

 World Marrow Donor Association	World Marrow Donor Association			
	International Standards for Unrelated Hematopoietic Progenitor Cell Donor Registries			
	Document Type:	Standards	WG/Committee:	STDC
	Document Reference:	20140101-STDC- Standards	Other (specify):	
	Version:	Effective January 1, 2014	Approved by:	WBRD
	Drafting Date:		Approval date:	20130405
Status	Public			

**WORLD MARROW DONOR ASSOCIATION
INTERNATIONAL STANDARDS FOR
UNRELATED HEMATOPOIETIC PROGENITOR CELL DONOR REGISTRIES**

Table of contents

	<u>Page</u>
A. INTRODUCTION AND DEFINITIONS	
1.0 Introduction	3
2.0 Definitions/abbreviations	4
B. STANDARDS	
1.0 General	8
2.0 General organisation of the registry	9
3.0 Donor recruitment, consenting, screening and testing of volunteer donors	10
4.0 Umbilical cord blood and maternal donor recruitment, consenting, testing and review/release of cord blood units	14
5.0 Information technology and information management	17
6.0 Facilitation of search requests	18
7.0 Second and subsequent donations of HPC and/or blood products for the same patient	20
8.0 Collection, processing and transport of HPC	20
9.0 Follow-up of patient and volunteer donor	22
10.0 Financial and legal liabilities	22
Appendix I	25
Appendix II	26

These standards are aimed at enhancing the quality of registries assisting the grafting physician responsible for patient treatment in the international search for an unrelated donor for their patient. Next to accreditation by other international organisations, related to registry operations (Appendix 1), accreditation or qualification of individual registries by the World Marrow Donor Association (WMDA) is an indication that these registries are committed to follow WMDA standards. These standards promote the quality of procedures necessary to obtain, in the shortest possible time, the appropriate quality and quantity of haematopoietic progenitor cells (HPC) of the best unrelated donor suitable for engrafting a patient while protecting the anonymity, health and well-being of the volunteer donors. These standards are based on recommendations previously published [Goldman J., Special Report: bone marrow transplants using volunteer donors – recommendations and requirements for a standardised practice throughout the world – 1994 update. Blood 84:2833-2839, 1994]. These standards set forth only the minimum guidelines for registries working through the WMDA to facilitate HPC transplantations.

The standards do not set forth all that may be required of the registry to conform to governmental regulations or the standard here prevailing in the relevant community. Each registry must determine and follow any additional laws, regulations, practices and procedures that apply in their particular community. The WMDA disclaims all representations or warranties, expressed or implied, that compliance with the WMDA standards will fulfil the requirements of all applicable governmental laws and regulations or the standard of care prevailing in the relevant community.

A. INTRODUCTION AND DEFINITIONS

1.0 Introduction

1.01 The first time a registry sends in an application package to the WMDA Office, the registry will receive a qualification certificate from the WMDA, if the registry complies with the “benchmark” standards. These standards have been indicated in bold. Other standards, not in bold, are not required during the initial qualification process. The first time qualification of any registry will cover a period of five years and will not include site visits. Registries applying for first time qualification and judged by the review committee as sufficiently prepared to meet all of the required standards, will be allowed to submit a full application package for accreditation after a minimum of two years following approval of qualification. The registry may opt to apply any time after the 2 years up to the full term of 5 years. Qualified and accredited registries are required to perform an annual self-evaluation during this period.

1.02 After the qualification period is completed, the word “must” indicates that deviations are not acceptable. There will be no difference between bolded benchmark standards and non-bolded standards containing the words “must”. The words

“should”, “might”, and “may” are used for recommendations that are not mandatory.

- 1.03 If governmental laws and regulations differ from the WMDA standards, the requirement to meet local legal standards will be accepted as a valid cause of deviation from WMDA standards.

2.0 Definitions/abbreviations

Note: The institutions providing HPC to a patient in another country vary in their organisational structures. The definitions below are aimed at defining the individual elements, which comprise this effort and are not intended to indicate the requirement for a specific organisational structure.

ABO: Major human blood group including erythrocyte antigens, A, B and O.

Blood collection centre: A medical facility where blood intended for transfusion is drawn and stored.

Bone Marrow Donors Worldwide (BMDW): BMDW is a voluntary collaborative effort of stem cell donor registries and cord blood banks whose goal is to provide centralised information on the HLA phenotypes and other relevant data of unrelated haematopoietic progenitor cell donors and cord blood units and to make this information easily accessible to the physicians of patients in need of a HPC transplantation.

Cell processing unit: A medical laboratory facility where HPC are manipulated prior to transplantation. These activities may include the depletion of specific cell types from the graft, selection for specific cell types for infusion, *ex vivo* manipulation of cells in the graft, or concentration of the cell product.

Central venous catheter (CVC): A catheter placed in a vein in the neck (internal jugular vein), chest (subclavian or axillary vein) or in the groin (femoral vein).

Collection centre: A medical facility where HPC collection from volunteer donors actually takes place. This collection might include marrow aspiration or apheresis. The collection centre, or designee, performs the medical work-up of the volunteer donor and provides the final approval of the volunteer donor for collection. The collection centre packages the donation for transport to the transplant centre.

