

	World Marrow Donor Association		
	International Standards for Unrelated Haematopoietic Stem Cell Donor Registries		
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WORLD MARROW DONOR ASSOCIATION
(WMDA)
INTERNATIONAL STANDARDS
UNRELATED HAEMATOPOIETIC STEM CELL DONOR REGISTRIES

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Table of Contents

FOREWORD	3
A. INTRODUCTION AND DEFINITIONS	4
1.0 Introduction	4
2.0 Definitions/abbreviations	4
B. STANDARDS.....	10
1.0 General.....	10
2.0 General organisation of the registry	11
3.0 Donor recruitment, consenting, screening and testing of donors.....	12
4.0 Umbilical cord blood and maternal donor recruitment, consenting, screening, testing and review/release of cord blood units.	16
5.0 Information technology and information management.....	19
6.0 Facilitation of search requests.....	21
7.0 Second and subsequent donations of HSC and/or cell products for the same patient.....	23
8.0 Collection, processing and transport of haematopoietic stem cells.....	23
9.0 Follow-up of patient and donor	26
10.0 Financial and legal liabilities.....	27

FOREWORD

The World Marrow Donor Association (WMDA) promotes product quality and global collaboration by creating and maintaining international standards, in order to improve access to life-saving haematopoietic stem cell transplantation for patients while assuring that donors' rights and safety are protected. WMDA members, clinicians, national authorities and donors trust evaluation by the WMDA Certification Body as an indication that high quality hematopoietic stem cell products are efficiently provided and donor safety is ensured. The WMDA certification process is based on the WMDA International Standards for Unrelated Haematopoietic Stem Cell Donor Registries, commonly referred to as "WMDA (International) Standards".

WMDA standards set forth the minimum guidelines to facilitate haematopoietic stem cell transplantation. The major objectives of the WMDA International Standards are to ensure efficient and secure:

- processing of incoming requests for access to donors/cord blood units from organisations in other countries;
- facilitation of outgoing requests for international donors/cord blood units for patients of transplant centres represented by the requesting organisation
- coordination of activities of donor, cord blood, collection, and transplant centres overseen by the registry.

A list of participating organisations, including their status, is available on the WMDA website. See the following link: <https://share.wmda.info/x/4gdcAQ>

The WMDA International 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 registry must determine and follow applicable 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 full WMDA Standards compliant:

- The first time that a registry applies, the registry will become WMDA Benchmark Level 1 or Level 2 if the registry complies with the '**benchmarked**' WMDA Standards. Depending on the level of activity of a registry, the registry will become either WMDA Benchmark Level 1 or WMDA Benchmark Level 2 (activity above a specific level).
- The second time that a registry applies, and if the registry has a sufficient level of activity, the registry will become WMDA Full Standards compliant if the registry complies with all required WMDA Standards. Full WMDA Standards compliance 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 terms "may" and "might" either describe examples or indicate that a practice is permissive (may) or possible (might).

2.0 Definitions/abbreviations

Note: Organisations, defined as a "registry" in the WMDA Standards, providing haematopoietic stem cells to a patient in another country vary in their administrative structures. The organisation may outsource processes or parts of processes but the responsibility for the service quality and compliance with WMDA Standards remains with the organisation. 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

Applicable laws and regulations:

Any local, national, or governmental law and/or regulation that is applicable to donation, collection, providing of haematopoietic stem cells from donors/cord blood units for cellular therapy.

ASHI:

American Society for Histocompatibility and Immunogenetics

Autologous:

Derived from and intended for the same individual

Backup (of data and/or systems):

The process of copying data to preserve it in case of equipment / software failure, site disaster, or widespread data corruption.

Back up donor:

A backup donor is the donor that will be requested for donation if the primary donor selected for workup is unable to proceed to donation. The main objective in securing a backup donor is to ensure that transplant will not be significantly delayed if the primary donor is unable to donate. This is different from an earlier search stage where the transplant centre may request more than one donor for verification typing because requesting a single donor might delay the transplant if not appropriately matched or available.

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 Benchmark L1 or Benchmark L2 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 haematopoietic 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 haematopoietic 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 haematopoietic stem cell products

Donor:

A person who is the source of cells for cellular therapy. 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 applicable laws and regulations 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, and 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.

