Guidelines for Auditing of Donor Centers

by the Working Group Quality and Regulation of the WMDA

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1 Foreword

These guidelines are intended for the audit of Donor Centres (DCs) by registries; they have been developed for registries relying on independent DCs for the recruitment and management of HPC donations from Unrelated Donors (UD), for e.g. verification typing and work up processes.

The main goal of these guidelines is to support registries in verifying and auditing their affiliated DCs to ensure they are compliant with the WMDA Standards. Registries are responsible, indirectly or directly, for ensuring the right donors are recruited and UD management based on their agreements with their DCs.

NOTE: Definitions used throughout these guidelines are as given in the WMDA Standards as of July 1, 2020.

WMDA Standard 1.06 states:

"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 must be documented in an agreement."

The present guidelines are based on the 2020 WMDA Standards. This means that the authors interpreted the current standards and deduced specific process steps and requirements for DCs. Registries need to be aware that these guidelines may not cover all aspects necessary to comply with local governmental laws and regulations. It is therefore the responsibility of each registry to determine and follow any additional governmental regulations and guidelines applicable to them. The registries are responsible for checking their national requirements that apply to the DCs and they are also responsible for adapting the checklists to meet these specific requirements. The guidelines lay the groundwork that should apply in most countries worldwide and help the registries to ensure that the WMDA Standards are followed by their DCs.

These guidelines do not supersede the forgoing established systems, but instead endeavour to embed these in the framework of donor management and ensure that the current WMDA

Standards, as well as WMDA recommendations, will be followed by the DCs. If the DCs have any other accreditation, such as FACT-JACIE, AABB (formerly known as the American Association of Blood Banks), European Federation of Immunogenetics (EFI) or American Society for Histocompatibility and Immunogenetics (ASHI), this should be demonstrated in their quality management system.

It is recommended that a full audit is conducted, including an on-site or remote/virtual inspection of any DC that is to be newly contracted by a registry. During the application period, all national and WMDA requirements must be considered. Once the potential DC is accepted and if the DC maintains a license or accreditation by national authorities or internationally recognised institutions, they will thereafter be audited only for those recommendations/requirements (including WMDA Standards) not covered by the respective license or accreditation as identified by the registry.

These guidelines and related checklists have been initiated to support registries in their daily activities. Each registry should establish its own auditing group of fully trained staff in audit procedures. As standards and requirements change in the future, registries are advised to make proposals for changes and additions. Feedback can be sent to the Working Group Quality & Regulation via the WMDA Office.

2 Abbreviations and definitions

AABB

Formerly known as American Association of Blood Banks

ASHI

American Society for Histocompatibility and Immunogenetics

BM

Bone Marrow

Collection Centre (CC)

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 donor and provides the final approval of the

potential donor for collection. The collection centre packages the stem cell donation for transport to the transplant centre

Donor Centre (DC)

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

DUMN

Declaration of Urgent Medical Need

EFI

European Federation of Immunogenetics

FACT-JACIE

Foundation for the accreditation of cellular therapy

Joint accreditation committee isct-ebmt

FDA (Food and Drug administration)

Food and Drug administration is the US governmental body responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs and biological products

Follow-up

Care given to the donor immediately after the donation and regular medical check-ups for long term period, including a mechanism for donors to contact the registry to report related medical concerns for a minimum of ten (10) years after donation.

GRID (Global registration identifier for donors)

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.

HLA

Human Leukocyte Antigen

HSC (hematopoietic stem cells)

Defined also as Hematopoietic progenitor cells-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.

KPI (Key Performance Indicators)

The Working Group Quality and Regulation has defined key performance indicators (KPI) for hematopoietic stem cell donor registries. These KPIs are based on the WMDA global trends report and assessed every year.

IDM

Infectious disease markers

PE (Physical examination)

Physical examination is the medical examination performed by a physician during the work up to establish the suitability of the donor for the donation

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.

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.

S(P)EAR

The SPEAR 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.