Cord blood bank: A facility responsible for donor management and the collection, processing, testing, cryopreservation, storage, listing, reservation, release, and distribution of cord blood units.

Cord blood collection site: A location where the infant donor is delivered and the cord blood unit is collected.

Donor: A person who is the source of cells or tissue for a cellular therapy product. Donors are unrelated to the patient seeking a transplant. These Standards refer to three types of donors:

1. volunteer donors of HPC;
2. infant donor whose placenta and/or umbilical cord the cord blood is obtained;
3. maternal donor who carries the infant donor to delivery.

Donor centre: An organisation responsible for donor recruitment, consenting, testing, management and the collection of donor personal, genetic, medical data.

European Marrow Donor Information System (EMDIS): A system that facilitates electronic communication between registries.

Extended typing: This HLA typing includes the tests carried out on a specific donor/cord blood unit with the purpose of adding additional information (typing of additional loci or further subtyping at a higher resolution) to an existing HLA assignment. The additional HLA typing may be performed on a stored sample.

GCSF: Granulocyte colony-stimulating factor is a cytokine that stimulates the bone marrow to produce granulocytes (white cells) and HPC and causes these cells to mobilise (move) to the peripheral blood where they can be collected from the veins for transplantation.

Hematopoietic progenitor cells (HPC): The progenitor cells, which give rise to blood and immune system cells. These cells are found in bone marrow, growth factor stimulated peripheral blood, and umbilical cord blood.

Hematopoietic progenitor cell transplantation: A medical procedure involving transplantation of hematopoietic progenitor cells.

HLA: Human leukocyte antigen.

IDM: Infectious disease marker.

Must: To be complied with at all times.

Quality system: An organisational structure, personnel requirements including qualifications, training and competencies, responsibilities, procedures, process and resources defined for implementing and managing quality within the registry including all activities contributing to the quality, directly or indirectly. The quality system must cover detection, reporting and corrective action related to adverse events and complaints; identification, labelling and tracking of individuals and products; development, implementation, and review of policies and procedures; creation, review, control and maintenance of records; outcome analyses; facilities; and safety. The quality system must be described by the registry in written documents and a process to audit the quality system must be in place.

Registry: An organisation responsible for coordination of the search for haematopoietic progenitor cells from donors (including cord blood) unrelated to the potential recipient.

SAE: (serious adverse event): Any untoward occurrence associated with the procurement, testing, processing, storage, and distribution of tissues and cells that might lead to the transmission of an infectious disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalisation or morbidity.

SAR: (serious adverse reaction): An unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalisation or morbidity.

SEAR: (serious events and adverse reactions): A centralised international database recording adverse reaction occurring during procurement of HPC that have or may have resulted in harm to an unrelated donor and the outcome of any investigation to determine the cause of the event.

Search: The process of identifying a suitable donor to donate HPC for a patient in need of a transplant.

Should: Recommended or advised, but effective alternatives may exist.

Signed valid informed consent: Signed documentation indicating that a volunteer donor or the maternal donor of umbilical cord blood has been provided with information on the procedure and tests performed, the risks and benefits of the procedure, that they have understood the information provided, have had an opportunity to ask questions, have been provided with satisfactory responses and have confirmed that all information provided is true to the best of their knowledge. The consent is valid when it complies with national regulation.

SPEAR: (serious product events and adverse reactions): A centralised international database recording adverse reactions that impact the quality of a donated cellular product that have or may have resulted in harm to the recipient and the outcome of any investigation to determine the cause of the event.

Standard operating procedures (SOP): A compilation of written detailed instructions describing the steps in a process, including materials and methods to be used and the expected end product. The SOP must include a process to regularly review and update procedures. Changes to SOP must be documented and validated.

Testing laboratories: These laboratories perform the histocompatibility, blood group, infectious disease, and other testing of the prospective donors and patients. They may be under the direction of a registry, donor centre or transplant centre or may be separate from these entities.

Total nucleated cell Count (TNC): The number of cells with a nucleus in a cord blood unit.

Traceability: The ability to locate and identify a donor or recipient, their data and cell product, during any stage of the recruitment, testing, collection, donation, transplantation, and follow-up process. Traceability also includes the ability to identify the organisational entities (e.g. registry, donor centre, collection centre, cell processing unit and transplant centre) involved in the international exchange.

Transplant centre: A medical facility where a patient (recipient) receives a transplant (graft) with HPC from an unrelated donor or from an umbilical cord blood unit. The transplant centre (TC) oversees the immediate medical treatment and provides long-term follow-up of the recipient. The search unit undertakes the search for an unrelated donor for specific patients using criteria defined and documented by the TC. This entity may be contained within a TC or may be separate from the TC. If separate, the search unit may coordinate searches for one or several TCs. In the standards, reference to a TC should be interpreted as a TC and/or a search unit as appropriate. Transplant centres/search units seeking an international donor work through the registry in their country.

Validation: Establishing documented evidence that a process will consistently produce predetermined specifications. Evaluation and written documentation of the performance of equipment, a reagent, a process or a system with regard to its effectiveness based on its intended use.

Verification typing: This HLA typing includes the tests carried out on a fresh sample of a specific donor or on an attached-segment of a cord blood unit with the purpose of verifying the identity and concordance of an existing HLA assignment. This stage used to be referred to as "confirmatory typing (CT)".

