3.6.2 A Clinical Program treating paediatric patients shall have nurses formally trained and experienced in the management of paediatric patients receiving cellular therapy.

B3.6.3 Training shall include:

B3.6.3.1 Haematology/oncology patient care, including an overview of the cellular therapy process.

B3.6.3.2 Administration of preparative regimens.

B3.6.3.3 Administration of blood products, growth factors, cellular therapy products, and other supportive therapies.

B3.6.3.4 Care interventions to manage transplant complications, including, but not limited to, neutropenic fever, infectious and noninfectious processes,

mucositis, nausea and vomiting, and pain management.

B3.6.3.5 Recognition of cellular therapy complications and emergencies requiring rapid notification of the clinical transplant team.

B3.6.3.6 Palliative and end of life care.

B3.6.4 There shall be written policies for all relevant nursing procedures, including, but not limited to:

B3.6.4.1 Care of immunocompromised patients.

B3.6.4.2 Administration of preparative regimens.

B3.6.4.3 Administration of cellular therapy products.

B3.6.4.4 Central venous access device care. B3.6.4.5 Administration of blood products.

B3.6.5 There shall be an adequate number of nurses experienced in the care of transplant patients.

B3.6.6 There shall be a nurse/patient ratio satisfactory to manage the severity of the patients' clinical status.

B3.7 Consulting Specialists

B3.7.1 The Clinical Program shall have access to certified or trained consulting specialists and/or specialist groups from key disciplines who are capable of assisting in the management of patients requiring medical care, including but not limited to:

B3.7.1.1 Surgery.

B3.7.1.2 Pulmonary medicine.

B3.7.1.3 Intensive care.

B3.7.1.4 Gastroenterology.

B3.7.1.5 Nephrology.

B3.7.1.6 Infectious diseases.

B3.7.1.7 Cardiology.

B3.7.1.8 Pathology.

B3.7.1.9 Psychiatry.

B3.7.1.10 Radiology.

B3.7.1.11 Radiation oncology with experience in large-field (e.g., total body or total lymphoid) irradiation treatment protocols, if radiation therapy is administered.

B3.7.1.12 Transfusion medicine.

B3.7.1.13 Neurology.

B3.7.1.14 Palliative and end of life care.

B3.7.2 A Clinical Program treating paediatric patients shall have consultants, as defined in B3.7.1, qualified to manage paediatric patients.

B3.8 Quality Management Supervisor

B3.8.1 There should be a Clinical Program Quality Management Supervisor approved by the Program Director to establish and maintain systems to review, modify, and approve all policies and procedures intended to monitor compliance with these Standards and/or the performance of the Clinical Program.

B3.8.2 The Clinical Program Quality Management Supervisor shall participate regularly in educational activities related to the field of cellular therapy, and/or quality management.

B3.9 Support services staff

B3.9.1 The Clinical Program shall have one or more designated staff with appropriate training and education to assist in the provision of pre transplant patient evaluation, treatment, and post-transplant follow-up and care. Designated staff shall include:

B3.9.1.1 Pharmacy staff knowledgeable in the use and monitoring of pharmaceuticals used by the Clinical Program.

B3.9.1.2 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.

B3.9.1.3 Social services staff.

B3.9.1.4 Psychology services staff.

B3.9.1.5 Physical therapy staff.

B3.9.1.6 Data management staff sufficient to comply with B9.

B4 Quality Management

B4.1 There shall be an overall Quality Management Program that incorporates key performance data from clinical, collection, and processing facility quality management.

B4.1.1 The Clinical Program shall establish and maintain a written Quality Management Plan.

B4.2 The Quality Management Plan shall include an organizational chart of key personnel and functions within the cellular therapy program, including clinical, collection, and processing.

B4.2.1 The Quality Management Plan shall include a description of how these key personnel interact to implement the quality management activities.

B4.2.2 The Clinical Program Director or designee shall be responsible for the Quality Management Plan.

B4.2.2.1 The Clinical Program Director or designee shall have authority over and responsibility for ensuring that the Quality Management Program is effectively established and maintained.

B4.2.2.2 The Clinical Program Director or designee shall not have oversight of his/her own work if this person also performs other tasks in the Clinical Program.

B4.2.2.3 The Clinical Program Director or designee shall report on quality management activities, at a minimum, quarterly.

