

	World Marrow Donor Association			
	International Standards for Unrelated Hematopoietic Stem Cell Donor Registries			
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WORLD MARROW DONOR ASSOCIATION
WMDA
INTERNATIONAL STANDARDS
UNRELATED HEMATOPOIETIC STEM CELL DONOR REGISTRIES

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FOREWORD

The World Marrow Donor Association (WMDA) promotes product quality and global collaboration through accreditation and standardisation. WMDA members, clinicians, national authorities and donors trust WMDA accreditation as an indication that high quality hematopoietic stem cell products are efficiently provided and donor safety is ensured. The WMDA accreditation programme is based on the WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries.

The WMDA Standards set forth the minimum guidelines to facilitate hematopoietic stem cell transplantation and cell therapies. The major objectives of the 2020 edition of the WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries are to:

- process the incoming requests for access to donors/cord blood units arriving from organisations in other countries in a secure way;
- facilitate outgoing requests for international donors/cord blood units for patients in the country where the registry resides;
- coordinate the activities of donor, collection, and transplant centres, and cord blood banks within a registry.

These WMDA Standards are effective on January 1, 2020. All WMDA certified, qualified and accredited registries are expected to comply with these WMDA Standards.

A list of WMDA certified, qualified and accredited registries is visible on the WMDA website. See the following link: <https://share.wmda.info/x/DAAwBw>.

The WMDA Standards do not set forth all that may be required to conform to governmental regulations or the standards prevailing in the local legal environment. Each WMDA certified, qualified or accredited registry must determine and follow additional laws, regulations, practices and procedures that apply in their local legal and regulatory environment. 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 local legal and regulatory environment.

A. INTRODUCTION AND DEFINITIONS

1.0 Introduction

1.01 WMDA has a two-level process to become WMDA accredited:

- The first time that a registry applies, the registry will become WMDA certified or WMDA qualified if the registry complies with the '**benchmark**' WMDA Standards. Depending on the level of activity of a registry, the registry will become either WMDA certified (low activity) or WMDA qualified (activity above a specific level). The process to become a WMDA certified or WMDA qualified registry will not include an on-site inspection.
- The second time that a registry applies and if the registry has a sufficient level of activity, the registry will become WMDA accredited if the registry complies with all WMDA Standards. The process will include an on-site inspection. Accreditation status can be renewed.

1.02 For purposes of the WMDA Standards, the term "must" means that the Standard is to be complied with at all times. The term "should" indicates an

activity that is recommended or advised, and for which there may be effective alternatives. The term may or might is permissive, indicating that the practice is acceptable, and not necessarily recommended.

2.0 Definitions/abbreviations

Note: Organisations, defined as a “registry” in the WMDA Standards, providing hematopoietic stem cells to a patient in another country vary in their administrative structures. The definitions below are aimed at defining the individual elements that 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

Agreement:

A formal arrangement between organisations as to a course of action to supply a service

ASHI:

American Society for Histocompatibility and Immunogenetics

Benchmarked standards:

A subset of the WMDA Standards that are considered the most critical for registry quality. This subset of standards is the basis for the evaluation of certification or qualification status.

Blood collection centre:

A medical facility where blood intended for testing and/or transfusion is drawn and stored

Cell processing unit:

A medical laboratory facility where hematopoietic stem cells are manipulated prior to transplantation/cellular therapy. 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 hematopoietic stem cell collection from donors takes place. This collection might include marrow aspiration or apheresis. The collection centre physician, or designee, performs the medical workup of the potential donor and provides the final approval of the donor for collection. The collection centre packages the stem cell 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

Courier:

An individual trained and qualified in transport of hematopoietic stem cell products

Donor:

A person who is the source of cells or tissue for a cellular therapy product. Donors are volunteers and unrelated to the patient in need of a transplant.

The WMDA Standards refer to three types of donors:

- Volunteer donors who have passed a minimum age established by national law or their eighteenth (18th) birthday when no regulation exists;
- Infant donor from whose placenta and/or umbilical cord the cord blood is obtained;
- 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

EFI:

European Federation of Immunogenetics

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 purpose of this typing is to ascertain the level of HLA match between donor and potential recipient. The additional HLA typing may be performed on a stored sample. This typing may also serve as a verification typing if it is performed on a fresh sample from the donor or attached segment of the cord blood unit.