G-CSF:

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

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.

Haematopoietic stem cells (HSC):

Haematopoietic stem cells (defined also as haematopoietic progenitor cell-HPC) are the cells, that give rise to blood and immune system cells. These cells are found in bone marrow, growth factor stimulated peripheral blood, and umbilical cord blood.

Haematopoietic stem cell transplantation:

A medical procedure involving transplantation/cellular therapy with haematopoietic stem cells.

HLA:

Human Leukocyte Antigen.

Infectious Disease Marker (IDM):

Test that aid in the diagnosis of infectious disease

Must:

To be always complied with.

Patient/Recipient:

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

Policy/procedure:

Documented information that specifies the way to carry out an activity or a process and is controlled and maintained by the registry/cord blood bank.

Primary donor

The single selected volunteer that the transplant centre intends to be the source of cells for their patient.

Product:

A cellular therapy product that contains haematopoietic 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 equipment work correctly. For example, a new cord blood collection process must be validated; a shipping container used to transport cells must be qualified first.

Quality management system:

A system that documents policies, procedures and responsibilities for achieving quality within an organisation 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 coordinating the provision and/or procurement of haematopoietic stem cells and other cellular products from donors (including cord blood) unrelated to the potential recipient.

- The registry requesting a search (or “requesting registry”) is the registry that acts on behalf of their transplant centres.
- The registry providing the donor or cord blood unit (or “providing registry”) is the source of haematopoietic stem cells and other cellular products.

Rh factor:

Rhesus factor, a specific antigen present on the surface of red blood cells.

Serious Adverse Event (SAE) – 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

Serious Adverse Reaction (SAR) - 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 that 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.

Search (coordination) centre:

The search (coordination) centre undertakes the search for an unrelated donor for specific patients using criteria defined and documented by transplant centres. This entity may be contained within a transplant centre or may be separate from the transplant centre. If separate, the search centre may coordinate searches for one or several transplant centres. In the WMDA Standards, reference to a transplant centre should be interpreted as a transplant centre and/or a search centre as appropriate. Transplant centres/search centres seeking an international donor work through the registry in their country.

Should:

Recommended or advised, but effective alternatives may exist.

SPEAR Committee:

A WMDA committee of experts responsible for the review and reporting of all serious (product) events and adverse reactions (S(P)EAR) reported to WMDA (<https://share.wmda.info/x/YotOGg>).

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/cellular therapy, 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 haematopoietic 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.

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 regulations.

Validation:

Validation is the process of providing documented evidence that a specific process will consistently produce a product meeting its predetermined specifications and quality. For example, a new cord blood collection process must be validated; a shipping container used to transport cells 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 from a specific individual 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 patient/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 (DUA):

An agreement that covers the legal framework of all sharing personal and other sensitive data for the transmission and use of such data among organisations including WMDA in the context of haematopoietic stem cell search, match, and transplant procedures.

WMDA Share:

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

Workup:

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

B. STANDARDS

1.0 General

- 1.01 An organisation responsible for all of the following: (1) maintaining a searchable donor file of at least 500 adult volunteer donors and/or at least 100 umbilical cord blood units; (2) coordinating the search of this file for a source of haematopoietic stem cells (HSC) and other cellular products for an unrelated potential recipient; and (3) providing HSC; is eligible for WMDA Benchmark Level 1/2 as a first step, followed by WMDA Full Standards compliance as a second step.
- 1.02 If a registry is accredited and/or certified by an international organisation with standards that meet or exceed some or all of the WMDA Standards, that registry will be considered compliant with the relevant WMDA Standards following submission and evaluation of material documenting that accreditation/certification.**
- 1.02.1 **If not all the WMDA Standards are covered by this international accreditation and/or certification, evidence of compliance with the WMDA Standards that are not covered must be provided.**
- 1.02.2 If applicable laws and regulations differ from the WMDA Standards, the requirement to meet applicable legal standards will be accepted as a valid cause of deviation from WMDA Standards.
- 1.03 A registry that intends to request WMDA certification (Benchmark Level 1/2) or that has obtained WMDA certification (Benchmark Level 1/2 or WMDA Full Standards compliance) must participate in the annual WMDA Global Trends Report.**
- 1.04 The registry's operational and regulatory information must be available on 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 compliance must be brought to the attention of the WMDA in a timely fashion.**
- 1.06 The registry's policy must describe how the providing registry determines that a donor centre(s) or cord blood bank(s) under its oversight complies with WMDA Standards to recruit and characterise donors/umbilical cord blood units. The duties and responsibilities of the registry and donor centre(s)/cord blood bank(s) and the nature of the oversight must be documented.
- 1.06.1 A registry requesting a donor/umbilical cord blood from an organisation that is not directly under the requesting registry's oversight must have a policy or procedure describing how it determines that the safety and well-being of the haematopoietic stem cell source and intended recipient are protected.
- 1.07 The registry must ensure that transplant centres under its oversight comply with relevant WMDA Standards when requesting a haematopoietic stem cell product from another country. The duties and responsibilities of the requesting registry and transplant centre(s) and the nature of the oversight must be documented.
- 1.07.1 The requesting registry's policy must describe how the registry determines that the transplant centre(s) meet the following criteria: (1) donation of