Transplant centre (TC)

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

UD

Unrelated adult donor

Verification typing (VT)

This HLA typing includes the tests carried out on a fresh sample of a specific donor with the purpose of verifying the identity and concordance of an existing HLA assignment. The purpose of this typing is to ensure that the donor is the same individual whose HLA typing was listed on the search report used to select the donor.

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.

3 Format and timing of audits

Improving the safety of volunteer UDs during donation, as well as maintaining high standards for HPC product quality is what the WMDA strives for. From UD recruitment, consenting, testing, management and the collection of donor personal, genetic and medical data, the essential procedures rely on high-quality standards at DCs.

To ensure the safety of the volunteer UD, the registry is responsible for compliance with WMDA standards at all times before, during, and after HPC donation. As the registry provides the volunteer UD with all necessary information about their role as UD, the registry is also responsible for ensuring that they comply with WMDA standards as a minimum requirement. In some countries it may be the responsibility of the registry to ensure compliance with local governmental laws and regulations.

The structure of a registry can vary from country to country. In some countries, the activities of a registry may be performed by more than one entity. For example, the registry might be affiliated with independent DCs. Alternatively, the registry might itself recruit and manage UDs internally. Regardless of the structure of the registry, compliance with WMDA standards must be ensured as a minimum requirement for all units that contribute to the operation of a registry as related to the DC.

Regular audits provide the means of monitoring compliance. The registry should embed these audits within their own quality system. The following formats and frequencies of audits are recommended:

Before a new DC is contracted, it is recommended to conduct an on-site evaluation at the DC facility. If it is not possible to conduct the audit on-site, a remote audit can be considered, provided that the technical and data protection criteria are met. Additionally, a paper-based audit is required to ensure compliance with the WMDA Standards. For already contracted,

experienced DCs, a biennial paper-based audit should be conducted by the DC, reviewing at least the following points:

- Change of address or other important contact information to ensure that all critical communications with CC, TC, UD can be accomplished in a timely manner.
- Relevant staff changes (e.g., Medical Director, CEO, physicians or coordinators). Some additional country-specific positions could be required by registries.
- Changes in accreditation, registration, or license status.
- UD issues which may include the number of serious adverse events and serious adverse reactions occurring and reported to the registry.
- Changes in suppliers, laboratories or other affiliated facilities, if required by the registry.

It is recommended that once every 4 years the registry performs a full on-site audit based on these guidelines and the provided checklists.

Whenever a DC fails to meet the basic requirements, immediate clarification must be made and both corrective and preventative actions must be taken by the DC. Below, some frequently detected non-conformities that can be identified at DCs are described exemplarily for special attention:

- Frequent cancellations by UDs could be the result of insufficient information provided to the UD about their role, the procedures and the risks.
- UDs HLA data are showing an unusually high discrepancy rate (the annual HLA discrepancy survey may provide a benchmark).
- The DC does not respond in a timely manner and cannot guarantee communication in critical situations.

These are just the most frequent examples. We strongly recommend auditors to look closer into these issues and in case of non-conformities, discuss ways of finding solutions with the DCs.

4 General organisation & typing

4.1 General requirements

It is important to have a clear and defined organisational structure as this provides the basis for a quality program and ensures the structure reflects the needs of the registry, its affiliations and customers. The general organisation information includes the registry's organisational structure and the basis of operation. Cooperating affiliates such as donor centres (DC), laboratories, CCs etc. are functionally part of the DR's performance and are required to comply with WMDA standards.

There needs to be a sufficient number of trained personnel to carry out DC operations, and assurance that staff are qualified for the tasks they perform. Qualifications are identified based on job responsibility as well as assigned tasks.

Effective management of key DC processes is essential to promote the quality of operations and services to UDs and other key stakeholders. Decision-making should be based on relevant goals (KPIs) and regulations/standards as defined by the agreement between the DC and registry. This pertains to internal decisions in accordance with key objectives as well as efforts to meet national and international regulatory requirements and voluntary standards, e.g. WMDA.