B4.2.2.4 The Clinical Program Director shall report on the performance of the Quality Management Plan, at a minimum, annually.

B4.3 The Quality Management Plan shall include, or summarise and reference, personnel education, experience, and training requirements for each key position in the Clinical Program. Personnel requirements shall include at a minimum:

B4.3.1 A system to document the following for all medical and nursing staff:

B4.3.1.1 Initial qualifications and training.

B4.3.1.2 Competency for each critical function performed.

B4.3.1.3 Continued competency at least annually.

B4.3.1.4 Annual performance review.

B4.3.1.5 Provisions for continuing education.

B4.3.2 A policy and/or procedure for personnel training and competency assessment.

B4.4 The Quality Management Plan shall include, or summarise and reference, policies and procedures for development, approval, implementation, review, revision, and archival of all critical processes, policies, and procedures.

B4.5 The Quality Management Plan shall include, or summarise and reference, a system for document control. The document control system shall include at a minimum the following elements:

B4.5.1 Listing of all active critical documents that shall adhere to the document control system requirements.

B4.5.2 A procedure for preparation, approval, implementation, review, revision, and archival of all policies and procedures.

B4.5.2.1 Archived policies and procedures, the inclusive dates of use, and their historical sequence shall be maintained for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

B4.5.3 A standardised format for policies, procedures, worksheets, and forms.

B4.5.4 Assignment of numeric or alphanumeric identifier and title to each document and document version regulated within the system.

B4.6 The Quality Management Plan shall include, or summarise and reference, policies and procedures for establishment and maintenance of written agreements with third parties whose services impact the clinical care of the patient and/or donor.

B4.6.1 Agreements shall include the responsibility of the third-party facility performing any step in collection, processing, or testing to comply with applicable laws and regulations and these Standards.

B4.6.2 Agreements shall be dated, reviewed, and renewed on a regular basis.

B4.7 The Quality Management Plan shall include, or summarise and reference, policies and procedures for documentation and review of outcome analysis and product efficacy, as appropriate.

B4.7.1 Review of outcome analysis and product efficacy shall include at a minimum:

B4.7.1.1 For HPC products intended for hematopoietic reconstitution, a process for documentation and review of time to engraftment following product administration.

B4.7.1.2 For HPC products, overall and treatment-related morbidity and mortality

at 100 days and 1 year after transplantation.

B4.7.1.3 For other cellular therapy products, the criteria for product efficacy and/or the clinical outcome shall be determined and shall be reviewed at regular time intervals.

B4.7.2 The Clinical Program shall provide data on outcome analysis and product efficacy, including adverse events related to the patient and/or product, in a timely manner to entities involved in the collection, processing, and/or distribution of the cellular therapy product.

B4.8 The Quality Management Plan shall include, or summarise and reference, policies, procedures, and a timetable for conducting, reviewing, and reporting audits of the Clinical Program's activities to verify compliance with elements of the Quality Management Program and operational policies and procedures.

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

B4.8.2 The results of audits shall be used to recognise problems, detect trends, identify improvement opportunities, and implement corrective actions when necessary.

B4.8.3 The Clinical Program shall periodically audit at a minimum:

B4.8.3.1 Accuracy of data contained in the Transplant Essential Data Forms of the CIBMTR or the Minimum Essential Data-A Forms of the EBMT.

B4.8.3.2 Donor screening and testing.

B4.8.3.3 Verification of chemotherapy drug and dose against the orders and the protocol.

B4.8.3.4 Management of cellular therapy products with positive microbial culture results.

B4.8.4 Collection and analysis of data related to the audit shall be reviewed, reported, and documented, at a minimum, on an annual basis.

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

B4.9.1 Notification of the recipient.

B4.9.2 Recipient follow-up and outcome analysis. B4.9.3 Follow-up of the donor, if relevant.

B4.9.4 Reporting to regulatory agencies if appropriate.

B4.9.5 Criteria for the administration of cellular therapy products with positive microbial culture results.

B4.10 The Quality Management Plan shall include, or summarise and reference, policies and procedures for errors, accidents, adverse events, biological product deviations and complaints.

B4.10.1 Policies and procedures shall include methods for:
B4.10.1.1 Detection.
B4.10.1.2 Investigation.
B4.10.1.3 Evaluation.
B4.10.1.4 Documentation.
B4.10.1.5 Reporting.
B4.10.1.6 Corrective action.
B4.10.1.7 Follow-up for effectiveness of corrective action.