HSC will only be requested for patients for whom cellular therapy is a medically acceptable procedure; (2) medical and administrative prerequisites from search initiation through post-transplant care are met; (3) testing is carried out by laboratories that meet standards established by applicable regulation and/or international societies that ensure the quality of results; and (4) processing and storage procedures maintain product quality.

1.07.2 A registry receiving requests for donors/cord blood units from organisations that are not directly under the registry's oversight must have a policy or procedure describing how the registry determines that the criteria described in 1.07.1 are met.

1.07.3 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 requesting registry. The standards for transplant centres must be readily accessible to relevant healthcare professionals.

1.08 The registry's policy must describe how the providing registry determines that a collection centre(s) under its oversight complies with WMDA Standards for the collection of haematopoietic stem cells or other donor samples, for donor medical evaluation and for the follow-up of donors. The duties and responsibilities of the registry and collection centre(s) and the nature of the oversight must be documented.

1.09 The registry must have a policy and procedure 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 applicable laws and regulations 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 haematopoietic 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 haematopoietic 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, search 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 healthcare 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 haematopoietic stem cell donation requests 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 search processes.**
- 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 the unrelated donor search process 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

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 haematopoietic 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 duration of 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 haematopoietic stem cells or other 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 haematopoietic stem cell collection must have passed a minimum age established by applicable laws and regulations or their 18th birthday if no applicable laws and regulations exist.**

3.16.1 The upper age limit for prospective donors selected to donate haematopoietic 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 applicable 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 haematopoietic 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 the time of verification typing. Testing must monitor infection with human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, cytomegalovirus (CMV), *Treponema pallidum* (syphilis) and other infectious agents as defined by local regulation or incidences.**
- 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 of donors selected for specific patients at workup must include testing for diseases thought to be important to consider in haematopoietic cellular therapy. Testing must monitor infection with human immunodeficiency virus (HIV), human T-lymphotropic virus I and II, hepatitis B virus, hepatitis C virus, cytomegalovirus (CMV), *Treponema pallidum* (syphilis) and other infectious agents as defined by applicable regulation or incidences.**
- 3.24.1 Selected donors should be tested for local diseases that are important to consider in haematopoietic stem cell transplantation. Donors who have recently travelled outside their country should be evaluated for infectious diseases prevalent in the areas of travel.
- 3.24.2 The transplant centre should be informed regarding the infectious disease markers that will be routinely tested, those that may be available upon request, and those for which a sample can be provided for testing.
- 3.25 **Infectious disease markers must be measured within thirty (30) days of the haematopoietic 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, and 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 any health screening affecting the health status of the maternal or infant donor. The registry must have a policy whether and how the maternal donor is informed.

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 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 haematopoietic stem cell transplantation/cellular therapy.
- 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 haematopoietic stem cell 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 haematopoietic stem cell transplantation. Testing must monitor infection with human immunodeficiency virus (HIV), human T lymphotropic virus I and II, hepatitis B virus, hepatitis C virus, cytomegalovirus (CMV), *Treponema pallidum* (syphilis) and other infectious agents as defined by applicable regulation or incidences.**
- 4.20.1 Maternal donors should also be tested for local diseases that are important to consider in haematopoietic stem cell 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 documentation

- 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.**

5.10.1 The searchable database available for donor and cord blood selection should be updated as changes occur.

- 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.