World Health Organization (WHO): WHO is the directing and coordinating authority for health within the United Nations system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends.

World Marrow Donor Association (WMDA): A non-profit association that fosters international collaboration to facilitate the exchange of high quality HPC for clinical transplantation worldwide and to promote the interests of donors.

Work-up: At this stage, a volunteer donor has been identified as an acceptable match for a patient, agrees to donate HPC after a full donor information and counselling session, and is medically evaluated for their fitness to donate HPC.

B. STANDARDS

1.0 General

- 1.01 A registry that is an organisational member of the WMDA is eligible for qualification/accreditation by the WMDA.
- 1.02 If a registry is accredited for international exchange of hematopoietic progenitors cells (HPCs) by an international organisation with standards that meet or exceed WMDA standards, that registry may be given WMDA qualification/accreditation following submission of material documenting that accreditation.
- 1.03 A registry that intends to request WMDA qualification/accreditation or that has obtained WMDA qualification/accreditation must submit the WMDA annual report questionnaire.**
- 1.04 The import/export requirements of a qualified/accredited registry must be submitted for posting on the WMDA website. These requirements should be reviewed by the registry at least annually and updated as significant changes occur.**
- 1.05 Changes to the status of a WMDA qualified/accredited registry that may affect WMDA qualification/accreditation must be brought to the attention of the WMDA in a timely fashion.**
- 1.06 If a registry relies on an independent donor centre or cord blood bank to recruit and characterise donors/umbilical cord blood units, the registry must ensure that the donor centre/cord blood bank complies with relevant WMDA standards. The nature of these affiliations and the duties and responsibilities of each entity must be documented in a written agreement.
- 1.07 The registry must ensure that transplant centres affiliated with the registry and requesting a donor from another country meet standards designed to ensure that donation of HPC will only be requested for patients for whom transplantation is a medically acceptable procedure. The nature of these affiliations and the duties and responsibilities of each entity must be documented in a written agreement.
 - 1.07.1 These transplant centre standards should be defined by an appropriate national or international organisation. In absence of such standards, they must be defined by the registry.
 - 1.07.2 The standards for transplant centres must be readily accessible to health care professionals involved in HPC transplantation.

- 1.08 If a registry relies on an independent collection centre for the collection of donor HPC or other donor samples, for donor medical evaluation or for the follow-up of donors, the registry must ensure that the collection centre complies with WMDA standards in these areas. The nature of these affiliations and the duties and responsibilities of each entity must be documented in a written agreement.
 - 1.09 The registry must have a system to review WMDA recommendations.
- 2.0 General organisation of the registry
- 2.01 The registry must be a legal entity or be contained within a legal entity operating within the laws of the country in which the registry resides.**
 - 2.02 The authorised official of the legal entity is responsible for ensuring the registry's compliance with the WMDA standards and must authorise all official documents related to WMDA qualification/accreditation.**
 - 2.03 The director or key registry personnel must have demonstrated experience in program administration in a health care setting.
 - 2.04 The director or key registry personnel or consultants must have expertise in human histocompatibility and HPC transplantation as documented by the relevant education and experience. At least one of these individuals must be a physician. These individuals must possess a basic understanding of diseases treatable by HPC transplantation, comprehend alternative therapies and donor search problems associated with these diseases, understand HLA specificities (serologic and DNA-based) and haplotypes, and possess a knowledge of transplant centre, donor centre, collection centre, cord blood bank (if applicable), and registry protocols in their own country and abroad.**
 - 2.05 The registry must have a qualified and trained health care professional readily available to assist with routine medical decisions regarding donor selection and donation.
 - 2.05.1 The registry must have a procedure such as the availability of a medical review panel to assist the registry with making unbiased decisions regarding nonstandard, high risk or experimental HPC donation or other related procedures.
 - 2.06 The registry must have direct access to expert consultants in the areas pertinent to the operation of the registry to assist the registry in establishing policies and procedures.

2.07 The staff of the registry must be trained and knowledgeable about their duties. The registry must conduct and document staff training and maintain training records.

2.08 The registry must retain a staff large enough to assume the volume and variety of services required to perform international searches within a time based on WMDA metrics for unrelated donor search while maintaining the confidentiality of patient and donor.

2.09 The registry must have a fixed physical location.

2.09.1 The location must have sufficient space so that all work can be carried out in an environment designed to minimise errors, reduce risks to health and safety, and maintain confidentiality.

2.10 The registry must have sufficient communication links to facilitate searches. These links must include telephone, fax, and international telematics links (email, internet).

2.11 The registry must have a system of quality management to assess, ensure, conduct and improve the quality of its operations.

2.11.1 The registry must maintain written policies and protocols for all processes performed in the registry. This must include manual of operations, standard operating procedures, and forms.

2.11.2 The registry should have a plan to provide crisis response, business continuity and disaster recovery.

3.0 Donor recruitment, consenting, screening and testing of volunteer donors

Recruitment

3.01 Entities involved in donor recruitment must meet any relevant international and national laws and regulations.

3.01.1 A donor centre must transmit the donor's data necessary for the search process to the registry, through an efficient and secure system of communication that maintains the integrity of the data. The registry is responsible for making these donors available via search databases (e.g. EMDIS/BMDW).