B4.10.2 Documentation of each adverse event that occurs in the Clinical Program shall be reviewed in a timely manner by the Clinical Program Director.

B4.10.3 A written description of an adverse event shall be made available to the recipient's and/or donor's physician and the Collection and Processing Facilities, if appropriate.

B4.10.4 When applicable, adverse events shall be reported to the appropriate regulatory agencies within the required timeframes.

B4.10.5 Deviations from the following key standard operating procedures, B5.1.1, B5.1.6, and B5.1.7, shall be documented.

B4.10.5.1 Planned deviations shall be pre-approved by the Clinical Program Director or designee.

B4.10.5.2 Unplanned deviations and associated corrective actions shall be reviewed by the Clinical Program Director or designee.

B4.10.6 There shall be a defined process improvement plan that includes policies or procedures for the recognition and investigation of the cause of all issues that require corrective action.

B4.10.6.1 Follow-up activities shall be conducted to determine if the corrective actions were effective.

B4.10.7 There shall be a defined process to obtain feedback from patients and patient representatives.

B4.11 The Quality Management Plan shall include, or summarise and reference, policies and procedures for cellular therapy product tracking and tracing that allow tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

B4.12 The Quality Management Plan shall include, or summarise and reference, policies and procedures for actions to take in the event the Clinical Program's operations are interrupted.

B4.13 The Quality Management Plan shall include, or summarise and reference, policies and procedures for qualification of critical reagents, supplies, equipment, and facilities used for the marrow collection procedure.

B4.14 The Quality Management Plan shall include, or summarise and reference, policies and procedures for validation and/or verification of the marrow collection procedure.

B4.14.1 Changes to the marrow collection procedure shall be verified or validated to determine whether they create an adverse impact anywhere in the operation.

B5 Policies and procedures

B5.1 The Clinical Program shall establish and maintain policies and/or procedures addressing critical aspects of operations and management in addition to those required in B4. These documents shall include all elements required by these standards and shall address at a minimum:

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

B5.1.2 Donor and recipient consent.

B5.1.3 Donor and recipient confidentiality.

B5.1.4 Infection prevention and control.

B5.1.5 Administration of the preparative regimen.

B5.1.6 Administration of HPC and other cellular therapy products, including exceptional release.

B5.1.7 Administration of blood products.

B5.1.8 Facility management and monitoring.

B5.1.9 Disposal of medical and biohazard waste.

B5.1.10 Emergency and disaster plan, including the Clinical Program response.

B5.2 The Clinical Program shall maintain a detailed standard operating procedures

manual.

B5.2.1 The standard operating procedures manual shall include a listing of all current Standard Operating Procedures.

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

B5.3.1 A clearly written description of the objectives.

B5.3.2 A description of equipment and supplies used.

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

B5.3.4 A stepwise description of the procedure.

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

B5.3.6 A reference section listing appropriate literature, if applicable.

B5.3.7 Documented approval of each procedure by the Clinical Program Director or designated physician prior to implementation and every two years thereafter.

B5.3.8 Documented approval of each procedural modification by the Clinical Program Director or designated physician prior to implementation.

B5.3.9 A current version of orders, worksheets, reports, labels, and forms, where applicable.

B5.4 Copies of Standard Operating Procedures relevant to processes being performed shall be readily available to the facility staff.

B5.5 All personnel in the facility shall follow the Standard Operating Procedures related to their positions.

B5.6 Review and/or training by a staff member shall be documented before the staff member is allowed to perform new and revised policies and procedures.

B5.7 There shall be a process to address age-specific issues in the Standard Operating Procedures, as appropriate.

B6 Allogeneic and autologous donor selection, evaluation, and management

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

B6.1.1 Written criteria shall include criteria for the selection of allogeneic donors who

are minors.

B6.1.2 Written criteria shall include criteria for the selection of allogeneic donors when more than one donor is available and suitable.

B6.1.3 Information regarding the donation process should be provided to the potential allogeneic donor prior to HLA typing.

B6.2 Allogeneic and autologous donor information and consent to donate

B6.2.1 The collection procedure shall be explained in terms the donor can understand, and shall include the following information at a minimum:

B6.2.1.1 The risks and benefits of the procedure.