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 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 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 applicable laws and regulations 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 applications that process pseudonymized or identifiable donor or patient information, independent penetration testing must be performed. 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 that 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 that 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 haematopoietic stem cell therapy.**

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 The registry/cord blood bank must have a policy for reserving a donor/cord blood unit when requested for a specific patient.

6.02.3.1 Any changes in the patient or search status that impact the reservation of a donor/cord blood unit, should be communicated to the providing registry/cord blood bank in a timely manner.

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 the relevant healthcare professionals.

6.02.5 The registry should make their policy for accepting requests for a backup donor for a specific patient at the workup stage readily accessible to the relevant healthcare professionals.

6.02.5.1 Registries requesting donors for workup should ensure that a policy is in place describing if and under which circumstances a backup donor can be requested in addition to the primary donor.

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 HLA verification typing of the potential adult donor/cord blood unit and the potential recipient must confirm the identities of the individuals/unit.

6.04.1 All specimens requested by the transplant centre for verification HLA typing of the donor or cord blood unit should be tested accordingly and results provided to the providing registry in a timely manner. If not tested, the transplant centre should inform the providing registry as to the status of that donor/unit request.

6.04.2 Adult donor HLA verification typing results should be available prior to requesting a specific donor for workup. At the latest, results must be available before the donor begins mobilisation or proceeds to collection, or the patient begins with the preparative regimen, whichever is earliest. Cord blood unit verification typing results must be available prior to shipment for a specific patient.

6.04.3 HLA verification typing results of the potential recipient should be available prior to requesting a specific donor for workup. At the latest, results must be available before the donor begins mobilisation or proceeds to collection, or the patient begins with the preparative regimen, whichever is earliest. For cord blood unit procurement requests, recipient results must be available prior to shipment of the unit.

6.05 The HLA typing of the adult donor (or cord blood unit) and the potential recipient should be at high resolution and include sufficient loci to allow the evaluation of the pair matching appropriate for the clinical application. This HLA typing should be available prior to requesting a specific donor for workup and at the latest must be available before the donor begins mobilisation or proceeds to collection, or the patient begins with the preparative regimen, whichever is earliest. Cord blood unit typing results must be available prior to shipment for a specific patient.

6.06 The policy of the registry regarding repetition of the database search for a specific patient must be defined and readily accessible to the relevant health care professionals.

Workup – shipment request

- 6.07 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. 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.**
- 6.07.1 The registry must have a process to inform the donor about the proposed date of transplant.
- 6.07.2 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.
- 6.07.3 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.**
- 6.07.4 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

- 6.08 The registry must have a policy listing the conditions under which donors and recipients might be informed of each other's identity. This policy must comply with applicable regulation on disclosure.**
- 7.0 Second and subsequent donations of haematopoietic stem cells and/or cell products for the same patient
- 7.01 The registry must have a 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 healthcare professionals.
- 8.0 Collection, processing and transport of haematopoietic stem cells
- 8.01 Collection of haematopoietic stem cells and any other collected cells intended for cellular therapy, must be performed at a collection centre/cord blood collection site conforming to applicable 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 haematopoietic stem cells or other donor cellular products must be under the direction of trained and experienced healthcare professionals.**

- 8.04** If required, autologous donor blood must be collected at a blood collection centre conforming to the applicable regulation.
- 8.05** If a donor is subjected to a medical intervention as part of the collection process, the registry must have 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 a 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** 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 haematopoietic stem cells and cord blood units must be defined and qualified.
 - 8.08.5 In case of transport of a cryopreserved cellular product, the dry shipper must contain a 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 SPEAR 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 any 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 SPEAR 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 HSC 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 Events and Reactions affecting donors undergoing collection of HSC and/or other 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 Events and Reactions must be submitted to the WMDA S(P)EAR Committee.**
- 9.04 **The registry must comply with applicable 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.
- 9.07 The registry requesting a product for transplantation should have a policy for sharing basic patient outcome data with the registry or cord blood bank providing the product.
 - 9.07.1 The registry should ensure that a policy is in place that the patient provides an appropriate consent before their outcome data are shared.
 - 9.07.2 The registry providing a product should have a policy for sharing basic patient outcomes data with donors and affiliated entities.

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 applicable 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.