Global registration identifier for donors (GRID):

The global registration identifier for donors provides a format for registries and donor centres that issue donor identifiers. The GRID assures that every donor is assigned a globally unique identifier.

HSC:

Hematopoietic stem cells (defined also as hematopoietic progenitor cell-HSC) are the 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 stem cell transplantation:

A medical procedure involving transplantation/cellular therapy of hematopoietic stem cells

HLA:

Human Leukocyte Antigen

IDM:

Infectious Disease Marker

Must:

To be always complied with

Patient/Recipient:

Individual in need of transplantation/cellular therapy is a patient; a patient who has received a cellular therapy is a recipient.

Product:

A cellular therapy product that contains hematopoietic stem cells and/or other nucleated cells intended for therapeutic use

Product code:

Unique numeric or alphanumeric identifier by which it will be possible to trace any cellular therapy product to its donor and to all records describing the handling and final disposition of the product.

Qualification:

Qualification is the process of proving that a system, supplies and equipment work correctly. For example, a new cord blood collection process must be validated; a shipping container used must be qualified first. By convention, the word validation is always used for software.

Quality management system:

A system that documents policies, procedures and responsibilities for achieving quality within an organization and a process to audit the quality system. The system includes:

- Personnel requirements such as qualifications, training, competencies, and responsibilities;
- Detection, reporting of, and corrective action(s) taken, 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;
- Description of facilities and safety considerations.

Registry:

An organisation responsible for coordination of the search for hematopoietic stem cells from donors (including cord blood) unrelated to the potential recipient.

- The patient registry or requesting registry is the registry that acts on behalf of their transplant centres.
- The donor registry or providing registry is the registry that provides the hematopoietic stem cell product.

Rh:

A specific antigen present on the surface of red blood cells, Rhesus

SAE (Serious adverse event) – Risk of Harm:

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 recipients or which might result in, or prolong, hospitalisation or morbidity.

SAR (Serious adverse reaction) - Harm:

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

Search:

The process of identifying a suitable stem cell source for a patient in need of a transplant

Should:

Recommended or advised, but effective alternatives may exist.

S(P)EAR Committee:

A WMDA Committee responsible for review of all events/reactions reported to WMDA as potential risk of harm or harm. The Committee evaluates the events/reactions' imputability (i.e., whether the event can be attributed to the donation or transplantation process) and impact.

Standard operating procedures (SOP):

A compilation of documented 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 SOPs must be documented and authorised.

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 (TNC) count:

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 hematopoietic stem cells from an unrelated donor or from an umbilical cord blood unit. The transplant centre 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 transplant centres. This entity may be contained within a transplant centre or may be separate from the transplant centre. If separate, the search unit may coordinate searches for one or several transplant centres. In the WMDA Standards, reference to a transplant centres should be interpreted as a transplant centre and/or a search unit as appropriate. Transplant centres/search units seeking an international donor work through the registry in their country.

Valid signed informed consent:

Signed documentation indicating that a potential 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 informed consent is valid when it complies with applicable local legal regulations.

Validation/Qualification:

Validation is the process of providing documented evidence that a specific process will consistently produce a product meeting its predetermined specifications and quality. Qualification is the process of proving that a system, supplies and equipment work correctly. For example, a new cord blood collection process must be validated; a shipping container used must be qualified first. By convention, the word validation is always used for software.

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 of and concordance with an existing HLA assignment. The purpose of this typing is to ensure that the donor/cord blood unit is the same individual/unit whose HLA typing was listed on the search report used to select the donor. This stage was historically referred to as "confirmatory typing (CT)".

Written Information Security Policy (WISP):

A set of comprehensive guidelines and policies designed to safeguard all confidential and restricted data maintained at the registry

WMDA Data Use Agreement:

Agreement between WMDA and the registry listing donors and/or cord blood units

WMDA Share:

The membership website of WMDA with the domain name: <https://share.wmda.info>

World Marrow Donor Association (WMDA):

The World Marrow Donor Association, abbreviated as WMDA, strives to ensure that patients worldwide have equal access to high quality cells for transplantation from donors whose rights and safety are protected.