Management of key DC processes is achieved through process control methods such as SOPs. Performance goals should be specified and assurance provided that there are enough people working in each area to meet these goals.

Selecting dependable, quality suppliers who provide services to support DC functions is essential. A system of review and monitoring is important to assess and ensure conformance to the standards, regulations and policies and procedures. Monitoring and review methods are determined between the registry and DC and should include practices such as internal/external audits, laboratory proficiency testing, outcomes data, quality indicators and feedback from customers and other stakeholders.

4.2 DC organisational chart and external partners (e.g. collection centres, labs, registries) organisational chart of the entity in which the DC is included

The intent of this requirement is to ensure the organisational structure is adequate to meet the requirements of the functions performed by the DC. There should be an adequate number of trained staff to carry out operations, as a shortage or lack of trained personnel can increase the risk for errors. It is also important to ensure there are enough people performing each specific function so that operations are not impacted if one person is away on leave.

Specific performance goals should also be identified and reviewed and the DC should be able to demonstrate that enough people are working in each area to meet these goals. Mechanisms should also be in place to monitor performance of KPIs, as this is important for identifying any changes that may be required in staffing or processes.

Staff members must be made aware of the sensitive nature of their job, and the importance of confidentiality must be defined in policies and procedures, as per national regulatory and applicable standard requirements. It is important to ensure that staff are trained regarding maintaining anonymity of the potential donors and transplant recipients and to establish rules of disclosure.

4.3 Copy of the latest valid certificate (EFI, ASHI/ other national organisation) of the tissue typing laboratory accredited to perform HLA typing

It is important to establish and track the performance of service providers to document their quality. A form of systematic review and monitoring, e.g. audits, is important to assess and ensure conformance to the WMDA standards, applicable regulations and policies and procedures. Having mechanisms in place to monitor performance is also important for identifying any changes in quality that may require corrective action.

International societies have established accreditation programs for HLA-typing laboratories such as the European Federation for Immunogenetics (EFI) and the American Society for Histocompatibility and Immunogenetics (ASHI). To ensure quality of HLA-typing, samples should be typed in an ASHI- EFI- or equivalently accredited HLA laboratory, and a current certification must be available for review.

As per the WMDA standards, a procedure should be in place that describes how the quality of testing data is monitored and how the DC ensures the accreditation of testing entities is current. The standards also provide further guidance to demonstrate how quality of HLA typing can be assessed.

4.4 CV of the Medical Director of the donor centre

There are many medical issues that can arise during the day-to-day activity within a DC, including donor health/eligibility issues, unusual transplant centre requests or complications during the stem cell collection process. There should be a designated physician or physicians to review these issues in order to provide guidance and direction regarding each case. These physicians should be experts in the field of stem cell transplantation and histocompatibility and should have a broad familiarity with general medicine, in accordance with national regulations and registry specific requirements. Both the WMDA and FACT-JACIE provide further detail pertaining to required qualifications.

Ensure the organisational chart includes the name of the Medical Director and other experts as applicable, e.g. HLA expert. The Medical Director must also be able to demonstrate sufficient training and experience as outlined in the WMDA guidance. Additionally, details of continuing education or continuing professional development should also be made available for review.

4.5 Significant changes which occurred in the functioning of the DC and associated recruitment procedures/policies within the last 4 years

As per the WMDA standards, when a registry relies on a DC to recruit and characterise UD, the registry is responsible to ensure the DC is aware of and complies with relevant WMDA standards. Once WMDA qualification/accreditation status has been achieved, it is important to ensure any significant changes that could affect this status are reported to the WMDA for review and assessment to ensure continued compliance with the standards. The WMDA guidance provides specific examples of significant changes to be reported. The DC should have a procedure or policy, which describes how and when DC changes are reported to the registry and/or directly to the WMDA.