3.02 The recruitment of volunteer donors must be performed under the direction of individuals who are experienced in recruitment of donors and in management activities including education, consenting, counselling, confidentiality, and medical screening. These individuals must be appropriately qualified and provided with timely and relevant training. The training and experience of these individuals must be documented.

Volunteer donor rights

- 3.03 The willingness to become a donor must be the individual choice of each donor, that is, donations must be voluntary. Donors must be willing to donate on behalf of any patient being treated in any part of the world. Donors must not be paid for their donation but may be reimbursed for expenses incurred during the donation process, for example, time lost from work or travel to the collection centre.**
- 3.04 Donors must be informed regarding their potential role in the donation of HPC, the risks involved in the donation, and the tests that the donor may undergo.**
- 3.05 Donors must be informed about the use of any medical intervention (e.g., administration of GCSF) and its known risks and/or side effects.**
- 3.06 A volunteer donor must be free to withdraw at any time.**
- 3.07 To ensure confidentiality, the identity of donors must be protected. Approaches to ensure donor confidentiality must be established.**
- 3.08 The volunteer donor has the right to receive the results of their health screening.

Counselling, timing and format of consent

- 3.09 Signed valid informed consent must be obtained initially at the time of recruitment.**
- 3.10 Volunteer donors must be counselled when selected for further tests and when selected as a donor for a specific patient.**
- 3.10.1 Counselling for volunteer donors selected for specific patients must include anonymity of the donor and patient, requirement for further blood samples before donation, requirement for infectious disease and other testing, risk of donation, possible duration of loss of time from normal activities, location of the collection, the potential for collection of autologous blood, donor's right to withdraw and consequences for the patient, details of insurance coverage, possible subsequent donations of HPC or blood products, alternative collection methods and whether blood is reserved for research purposes.
- 3.11 Signed valid informed consent must be obtained from all volunteer donors at the time of work-up.**
- 3.11.1 Informed consent documents must meet established criteria based at a minimum on WMDA guidelines. In addition to information on the process, risks and benefits, documents must include information on the collection and protection of donor data and the right of the donor to medical confidentiality and to receive medical information.

Documents must be clearly written in terms understood by the donor and, at work-up, must include the signatures of qualified staff involved in donor counselling.

- 3.12 The identity of the volunteer donor must be verified, at a minimum, at work-up and at collection, by the qualified staff signing the consent form.
- 3.13 Signed valid informed consent must be obtained if donor blood or other biological material or information is stored and/or used for the purpose of an ethically approved research project.**
- 3.14 Consent documents signed by volunteer donors must be available for review by individuals designated by the registry or national authorities to evaluate the registry.**

Donor characteristics

- 3.15 Information on donor age and gender must be collected at the time of recruitment.**
- 3.16 Prospective unrelated volunteer donors selected for HPC collection must have passed a minimum age established by national regulations or their 18th birthday if no regulations exist and an upper age-limit for donation must be stipulated after which donors will be removed from the registry.**

3.16.1 The upper age limit for prospective unrelated volunteer donors selected for HPC collection should not exceed 60 years.

Donor testing

- 3.17 Testing must be carried out by laboratories that meet standards established by the government or prevailing in the relevant community for performing these services.

3.17.1 Testing must be carried out in a manner to ensure the accuracy of the data.

- 3.18 Registries must have established approaches to monitor and ensure the accuracy and completeness of the data listed in the donor database, including a system to ensure the quality of HLA typing results.
- 3.19 The results of the donor assessment including the results of any laboratory tests and medical evaluation must be documented and maintained.

Histocompatibility testing and ABO grouping

- 3.20 A minimum of HLA-A,-B,-DRB1 should be defined prior to listing newly recruited volunteer donors on the registry. If not all the newly recruited donors are DR typed, the registry should have a reasonable policy and strategy for selective DR typing of some donors.
- 3.21 The ABO blood group and Rh factor testing of volunteer donors must be done at the verification typing stage if the donor's blood group has not been previously determined.**

Medical assessment and infectious disease testing

3.22 Donor health requirements affecting the suitability of volunteer donors must be established.

3.22.1 An initial health screening should be performed at the time of recruitment.

3.22.2 A health screening must be performed at time of verification typing.

3.22.2.1 Information on donor parity and history of other prior sensitizing events such as transfusion must be obtained from volunteer donors during the verification typing stage.

3.22.3 Policies for testing the volunteer donor selected for work-up must be established and must include medical history, physical exam, and laboratory tests in order to determine the volunteer's fitness to donate.

3.22.3.1 This examination must be performed or supervised by a physician who is not a member of a team who has cared for the patient.

3.22.3.2 Female volunteer donors of childbearing potential must have a pregnancy test performed during the work-up stage.

3.23 The volunteer donor's medical history taken at the time of medical examination for donation must include questions to identify persons at risk of disease transmissible through transplantation (e.g., infectious diseases, genetic defects or disseminated malignancies) according to WMDA recommendations.