B6.2.1.2 Tests and procedures performed on the donor to protect the health of the donor and the recipient.

B6.2.1.3 The rights of the donor and parent of the donor who is a minor to review the results of such tests according to applicable laws and regulations.

B6.2.1.4 Alternative collection methods.

B6.2.1.5 Protection of medical information and confidentiality.

B6.2.2 The donor shall have an opportunity to ask questions.

B6.2.3 The donor shall have the right to refuse to donate.

B6.2.3.1 The allogeneic donor shall be informed of the potential consequences to recipient of such refusal.

B6.2.4 Donor informed consent for the cellular therapy product donation shall be obtained and documented by a licensed health care professional familiar with the collection procedure.

B6.2.4.1 Informed consent from the allogeneic donor should be obtained by a licensed health care professional other than the intended recipient's primary transplant physician.

B6.2.5 In the case of a minor donor, informed consent shall be obtained from the donor's parent or legal guardian in accordance with applicable laws and regulations and shall be documented.

B6.2.6 The allogeneic donor shall give informed consent and authorization in advance to release the donor's health information to the transplant physician and/or the recipient as appropriate.

B6.2.7 Documentation of consent shall be available to the Collection Facility staff

prior to the collection procedure.

B6.3 Allogeneic and autologous donor suitability for cellular therapy product collection

B6.3.1 There shall be criteria and evaluation procedures in place to protect the safety of donors during the process of cellular therapy product collection.

B6.3.1.1 Any abnormal finding shall be reported to the prospective donor with documentation in the donor record of recommendations made for follow-up care.

B6.3.1.2 Allogeneic donor suitability should be evaluated by a licensed health care professional who is not the primary transplant physician or health care professional overseeing care of the recipient.

B6.3.1.3 Autologous donors shall be tested as required by applicable laws and regulations.

B6.3.2 The risks of donation shall be evaluated and documented, including:

B6.3.2.1 Possible need for central venous access.

B6.3.2.2 Mobilization therapy for collection of HPC, Apheresis.

B6.3.2.3 Anesthesia for collection of HPC, Marrow.

B6.3.3 The donor should be evaluated for the risk of hemoglobinopathy prior to administration of the mobilization regimen.

B6.3.4 A pregnancy assessment shall be performed for all female donors with childbearing potential within seven (7) days preceding donor mobilization, cellular therapy product collection, or initiation of the recipient's preparative regimen, whichever occurs earliest.

B6.3.5 Laboratory testing of all donors shall be performed by a laboratory accredited, registered, or licensed in accordance with applicable laws andregulations using one or more donor screening tests approved or cleared by the governmental authority.

B6.3.5.1 The Clinical Program shall inform the Collection Facility and Processing Facility of donor test results or if any testing was not performed.

B6.3.6 A donor advocate should be available to represent allogeneic donors who are minors or who are mentally incapacitated.

B6.3.7 Collection from a donor who does not meet Clinical Program collection safety criteria shall require documentation of the rationale for his/her selection by the transplant physician.

B6.3.8 Issues of donor health that pertain to the safety of the collection procedure

shall be communicated in writing to the Collection Facility staff.

B6.3.9 There shall be a policy for follow-up of donors that includes routine management and the management of collection-associated adverse events.

B6.4 Additional requirements for allogeneic donors

B6.4.1 Allogeneic donors and allogeneic recipients shall be tested for ABO group and Rh type using two independently collected samples. Discrepancies shall be resolved and documented prior to issue of the cellular therapy product.

B6.4.2 A red cell antibody screen shall be performed on allogeneic donors and allogeneic recipients.

B6.4.3 Allogeneic donors shall be evaluated for risk factors that might result in disease transmission from the cellular therapy product by medical history, physical examination, examination of relevant medical records, and laboratory testing.

B6.4.4 The medical history for allogeneic donors shall include at least the following:

B6.4.4.1 Vaccination history.

B6.4.4.2 Travel history.

B6.4.4.3 Blood transfusion history.

B6.4.4.4 Questions to identify persons at high risk for transmission of communicable disease as defined by the applicable governmental authority.

B6.4.4.5 Questions to identify persons at risk of transmitting inherited conditions.