5 KPIs

The key performance indicators (KPIs) represent a quantitative assessment of key activities of a registry; and their main objective is to instigate registries to improve their processes by defining achievable target values. This would result in faster services for transplant recipients. These KPIs are based on the WMDA annual report and the HLA discrepancy report as evaluated each year by the WGQR. The defined KPIs represent a quantitative assessment of key activities of a registry, which in turn reflect the activity of associated DCs as a whole. More information can be found on the WMDA website.

By setting KPIs for participating institutions (registries and DCs), the WMDA aims to improve the quality of certain processes. This includes, for example, the turnaround time for providing samples or products, or the response rate, so that a higher percentage of UDs are available when being requested for testing or workup.

An attempt to implement appropriate measures should be instigated if it is identified that there are issues within an institution, which are negatively influencing the KPIs, and improvements could be made. Thus, actions would not only be limited to the institution's calculated KPI but would also explore the reasons for UD unavailability or for delays in the provision of samples or services, and if counter-measures would be possible and appropriate.

There should be procedures in place for establishing and evaluating the institution's KPIs in relation to the WMDA recommendations, as well as for analysing associated procedures if shortfalls are identified, to decide on a suitable action plan. The institution's KPIs can also be compared to the data of other institutions of similar size (see WMDA report). Results and evaluations should be documented. Monitoring of KPIs should be on an annual basis, since results are collected and published by the WMDA annually.

6 Step by step from recruitment to follow-up

6.1 Recruitment

6.1.1. General requirements

There is some variability of donor recruitment process between registries, including the target groups they may focus on. Some countries have government regulations that guide recruitment activities while others have policies and procedures that indicate how donors are recruited.

WMDA standard 3.02 states:

"*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*. "

Recruiters may be employees or volunteers of the DC and are actively involved in the recruitment process. They are often the first point of contact for potential new registrants and have an important role in educating potential registrants as well as ensuring availability and commitment of registered donors. Other responsibilities include confirming eligibility as per established requirements, obtaining informed consent, ensuring confidentiality of registrant data and management of HLA samples. A supervisor may also be in place to oversee the recruitment process. Due to the important work involved with stem cell recruitment, a rigorous training program should be in place for recruiters and recruitment supervisors. The WMDA has developed recommendations for the qualification and training of stem cell donor recruiters to ensure competency in educating potential registrants about stem cell donation, the importance of the donor role and long-term donor availability.

A procedure for staff training should be designed and followed. If special licences or permits are required for recruitment activity by local law, these documents should be obtained and filed by the DC.

6.1.2 Procedure for the donor management at time of registration - SOPs, policies and recruitment material

A procedure which clearly outlines the responsibility and tasks of the DC for donor recruitment activities must be in place. Effective management of documents, including SOPs, manuals, recruitment materials, and records, ensures staff are performing activities according to defined requirements and demonstrates ability to record, trace and retain information in various forms.

It is important to confirm how essential documents are controlled and managed to ensure staff have access and are trained to the most current versions. This is especially important for critical processes such as management of donor consents and samples to ensure privacy, confidentiality, integrity and traceability. For example, labelling of donor samples is vital to ensure the correct linkage of the donor's personal data with the corresponding sample sent for HLA-typing.

6.1.3 Review several completed consent forms of donors recruited in the last 4 years

When recruiting donors, it is important to ensure they have received appropriate counselling and provide the necessary informed consent. Informed consent is to be written according to national laws and regulations and must adhere to WMDA standards as well as registry policy. Donors must sign/electronically submit a consent form at the recruitment stage. Written information must be given out to reinforce other forms of communication.

There should be a written policy in place outlining the elements to be included as part of the donor counselling process. The policy should include the importance of donor commitment and the obligation involved when registering as a donor, including the time required to complete the donation process and potential financial impacts if the donor does not receive payment from their employer for time they are absent from work. The testing, workup and final donation procedures require the individual to take time out of work, studies and family commitments. There must be a policy in place regarding donor reimbursement, and the DC should describe how and when this information is communicated to the donor.