WMDA promotes global collaboration and the sharing of best practices among its members for the benefit of stem cell donors and patients.

WMDA aims:

- *Optimising 'Search, Match & Connect'*: Provide a global platform that facilitates access to the most suitable stem cell source for a transplant patient;
- *Supporting global development*: Support members to develop and grow, so that more transplant patients find the most suitable match;
- *Promoting donor care*: Ensure that the rights and safety of stem cell donors are promoted and protected;
- *Ensuring quality*: Promote product quality and global collaboration through accreditation and standardisation.

Workup:

At this stage, a potential donor has been identified as an acceptable match for a patient, agrees to donate hematopoietic stem cells after a full donor information and counselling session, and is medically evaluated for their fitness to donate hematopoietic stem cells.

B. STANDARDS

1.0 General

- 1.01 A WMDA regular member organisation is eligible for WMDA certification or WMDA qualification as a first step, followed by WMDA accreditation as a second step.
- 1.02 If a registry is accredited for international exchange of hematopoietic stem cells by an international organisation with standards that meet or exceed WMDA Standards, that registry may be given WMDA qualification following submission and evaluation of material documenting that accreditation.**
- 1.02.1 **If not all the WMDA Standards are covered by this international accreditation, evidence of compliance with the WMDA Standards that are not covered must be provided.**
- 1.02.2 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.
- 1.03 A registry that intends to request WMDA certification or WMDA qualification or that has obtained WMDA certification, qualification or WMDA accreditation must participate in the annual WMDA Global Trends Report.**
- 1.04 The registry's operational and regulatory information as per the WMDA survey must be available on the WMDA Share. This information should be reviewed by the registry at least annually and must be updated as significant changes occur.**
- 1.05 Changes to the status of a registry that may affect WMDA certification, qualification or 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 an 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 HSC 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 an 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.
- 1.08 If a registry relies on an independent collection centre for the collection of hematopoietic stem cells 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. The nature of these

affiliations and the duties and responsibilities of each entity must be documented in an agreement.

- 1.09 The registry must have a policy and procedure to review WMDA recommendations.

2 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. The authorised official must authorise all official documents.**
- 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 hematopoietic stem cell transplantation and cell therapies 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 hematopoietic stem cell transplantation, comprehend alternative therapies and donor search problems associated with these diseases, understand HLA antigens/alleles 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 to access a medical review panel to assist the registry with making unbiased decisions regarding nonstandard, high risk or experimental hematopoietic stem 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 registry staff must be trained and knowledgeable about their duties. The registry must conduct and document staff training and maintain training records.
 - 2.07.1 At least one member of the registry staff must be able to communicate in English and be available as needed to facilitate international searches.**
- 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 timeframe in accordance with 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 to ensure 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 a system of quality management to assess, ensure, conduct and improve the quality of its operations.
 - 2.10.1 **The registry must maintain documented policies and procedures for all processes performed in the registry. This must include manual of operations, standard operating procedures, and forms.**
 - 2.10.2 The registry should have a plan to provide crisis response, business continuity and disaster recovery.
 - 2.10.3 The registry should have a documented risk management plan to mitigate against risks, and processes to manage risks or incidents should they arise.
 - 2.10.4 The registry should have a strategic plan.
- 3.0 Donor recruitment, consenting, screening and testing of donors

Recruitment

- 3.01 The registry must ensure that entities involved in donor recruitment meet applicable laws and regulations.
- 3.02 Recruitment of donors must be performed by professionals trained for recruitment, 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.

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 and may be reimbursed for expenses incurred during the donation process.**
- 3.04 **Donors must be informed regarding their potential role in the donation of hematopoietic stem cells, 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 and its known risks and/or side effects.**
- 3.06 **A donor must be free to withdraw at any time.**
- 3.07 **To ensure confidentiality, the identity of donors must be protected. The registry must have policies and procedures in place to ensure donor confidentiality.**
- 3.08 The donor has the right to receive the results of any health screening affecting their health status. The registry must have a policy regarding the provision of such information.