3.24 Infectious disease testing of volunteer donors selected for specific patients must include testing for diseases thought to be important to consider in HPC transplantation. Testing must monitor infection with human immunodeficiency virus (HIV), Human T-cell lymphotropic virus I and II, Hepatitis B virus, Hepatitis C virus, Cytomegalovirus (CMV), *Treponema pallidum* (syphilis) and other infectious agents as defined by national health authorities.

3.24.1 Selected volunteer donors should also be tested for local diseases that are important to consider in transplantation. Donors who have recently travelled outside their country should also be evaluated for infectious agents prevalent in the areas of travel.

3.25 Infectious disease markers must be measured within 30 days of the HPC collection and the results must be provided to the transplant centre before commencement of patient conditioning.

- 3.26 The volunteer donor must be counselled in case of positive disease results.
- 4.0 Umbilical cord blood and maternal donor recruitment, consenting, screening, testing and review/release of cord blood units.

Recruitment and collection

- 4.01 All parties involved in maternal donor recruitment and in cord blood collection must meet any relevant national laws and/or international regulations.
- 4.01.1 The cord blood bank must transmit all cord blood unit data necessary for the search process to the registry, through an efficient and secure system of communication that maintains the integrity of these data. The registry is responsible for making these cord blood units available via search databases (e.g. BMDW/EMDIS).
- 4.02 The recruitment of maternal donors must be performed under the direction of individuals who are experienced in recruitment of maternal donors and in management activities including education, consenting, counselling, confidentiality, and medical screening. These individuals must be appropriately qualified and provided with timely and relevant training.

Maternal donor and infant donor rights

- 4.03 The willingness to donate cord blood must be the individual choice of each maternal donor, that is, donations must be voluntary. The maternal donor must be willing to donate to any patient being treated in any part of the world and must not be paid for their donation.**
- 4.04 Maternal donors of cord blood units must be informed regarding their role in the donation of cord blood, the collection procedure, the long-term storage of the cord blood, the possible risks for and benefits to the maternal donor and/or infant donor, the tests to be performed on the maternal biological samples and on the donated cord blood unit.**
- 4.05 The maternal donor must be informed about the right to withdraw her consent for the donation of cord blood without prejudice at any time before delivery.**
- 4.06 To ensure confidentiality, the identity of maternal donors and infant donors must be protected. Policies and procedures must be in place to ensure donor confidentiality.**
- 4.07 The maternal donor has the right to receive the results of the maternal and infant donor health screening, if the test results are available.

Counselling, timing and format of consent

4.08 Signed informed valid consent must be obtained and documented while the maternal donor is able to concentrate on the information, before the maternal donor goes into active labour.

4.08.1 Informed consent documents must meet established criteria. In addition to information on collection procedure, intent of donation for unrelated use, possible risks and benefits, documents must include information on the protection of donor identity, donor data and the right of the donor to medical confidentiality and to receive medical information. Documents must be clearly written in terms understood by the maternal donor and must include the signatures of qualified staff involved in maternal donor recruitment.

4.09 Signed informed valid consent must be obtained if maternal or infant donor blood, cord blood units or other biological material or information is stored and/or used for the purpose of an ethically approved research project.

4.10 Consent documents signed by maternal donors must be available for review by individuals designated by the registry or national authorities to evaluate the registry.

Cord blood unit characteristics

4.11 Date of birth, time of collection and gender associated with the cord blood unit must be registered at the time of collection.

4.12 The total nucleated cell count (TNC) must be obtained in the final product prior to cryopreservation for listing a unit in the registry database.

Testing

4.13 Testing of maternal and infant donor samples must be carried out by laboratories that meet standards established by the government or prevailing in the relevant community for performing these services.

4.13.1 Testing must be carried out in a manner to ensure the accuracy of the data.

4.14 Registries must have established approaches to monitor and ensure the accuracy and completeness of the data listed in the cord blood unit database, including a system to assure the quality of HLA typing results.

4.15 The results of the maternal and infant donor assessment including the results of any laboratory tests and medical evaluation must be documented and maintained.

Histocompatibility testing and ABO grouping

4.16 A minimum of HLA-A,-B,-DRB1 should be defined prior to listing umbilical cord blood units in the registry database.

4.17 The ABO blood group and Rh factor testing must be done prior to listing a cord blood unit in the registry database.

Medical assessment and Infectious disease testing

4.18 Requirements for maternal and infant donor health affecting the eligibility of donation must be established.

4.19 A health screening of the maternal donor for diseases transmissible through transplantation must be performed and included in the status at the time of delivery.

4.20 A maternal blood sample, obtained within 7 days before or after collection of the cord blood unit, must be tested for diseases thought to be important to consider in HPC transplantation. Testing must monitor infection with human immunodeficiency virus (HIV), Human T-cell lymphotropic virus I and II, Hepatitis B virus, Hepatitis C virus, Cytomegalovirus (CMV), *Treponema pallidum* (syphilis) and other infectious agents as defined by national health authorities.

4.20.1 Maternal donors should also be tested for local diseases that are important to consider in transplantation. Maternal donors who have recently travelled outside their country should also be evaluated for infectious agents prevalent in the areas of travel.

4.21 A medical and genetic history of the infant donor's family must be obtained and documented.

4.22 Hemoglobinopathy testing on the infant donor or the cord blood unit must be performed prior to shipment of the cord blood unit for transplantation.