B6.4.4.6 Questions to identify persons at risk of transmitting hematological or immunological disease.

B6.4.4.7 Questions to identify a past history of malignant disease.

B6.4.4.8 The allogeneic donor shall confirm that all the information provided is true to the best of his/her knowledge.

B6.4.5 Within thirty (30) days prior to collection, allogeneic HPC donors shall be tested for evidence of clinically relevant infection by the following communicable disease agents using tests as required by applicable laws and regulations:

B6.4.5.1 Human immunodeficiency virus, type 1.

B6.4.5.2 Human immunodeficiency virus, type 2.

B6.4.5.3 Hepatitis B virus.

B6.4.5.4 Hepatitis C virus.

B6.4.5.5 Treponema pallidum (syphilis).

B6.4.6 If required by applicable laws and regulations, allogeneic HPC donors shall also be tested within thirty (30) days prior to collection for evidence of clinically relevant infection by the following disease agents:

B6.4.6.1 Human T cell lymphotrophic virus I.

B6.4.6.2 Human T cell lymphotrophic virus II.

B6.4.6.3 West Nile Virus.

B6.4.6.4 Trypanosoma cruzi (Chagas' Disease).

B6.4.7 Additional tests shall be performed as required to assess the possibility of transmission of other infectious or non-infectious diseases.

B6.4.8 For viable, lymphocyte rich cells, including therapeutic cells and other cellular therapy products, each allogeneic donor shall be tested for communicable disease agents listed in B6.4.5 and B6.4.6 within seven (7) days prior to or after collection in the U.S. or 30 days prior to collection in Europe, or in accordance with applicable laws and regulations.

B6.4.9 Allogeneic donors shall be tested for CMV (unless previously documented to be positive).

B6.4.10 Allogeneic donors and recipients shall be tested at a minimum for HLAA, B, DRB1 type by a laboratory accredited by ASHI, EFI, or equivalent. HLA-C testing shall be performed for unrelated allogeneic donors and related allogeneic donors other than siblings.

B6.4.10.1 DNA high resolution molecular typing shall be used for DRB1 typing.

B6.4.10.2 Verification typing shall be performed using an independently collected sample prior to allogeneic donor selection.

B6.4.11 Allogeneic donors shall be tested for red cell compatibility with the recipient where appropriate.

B6.4.12 Allogeneic donor eligibility, as defined by applicable laws and regulations, shall be determined by a physician after history, exam, medical record review, and testing, and shall be documented in the recipient's medical record before the recipient's preparative regimen is initiated and before the allogeneic donor begins mobilisation regimen.

B6.4.13 The use of an ineligible allogeneic donor shall require documentation of the rationale for his/her selection and suitability by the transplant physician, urgent medical need documentation, and the documented informed consent of the donor

and the recipient.

B6.4.14 Allogeneic donor eligibility and suitability shall be communicated in writing to the Collection and Processing Facilities.

B6.4.15 There shall be a policy covering the creation, regular review, and retention of allogeneic donor records.

B6.4.15.1 Allogeneic donor records shall include donor eligibility determination, including the name of the responsible person who made the determination and the date of the determination.

B7 Therapy administration

B7.1 The attending physician shall verify the availability and suitability of a donor or cellular therapy product prior to initiating the recipient's preparative regimen.

B7.1.1 The clinical service shall notify the Processing Facility prior to requesting a cryopreserved cellular therapy product from a cord blood bank or registry.

B7.2 There shall be a policy addressing safe administration of the preparative regimen.

B7.2.1 There shall be a policy addressing safe administration of chemotherapy.

B7.2.1.1 The treatment orders shall include the patient height and weight, specific dates, daily doses (if appropriate), and route of administration of each agent.

B7.2.1.2 Pre printed orders or electronic equivalents shall be used for protocols and standardised regimens. These orders shall be verified and documented by an attending physician.

B7.2.1.3 The pharmacist preparing the chemotherapy shall verify and document the doses against the protocol or standardized regimen listed on the orders.

B7.2.1.4 Prior to administration of chemotherapy, two (2) persons qualified to administer chemotherapy shall verify and document 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.

B7.2.2 There shall be a policy addressing safe administration of radiation therapy.

B7.2.2.1 There shall be a consultation with a radiation oncologist prior to initiation of therapy if radiation treatment is used in the preparative regimen.