Counselling, timing and format of consent

3.09 Valid informed consent must be obtained initially at the time of recruitment.

3.10 Donors must be counselled when selected for further tests and when selected as a donor for a specific patient.

3.10.1 Counselling for 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 loss of time from normal activities and duration thereof, 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 hematopoietic stem cells or cellular products, alternative collection methods and whether blood or other biological material is reserved for research purposes.

3.11 Valid signed informed consent must be obtained from donors at the time of workup.

3.11.1 Informed consent documents must meet established criteria. 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. Documentation must be in a language understood by the donor and, at workup, must include the signature(s) of qualified staff involved in donor counselling.

3.12 The identity of the donor must be verified, at a minimum, at workup and at collection, by the qualified staff signing the consent form.

3.13 Valid signed 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 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 donors selected for hematopoietic stem cell collection must have passed a minimum age established by applicable law or their 18th birthday if no local regulations exist.

3.16.1 The upper age limit for prospective donors selected to donate hematopoietic stem cells should not exceed sixty (60) years. The registry must have a policy and procedure to remove donors from the registry.

Donor testing

3.17 Testing must be carried out by laboratories that meet standards established by local regulation.

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, -C, -DRB1 DNA-based typing results must be defined prior to listing newly recruited donors.
 - 3.20.1 The registry must use HLA testing laboratories that are capable of carrying out DNA-based intermediate and high-resolution HLA-typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or other accrediting organisations providing histocompatibility services appropriate for hematopoietic stem cell transplantation.
- 3.21 The ABO blood group and Rh factor testing of 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 regarding the suitability of 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 including infectious disease testing must be performed at time of verification typing.**
 - 3.22.2.1 Information on the number of pregnancies (including all pregnancies, whether or not a child was born) and history of other prior sensitizing events such as transfusion must be obtained from donors at time of verification typing.
 - 3.22.3 **Policies for testing the donor selected for workup must be established and must include medical history, physical examination, and laboratory tests in order to determine the donor's fitness to donate.**
 - 3.22.3.1 This examination must be performed or supervised by a physician who is not the primary treating physician overseeing the care of the patient.
 - 3.22.3.2 **Female donors of childbearing potential must have a pregnancy test and be counselled to avoid pregnancy during the workup stage before use of mobilising agents, collection or initiation of the recipient's preparative regimen, whichever occurs first.**
- 3.23 The donor's medical history taken at the time of medical examination for donation must include questions to identify risk of disease transmissible through transplantation.**
- 3.24 Infectious disease testing, as defined in 3.22.2, of donors selected for specific patients must include testing for diseases thought to be important**

to consider in hematopoietic stem cell 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 local regulation.

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

3.25 Infectious disease markers must be measured within thirty (30) days of the hematopoietic stem cell/cellular product collection and the results must be provided to the transplant centre before commencement of patient conditioning.

3.26 The donor must be counselled in case of positive transmissible disease test results.

4.0 Umbilical cord blood and maternal donor recruitment, consenting, screening, testing and review/release of cord blood units.

Recruitment

4.01 All parties involved in maternal donor recruitment and in cord blood collection must meet applicable laws and regulations.

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. The training and experience of these individuals must be documented.

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 potential 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.

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. Documented 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 Valid signed informed consent must be obtained and documented while the maternal donor is able to concentrate on the information and is not distracted by aspects of labour.

4.08.1 Informed consent documents must meet established criteria. In addition to information on the 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 maternal donor to medical confidentiality and to receive medical information. Documentation must be in a language understood by the maternal donor and must include the signature(s) of qualified staff involved in maternal donor recruitment.

4.09 Valid signed informed 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 collection, 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 local regulation.

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, -C, -DRB1 DNA-based typing results must be defined prior to listing umbilical cord blood units.

4.16.1 The cord blood bank must use HLA testing laboratories that are capable of carrying out DNA-based intermediate and high-resolution HLA-typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or other accrediting organisations providing histocompatibility services appropriate for hematopoietic stem cell transplantation.