4.23 A history of the current pregnancy, delivery and the infant donor's status at birth must be obtained, documented and reviewed to include any findings that might suggest the possibility of disease transmission through the cord blood unit.

4.23.1 The history of the infant donor must be updated and maternal screening should be repeated within a reasonable time frame post delivery to capture risks not immediately detected at birth, in particular in cases where the first screening was done early in pregnancy.

4.23.2 The maternal donor must be informed about the importance of contacting the cord blood bank if the infant donor develops a serious disease later in life.

4.24 The maternal donor must be counselled in the case of positive disease results that pose health risks to the maternal donor or infant donor.

4.25 The cord blood bank must review all source documentation prior to shipment of the cord blood unit for transplantation and must have policies and procedures in place describing what information

should be passed on to the transplant centre and how that communication will take place.

- 4.26 Prior to shipment, the identity of the cord blood unit must be verified through verification typing from attached segment of the cord blood unit or through any other validated procedure.

5.0 Information technology and information management

General information management

5.01 The registry must maintain records of its activities and must maintain a database of volunteer donor information.

5.01.1 The donor centre/cord blood bank must use a validated process for transmitting donor data/cord blood unit information necessary for search process to the registry.

- 5.02 Any HLA-related information stored, presented or communicated by the registry must follow WHO nomenclature and WMDA guidelines for the use of HLA nomenclature.

5.03 All patient and donor communications and records must be stored to ensure confidentiality and to allow for traceability of the donors/cord blood units and steps of the donation process.

- 5.04 To ensure confidentiality, the identity of donors/cord blood units must be protected. The registry, or its designee, must assign a unique and anonymous identifier to each volunteer donor, each maternal donor and each cellular product. This identifier must be used to track each volunteer donor and cord blood unit with their associated data and biological material and their participation in the donation process long term.

- 5.05 The system of quality management must include an assessment of all electronic functions to ensure that errors and problems are reported and resolved.

- 5.06 The access to donor and patient data information in the registry as well as the transmission of this information to and from the registry must be organised in a way that accidental or unauthorised access, destruction or modification is prevented.

- 5.07 Records must be maintained for an appropriate period of time, at least as dictated by national laws or standards. Key documents related to donor traceability must be maintained at a minimum for thirty (30) years following donation. Data storage may be on paper or in electronic form.

System administration

- 5.08 The key components of a registry's hardware, software and network architecture and external connections must be adequately documented.

- 5.09 Electronic connection and communication between establishments must be organised and performed with greatest possible care minimizing vulnerabilities and exploitation risks.
- 5.10 Redundant and reliable software and hardware architecture should be used to minimise the probability of failure or data loss and the possible length of a down time.
- 5.11 Backup of all systems and data must be performed regularly at reasonable intervals. Backups must be validated by data restoration tests. These activities must be documented.
- 5.12 The overall system documentation must provide all information necessary for trained and skilled staff to keep the Information Technology systems operational.

System development

- 5.13 A procedure for the definition, specification, implementation, validation and authorization of relevant systems (software, hardware and network) must be established and documented. Each such process itself must be appropriately documented on a continuous basis.
- 5.14 Any system installed must be accompanied with adequate documentation for its qualification, maintenance (in particular detail if developed in house), administration and operation.
- 5.15 Any modifications to such systems must be performed in a way fulfilling 5.13 and 5.14.
- 5.16 Any function needed for information management may be performed by or with the help of qualified third parties (e. g. a company or a university). Responsibilities of both parties must be described in writing.

Functionality of information technology systems

- 5.17 Search algorithms must provide lists of suitably matched donors in a reasonable time frame.
- 5.18 Each printed report must be dated.
- 5.19 Each step in the search process (e. g. patient registration and any request, result or update) must be documented with all relevant attributes and a time stamp.
- 5.20 The information history of relevant data must be recorded.

6.0 Facilitation of search requests

6.01 Critical communications between registries or between a registry and a transplant centre must be in writing, or via electronic established system.

- 6.01.1 These communications should contain a signature of authorization and be sent by fax or email or should be submitted through authorised access to a communication system.

6.02 Registries must respond to search requests and to requests for additional information and/or an aliquot of donor (or maternal if cord blood) sample within a time period consistent with WMDA metrics and in a defined manner.

6.02.1 Registries or their associated donor centres/cord blood banks must have the capability of shipping samples, if available, to the appropriate transplant centre if required for further testing. The sample must be appropriate for the testing required.

6.02.2 Verification typing of the donor/cord blood unit at a minimum of HLA-A, -B, -DRB1 must be performed prior to donation/shipment for a specific patient.

6.02.3 The policy of the registry regarding repetition of the database search for a specific patient must be defined and readily accessible to health care professionals involved in HPC transplantation.

6.02.4 The registry must have an effective mechanism to provide access to international patients.

6.03 A donor selected for a specific patient must be placed on a “reserved” status from the time of verification typing until the donation date is reached.

6.03.1 If the donation/shipping date is not scheduled or is delayed, a maximum time limit and the procedures for granting exceptions for this status must be set in writing and be readily accessible to health care professionals involved in HPC transplantation.