B7.2.2.2 The patient's diagnosis, pre-existing co-morbid conditions, and proposed preparative regimen shall be made available to the consulting radiation oncologist in writing.

B7.2.2.3 A documented consultation by a radiation oncologist shall at a minimum address any prior radiation treatment the patient may have received and any other factors that may increase the toxicity of the radiation.

B7.2.2.4 The consultation shall also include radiation planning.

B7.2.2.5 Prior to administration of each dose of radiation therapy, the dose shall be verified and documented as per radiation therapy standards.

B7.2.2.6 A final report of the details of the radiation therapy administered shall be documented in the patient medical record.

B7.3 There shall be a policy addressing safe administration of Extracorporeal photopheresis (ECP).

B7.3.1 There shall be a consultation with the facility that performs ECP prior to initiation of therapy.

B7.3.2 Before ECP is undertaken, there shall be a written order from a physician specifying, at a minimum, the patient's diagnosis, proposed regimen, timing of the procedure, and any other factors that may affect the safe administration of ECP.

B7.3.3 A final report of the details of ECP administered, including an assessment of the response, shall be documented in the patient's medical record.

B7.3.4 The ECP procedure shall be performed according to written standard operating procedures of the facility performing the procedure appropriate for the clinical condition of the patient.

B7.3.5 Outcomes, including adverse events, related to the administration of ECP to patients within the Clinical Program shall be analysed annually.

B7.4 There shall be a policy addressing safe administration of cellular therapy products.

B7.4.1 There shall be a policy for determining the appropriate volume and the appropriate dose of red blood cells, cryoprotectants, and other additives.

B7.4.1.1 Cord blood units that have not been red cell reduced shall be diluted and/or washed.

B7.4.1.2 Cord blood units that have been red cell reduced should be diluted and/or washed.

B7.4.1.3 For double cord blood transplants, the first unit shall be administered safely prior to administration of the second unit.

B7.4.2 Two (2) qualified persons shall verify the identity of the recipient and the product and the order for administration prior to the administration of the cellular

therapy product.

B7.4.2.1 Verification of the identity and the order shall be documented.

B7.4.3 There shall be documentation in the patient medical record of the unit identifier and a copy of the distribution record.

B7.4.4 A circular of information for cellular therapy products shall be available to staff.

B8 Clinical research

B8.1 If required by applicable laws and regulations, Clinical Programs shall have formal review of investigational treatment protocols and patient consent forms by a process that is approved by the appropriate governmental authority.

B8.1.1 Those Clinical Programs utilising applicable investigational treatment protocols shall have in place a pharmacy equipped for research activities, including a process for tracking, inventory, and secured storage of investigational drugs.

B8.2 Documentation for all research protocols performed by the Clinical Program shall be maintained in accordance with institutional policies and applicable laws and regulations, including all audits; documentation of approval by the Institutional Review Board, Ethics Committee, or equivalent; correspondence with regulatory agencies; and any adverse outcomes.

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

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

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

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

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

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

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

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

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

B9 Data management

B9.1 The Clinical Program shall collect all the data necessary to complete the Transplant Essential Data Forms of the CIBMTR or the Minimum Essential Data- A forms of the EBMT.

B10 Records

B10.1 Clinical Program records related to quality control, personnel training and competency, facility maintenance, facility management, complaints, or other general facility issues shall be retained in accordance with applicable laws and regulations, or a defined program or institution policy, unless otherwise specified in these Standards.

B10.1.1 Employee records shall be maintained in a confidential manner and as required by applicable laws and regulations.

B10.2 Patient and donor records including, but not limited to, consents and records of care, shall be maintained in a confidential manner as required by applicable laws and regulations for a minimum of ten (10) years after the administration of the cellular therapy product, or, if not known, ten (10) years after the date of the distribution, disposition, or expiration, whichever is latest.

B10.3 Research records shall be maintained in a confidential manner as required by applicable laws and regulations for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.

B10.4 Records in case of divided responsibility

B10.4.1 If two (2) or more facilities participate in the collection, processing or administration of the cellular therapy product; the records of each facility shall show plainly the extent of its responsibility.

B10.4.2 The Clinical Program shall furnish to other facilities involved in the collection or processing of the cellular therapy product outcome data in so far as they concern the safety, purity, or potency of the cellular therapy product involved.