4.17 The ABO blood group and Rh factor testing must be done prior to listing a cord blood unit for search.

Medical assessment and Infectious disease testing

- 4.18 Requirements for maternal and infant donor health regarding 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 seven (7) days before or after collection of the cord blood unit, must be tested for diseases thought to be important to consider in hematopoietic stem cell 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 local regulation.**
- 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 diseases 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 should 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 provided with information to contact 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 an attached segment of the cord blood unit or through any other validated procedure.

5.0 Information technology and information management

System administration

- 5.01 Any registry system must be accompanied with adequate documentation detailing its specification, validation, maintenance, administration and operation; including hardware, software, the network architecture and external connections.

System security

- 5.02 Electronic connection and communication between organisations must be coordinated and performed with greatest possible care minimising vulnerabilities and exploitation risks.

Business continuity

- 5.03 Redundant, 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.
- 5.04 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.**
- 5.05 In the event of termination of operations, the registry should ensure continued adherence to data protection and record retention standards.

Maintenance

- 5.06 The system of quality management must include an assessment of all electronic functions to ensure that errors and problems are reported and resolved.
- 5.07 System modifications must be managed through a documented change management process.
- 5.08 Registry information technology systems must be maintained to ensure that the used software is up to date to minimise security risks and to make sure that all systems are running properly.

Software development

- 5.09 Registry software developed in-house must follow a documented software development process.

Registry operations - traceability

- 5.10 The registry must maintain records of its activities and must maintain a database of donor and/or cord blood unit information.**
- 5.11 All patient and donor/cord blood unit communications and records must be stored to allow for traceability of the donors/cord blood units from recruitment through the donation process, and post-donation/shipment.**
- 5.12 Each step in the search process must be documented with all relevant attributes, including a date and time stamp.
- 5.13 The information history of relevant data must be recorded.

Registry operations - data transmission

- 5.14 The registry must have sufficient communication links to facilitate searches, including backup methods if the principal link is unavailable.**

- 5.15 When transferring data between organisations, there must be a validated protocol for the transfer of data. Both the transferring organisation and the receiving organisation must have policies to verify data.
- 5.15.1 **Any HLA-related information stored, presented or communicated by the registry must follow WMDA guidelines for the use of HLA nomenclature.**
- 5.15.2 **The registry, or its designee, must assign a unique and anonymous identifier to each donor, each maternal donor and each cellular product to ensure confidentiality. This identifier must be used to track each donor and cord blood unit with their associated data and biological material and their participation in the donation process long term.**
- 5.16 The registry listing donors must use GRID to issue donor identifiers at the time that WMDA makes GRID mandatory.

Registry operations - quality

- 5.17 **Search reports must generate lists of suitably matched donors/cord blood units in a reasonable time frame.**
- 5.18 **Each printed report must be dated.**

Registry operations - protection personal data

- 5.19 **The access to personal donor and patient data as well as the transmission of these data between organisations must be coordinated in a way that accidental or unauthorised access, destruction or modification is prevented.**
- 5.20 The registry must formally assign a security role to be accountable for the oversight and governance of the registry's security and privacy risks and related controls.
- 5.21 The name and contact information of the security role must be posted on the registry's information profile on WMDA Share.
- 5.22 **A Written Information Security Policy must be documented and maintained.**
- 5.23 Prior to collecting, processing or sharing personal information, all unnecessary identifiers must be removed from the data set. Where it has not been possible to remove all personal identifiers, the data should be encrypted before it is copied to removable or portable media, or transmitted using unsecured channels.
- 5.24 Evidence of compliance to the requirements for data protection must be maintained for a minimum of six (6) years.
- 5.25 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.
- 5.26 If the registry has internet-facing web applications which process pseudonymized or identifiable donor or patient information, independent penetration testing must be performed annually. Any identified security vulnerabilities must have a documented remediation plan. Risks identified by this testing must be formally overseen by the registry's security role.

- 5.27 If the registry downloads the WMDA global file containing pseudonymised donor and cord blood data, it must perform annual security assessments against all systems which process data from the WMDA donor file. Any identified security vulnerabilities must have a documented remediation plan. The assessment, results and remediation plan must be formally overseen by the registry's security role.**

Third parties

- 5.28 If the registry has functions needed for information management that are performed by, or with the help of, qualified third parties, the third party appointed must comply with the relevant WMDA security standards and WMDA Data Use Agreement for the functions which they are providing. Responsibilities of both parties must be described in writing.