6.04 The donor centre/cord blood bank must be informed of the proposed date(s) of transplant at the time a specific donor/cord blood unit is requested for transplantation for a specific patient. If a volunteer donor will be the source of HPC, the donor must also be informed. The transplant centre must specify the latest date by which the donor centre must approve the eligibility of a donor for donation of HPC for a specific patient (i.e., provide donor clearance).

6.05 The registry must make their policy for the minimum criteria needed to allow a specific donor to be available for a specific patient readily accessible to the appropriate parties, such as national/international organisations authorised to provide hematopoietic progenitor cell treatment.

6.06 Prior to transplantation, the registry must have a process for communicating the volunteer donor’s preference to the appropriate transplant centre in a timely fashion to indicate the type of cells and to communicate any other donor-specific issues) that may impact the transplantation. Nevertheless, the volunteer donor must be free to change their mind at a later date.

- 6.07 Donor and patient identity must remain confidential throughout the search process so that only appropriate registry personnel have access to these data.**
 - 6.07.1 The registry must have a written policy listing the conditions under which volunteer donors and recipients might be informed of each other's identity. These policies must comply with governmental laws on disclosure.**

- 7.0 Second and subsequent donations of HPC and/or blood products for the same patient
 - 7.01 The registry must have a written policy regarding the process to be followed when a transplant centre requests a subsequent donation and the time frame for the process of approval.**
 - 7.01.1 This policy must include the specific details that should be provided by the transplant centre to document the need for a subsequent donation.
 - 7.01.2 This policy must be readily available to health care professionals involved in HPC transplantation.

- 8.0 Collection, processing and transport of haematopoietic progenitor cells
 - 8.01 Collection of HPC and any other collected cell products intended for therapeutic use, must be performed at a collection centre/cord blood collection site that fulfils standards established by the government or prevailing in the relevant community for such a facility.**
 - 8.02 The collection centre/cord blood collection site must ensure the identity, safety and privacy of the donor.**
 - 8.03 The collection centre/cord blood bank collection site and the procurement of HPC must be under the direction of trained and experienced health care professionals.**
 - 8.04 If required, autologous donor blood must be collected at a blood collection centre that fulfils national and/or regional and/or international guidelines for such a facility.**
 - 8.05 If a volunteer donor is subjected to a medical intervention (e.g., administration of GCSF) as part of the HPC collection process, the registry must have appropriate policies and procedures to protect the health and safety of the donor and of the recipient.**
 - 8.05.1 These policies should include the procedure regarding the type of collection (HPC, apheresis versus HPC, Marrow) in case of failed mobilization.

- 8.05.2** The registry must have a policy concerning the use of a central venous catheter (CVC) in volunteer donors to assure that a CVC is only used in exceptional circumstances. Those circumstances must be documented.
- 8.05.3** The registry must have a policy that protects the safety of the volunteer donors with a CVC inserted.
- 8.06** Written policies and procedures must be in place to ensure the identity, quality and quantity of the collected cells. These must include policies for communication between the transplant centre, collection centre/cord blood bank and cell processing unit regarding the number of cells required.
- 8.07** Written documentation of the characteristics of the collected product important in facilitating transplantation must be provided with the cells according to applicable guidelines. The documentation and/or label, at a minimum, must include information on the name of the product, the number of cells collected, the donor's unique identification code, donor ABO/Rh group, identification of the patient, date and time of collection (only in case of volunteer donor), any processing details, and name and contact information of the transplant centre. Labelling of the product must ensure the identity of the product.
- 8.08** Cells must be transported in a timely and reliable fashion to meet transplant centre requirements for the quality and quantity of the cell product upon arrival at the transplant centre. Packaging must comply with national and international regulations. Policies and procedures documenting the transport process must be stipulated.
- 8.08.1** In case of transport of a cord blood unit the dry shipper must contain an electronic data logger that continuously monitors temperature throughout the transportation or shipping period.
- 8.09** SAE affecting a cellular product intended for a specific patient must be identified, documented, investigated and remedial and/or corrective action taken.
- 8.10** SAR impacting the cellular product and hence potentially the patient's health must be submitted to a WMDA sponsored international centralised database of such events (SPEAR).
- 8.10.1** Reports of SAR affecting the donated cellular product must be communicated to the registry involved in the donation if the event might affect the transplantation. Other individuals or groups should be notified as appropriate.

8.10.2 The registry must comply with governmental regulations including requirements to report such adverse reactions to a regulatory agency.

9.0 Follow-up of patient and volunteer donor

9.01 The registry must have policies and procedures for the first year following donation for the follow-up and care of volunteer donors for conditions related to the HPC donation.

9.02 The registry must have policies and procedures for the long-term follow-up and care of volunteer donors for conditions related to the HPC donation. Long-term is defined as the time period following the first year after donation and extending for at least ten years.

9.03 SAR affecting donors undergoing collection of HPC and occurring both in the long term and/or the short term as a consequence of the donation must be identified, documented, investigated and remedial and/or corrective action taken.

9.03.1 Similar actions must be taken for adverse reactions occurring due to registry operations and impacting the health and safety of donors or patients.

9.04 SAR (either short- or long-term) affecting donors undergoing collection of HPC must be submitted to a WMDA sponsored international centralised database of such events (SEAR).