6.0 Facilitation of search requests

Communication

- 6.01 Critical communications among registries and other organisations must be in legible writing or transmitted via an electronic system.**

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

6.01.2 Donor and patient identity must remain confidential throughout the search process so that only appropriate registry or affiliated personnel have access to these data.

General requirements

- 6.02 The registry must have a mechanism to assess donor requests from organisations acting on behalf of international patients.

6.02.1 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 stem cell treatment.

6.02.2 If the registry criteria are not met, the registry must raise any concerns or questions to the requesting organisation.

6.02.3 A donor/cord blood unit selected for a specific patient must be placed on a "reserved" status from the time of verification typing until the donation/cord blood unit shipment date is reached.

6.02.4 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 hematopoietic stem cell transplantation.

Testing

- 6.03 Registries must respond to search requests and to requests for additional information and donor/cord blood/maternal samples within a time period consistent with WMDA metrics and in a defined manner.**

- 6.03.1 Registries or their associated donor centres/cord blood banks must have the capability of shipping samples, if available, to the facility indicated by the transplant centres if required for further testing. The sample must be appropriate for the testing required.
- 6.04 Verification typing of:
 - 6.04.1 the adult donor at a minimum of HLA-A, -B, -C, -DRB1 DNA based typing at high resolution must be performed prior to a hematopoietic stem cell donation for a specific patient.
 - 6.04.2 the cord blood unit at a minimum of HLA-A, -B, -DRB1 DNA based typing must be performed prior to shipment for a specific patient in a way that at least one typing result (previous or extended typing) for each locus is at high resolution.
- 6.05 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 hematopoietic stem cell transplantation.

Workup – shipment request

- 6.06 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 donor will be the source of HSC, 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 HSC for a specific patient.**
 - 6.06.1 Prior to transplantation, the registry must have a process for communicating the 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 donor must be free to change their mind at a later date.
 - 6.06.2 **The registry must have a process to communicate issues related to donor health and the release of an increased risk product to the transplant centre.**
 - 6.06.3 An increased risk product should be released by exception only when there is a documented clinical need for the product and when approved by the physician of the transplant centre.

Post donation

- 6.07 The registry must have a documented policy listing the conditions under which donors and recipients might be informed of each other's identity. This policy must comply with local regulation on disclosure.**
- 7.0 Second and subsequent donations of HSC and/or cell products for the same patient
 - 7.01 The registry must have a documented 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 the transplant centre should provide to justify the need for a subsequent donation.

7.01.2 This policy must be readily available to relevant health care professionals.

8.0 Collection, processing and transport of hematopoietic stem cells

8.01 Collection of hematopoietic stem cells and any other collected cells intended for therapeutic use, must be performed at a collection centre/cord blood collection site conforming to local regulation.

8.02 The collection centre/cord blood collection site must ensure the identity, safety and privacy of the donor and the confidentiality of the donor and cord blood data.

8.03 The collection centre/cord blood bank collection site and the collection of hematopoietic stem cells or other donor cellular products 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 conforming to the local regulation.

8.05 If a donor is subjected to a medical intervention as part of the collection process, the registry must have documented policies and procedures to protect the health and safety of the donor and of the recipient.

8.05.1 These policies must include the procedure to follow in case of failed mobilisation, including the potential to switch to a bone marrow collection if necessary.

8.05.2 **The registry must have a policy concerning the use of Central Venous Catheter in donors to ensure that a Central Venous Catheter 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 donors with a Central Venous Catheter inserted.**

8.06 Documented policies and procedures must be in place to ensure the identity, quality and quantity of the collected cells are communicated appropriately amongst the transplant centre, collection centre/cord blood bank and cell-processing unit.

8.07 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 and product code, the number of cells collected, the donor's unique identifier, donor ABO/Rh group, identification of the patient, date and time of collection, any processing details, and name and contact information of the transplant centre.

8.07.1 The registry should utilise an international coding and labelling system for the donation number to ensure the identity of the product.

8.08 Critical transport conditions, such as temperature and time limit must be defined to maintain the required cell properties.

- 8.08.1 **Cells must be transported by a trained person in a timely and reliable fashion to meet transplant centre requirements for the quality of the cell product upon arrival at the transplant centre.**
- 8.08.2 Policies and procedures for training and qualification of individuals acting as courier and documenting the transport process should follow WMDA guidelines. The entity providing the courier is responsible for ensuring that the transport takes place according to WMDA guidelines.
- 8.08.3 The container/package must be secure and ensure that the cells are maintained in the specified conditions. All containers and packages need to be qualified as fit for purpose.
- 8.08.4 Procedures for transportation and shipping of collected hematopoietic stem cells and cord blood units must be defined and qualified.
- 8.08.5 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.
- 8.08.6 Records of transport must be maintained to allow tracing of the product.
- 8.09 **Serious Adverse Events affecting a cellular product intended for a specific patient must be identified, documented, investigated and remedial and/or corrective action taken. The Serious Adverse Events must be submitted to the WMDA S(P)EAR Committee.**
- 8.10 **Serious Adverse Reactions impacting the cellular product and hence potentially the patient's health must be identified, documented, investigated and remedial and/or corrective action taken. The Serious Adverse Reactions must be submitted to the WMDA S(P)EAR Committee.**
 - 8.10.1 Reports of Serious Adverse Reactions affecting the donated cellular product must be communicated to the registry/organisations involved in the transplant if the event might affect the transplantation or subsequent donation. Other individuals or groups should be notified as appropriate.
 - 8.10.2 **Serious Adverse Reactions occurring due to registry operations and impacting the health and safety of donors or patients must be identified, documented, investigated and remedial and/or corrective action taken. The Serious Adverse Reactions must be submitted to the WMDA S(P)EAR Committee.**

9.0 Follow-up of patient and donor

- 9.01 **The registry must have policies and procedures for the follow-up and care of donors immediately following the donation.**
- 9.02 The registry must have policies and procedures for the long-term follow-up and care of donors for conditions related to the HPC donation, including a mechanism for donors to contact the registry to report related medical concerns for a minimum of ten (10) years after donation.

- 9.03 Serious Adverse Reactions affecting donors undergoing collection of HSC and/or cellular product, 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. The Serious Adverse Reactions must be submitted to the WMDA S(P)EAR Committee.**
- 9.04 The registry must comply with local 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 an HSC/cellular product from that donor must be reported to the requesting registry/transplant centre.**
- 9.06 Registries should require their national transplant centres to submit data to regional or international patient outcome databases in order to collect clinical outcome data of the transplanted recipients.**

10.0 Financial and legal liabilities

Responsibilities

- 10.01 The registry must keep complete and accurate financial records for services provided and requested according to local regulations.**
- 10.02 A registry must have adequate administrative structures and financial resources to guarantee the settlement of all invoices in due course and to perform accounting duties.**

Fee schedule

- 10.03 The registry must have available a fee schedule detailing payment terms for extended and verification HLA testing, infectious disease marker testing, product procurement, cancellation fee and other related services upon request.
 - 10.03.1 The registry should have a procedure to communicate changes in the fee schedule to interested parties thirty (30) calendar days prior to implementation.
- 10.04 The registry should have a procedure to communicate any cost not standardised or, for any reason, not accessible through a fee schedule and to ensure that the requesting registry is informed in advance.

Invoicing

- 10.05 The providing registry must have a procedure to invoice to the requesting registry/transplant centre for requested services.
- 10.06 Invoicing should occur within sixty (60) calendar days of service completion.

Payment

- 10.07 The requesting registry must have a procedure to ensure guarantee of payment for requested services.
 - 10.07.1 If the requesting registry cancels the service, the registry providing the service may expect full payment, provided that the services cannot be cancelled, and results are reported within thirty (30) calendar days of the cancellation date.

- 10.08 The requesting registry is liable for all expenses incurred on behalf of the organisations they serve.

Legal liability

- 10.09 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 donor should assume financial liability for any portion of the follow up testing and/or HSC procurement process. The registry is responsible for all reasonable expenses incurred by the donor.**
- 10.10 The registry, or its designee, should offer disability and death benefits to donors.
- 10.11 The registry should maintain liability insurance.