9.04.1 Reports of adverse reactions during a donation that might affect the initial or subsequent donation must be communicated to the patient outcome registry or transplant centre as appropriate.

9.04.2 The registry must comply with governmental regulations including requirements to report such adverse reactions to a regulatory agency.

9.05 Donor health issues post-donation potentially affecting the health of a patient having received a HPC donation from that donor must be reported to the transplant centre.

9.06 WMDA qualified/accredited registries should require their national transplant centres to submit data to a regional or international patient outcome databases in order to collect clinical outcome data of the transplanted patients.

10. Financial and legal liabilities

Responsibilities

10.01 The registry must keep complete and accurate financial records for all services provided and requested according to national laws and regulations as well as international standards.

Fee structure

- 10.02 A clear fee schedule detailing payment terms for extended and verification HLA testing, infectious disease marker testing, procurement and other related services must be available upon request. Changes in the fee schedule should be provided to interested parties thirty days prior to implementation.
- 10.03 Any cost not standardised or, for any reason, not accessible through such a schedule should be estimated and communicated in advance to the requesting registry and/or transplant centre.
- 10.04 If the procurement procedure is cancelled after the final donor selection, collection centre and/or donor centre and/or registry are entitled to charge for services performed prior to notice of cancellation. This practice must be noted on the fee schedule.

Billing

- 10.05 The registry providing HPC products or any other requested service must bill to and request payment from the registry/transplant centre requesting the hematopoietic progenitor cell products or service.
- 10.06 Billing must occur within sixty (60) days of service completion.

Payment

- 10.07 A registry requesting a service for a patient or forwarding such a request from a transplant centre guarantees the payment of completed services. If the requesting registry cancels the service, the reporting registry must expect full payment provided that the services are completed and reported within thirty (30) days of the cancellation date.
- 10.08 A registry must have adequate administrative structures and financial resources to guarantee the settlement of all invoices in due course.**
- 10.09 It is the responsibility of the requesting registry to collect funds from any person or institution ultimately covering these expenses. If it is unable to collect funds from the originating institution, the registry must be liable for the expenses incurred.

Legal liability

- 10.10 The registry must assume responsibility and establish procedures for all donor medical expenses including the pre-collection physical examination, the collection procedure and all post-collection medical expenses that are directly related to the donation. No volunteer donor should assume financial liability for any portion of the follow up testing and/or HPC procurement process. The registry is responsible for all reasonable expenses incurred by the donor.**

- 10.11 The registry, or its designee, should offer disability and death benefits to all volunteer donors.
- 10.12 The registry should maintain liability insurance.

Appendix I

Examples of organisations offering accreditation, on an international level, related to registry operations.

Area of Accreditation	Organisation
Transplant centre	Joint Accreditation Committee ICST (International Society for Cellular Therapy) and EBMT (European Group for Blood and Marrow transplant) (JACIE)
	Foundation for the Accreditation of Cellular Therapy (FACT)
Collection centre (marrow and/or peripheral blood progenitor cells)	FACT-JACIE
	AABB
Umbilical cord blood bank operations	Netcord-FACT
	AABB
Processing laboratory	AABB
	FACT-JACIE
Histocompatibility assessment	European Federation for Immunogenetics (EFI)
	American Society for Histocompatibility and Immunogenetics (ASHI)
General administration and other relevant sections	International Organization for Standardization (ISO 9001)
The international information technology standard for transfusion medicine and transplantation.	International Society Blood Transfusion (ISBT)

Appendix II

Changes to Standards document

Date of Revision	Alterations to Document	Status
May, 2003	Completion of standards	Board approved, Discussed at Dreieich meeting & approved subsequently
May, 2004	Reworded standard 1.01 in Overview and definitions to remove the word "pilot"	Board approved, Tokyo meeting
March, 2005	Added new standard 6.08 on contact of transplant centre with donor requests for harvest type etc.	Board approved, Prague meeting
November, 2005	Revised Chapter 10; added changes to 6.01.1 on communication with signature	Board approved, Minneapolis;
May, 2006	Revised standards based on EU directives	Board approved, Cape Town meeting
November, 2006	Revised Chapter 5; added changes to 6.02.2	Board approved, Minneapolis;
March, 2007	Added changes in 2.05, 3.0, 3.06.1, 4.05, 4.06 9.03, 10.02.3	Board approved, Lyon
November 2007	7.03.2 changed from "should" to "must" on making policy publicly available 8.07 new standard on SPEAR but it is a "should"	Board approved, e-mail communication November 2007
April 2008	Changes made to incorporate cord blood into the standards	Board approved
June 2010	Reworded definitions. Added changes in 1.01, 1.04.2.2, 3.05.5, 3.06.1, 4.05, 4.07.1, 5.01.5, 6.08, 7.02, 8.06, 9.04.3, 9.06. Added new standards: 1.06, 3.05.6, 3.06.2.4, 3.06.3.3.1, 3.06.3.5, 4.03.1	Board approved
April 2013	Changes made to reorder and to introduce a dedicated chapter for cord blood, etc. New standard: 1.04, 6.05, 8.05.2, 8.05.3, 8.08.1	Board approved