The WMDA provides specific guidance to be included, as part of the counselling and consent process and this should be used as a reference tool while reviewing completed consent forms. Recruitment brochures and other forms of written material provided to the donor at the time of recruitment should also be reviewed.

6.1.4 Information material provided to the donor

It is important to ensure the donor is adequately informed about their potential role in the donation process. Information may be provided to the donor through various forms such as literature, web-based materials, videos, over the telephone or face-to-face. Written information should always be provided to reinforce other forms of communication. Basic information regarding peripheral blood stem cell and bone marrow collection should be provided in terms that can easily be understood. The safety of the procedures should be emphasized, however basic information about the risks of the procedures should also be provided, as well as information on the potential risks associated with any medical intervention, such as the use of GCSF. Stressing the importance of commitment from potential donors is essential at the recruitment stage, especially during patient appeals.

It is important to have adequate controls in place for management of essential documents to ensure staff have access and are trained to the most current versions, including access to the most current versions of recruitment materials in their various forms.

As per WMDA guidance, a procedure/policy explaining the information/documentation to be provided to the donor at the time of registration should be in place.

6.1.5 Assess rules for donor eligibility, age and gender

The legal age of consent must be considered when recruiting and registering adult volunteer donors and at the point of stem cell or bone marrow donation.

A policy should be available which outlines information to be collected from a donor at the time of registration and this must include donor age and gender as per WMDA requirements. Tools such as a medical health questionnaire or checklist may also be used to capture this information. The donor should be in good health, and staff should have access to guidance

material which defines and clarifies all medical criteria that would exclude an individual from joining the registry based upon safety considerations for the donor, as well as considering safety of the patient. The WMDA provides minimum standards for which potential donors should be assessed.

Additionally, as per WMDA guidance, there should be a policy in place describing the circumstances for when a donor may receive the results of their health screening and the method of communicating these results to the donor must be appropriate to the situation based on privacy, regulatory and/or legal requirements where applicable.

6.1.6 Description of the interfaces with the registry (to maintain confidentiality of donor data, including transporting, transmitting, storing and protecting data integrity).

Each country has its own laws and regulations relating to privacy, confidentiality and the protection of personal data.

Policies and procedures regarding information management should be in place which indicate how data are captured/entered by DC staff and how the data are verified, saved and transferred to the registry database.

All information systems must uniquely identify and appropriately authenticate users or processes as per internal compliance requirements. Access and transmission of donor information to and from the registry must be managed in a way that unintended or unauthorised access, destruction or modification of data is prevented and confidentiality maintained. It should also be confirmed that access to electronic data is limited to authorised individuals.

The search for an unrelated donor is an anonymous process, and as a result the donor and patient must remain anonymous to each other. The WMDA standards require policies and procedures to be in place to ensure donor confidentiality, which includes the assignment of an anonymous identifier to the donor so their identity can be protected during the search process.

6.1.7 Training matrix and training records for donor recruiters

The WMDA has developed recommendations for minimum qualifications and training of stem cell donor recruiters that should be used as a guideline for management of recruitment personnel. There must be a means of clearly capturing training requirements for each role as this ensures that those performing the specific requirements for that role e.g. training matrix consistently meet training requirements. Documentation of training is a means of maintaining a historical record that training has taken place. Documentation should also be available for training performed at the time of hire and on an on-going basis.

6.2 Verification/ extended typing

As per the guidance to the standards and the on-site checklists of the WMDA, auditing of the VT process should include all aspects of the process: from maintenance of appropriate policies on suitable donor counselling, maintaining confidentiality, adherence to the respective health screening and testing requirements, correct sample collection, labelling and shipment procedures, as well as timely and accurate processing of requests and transmission of results.

Donor screening and testing, as well as questionnaires that evaluate and asses to detect conditions that increase risk of donation, can be found in WMDA guidelines and the donor medical suitability website, AABB and FDA regulations and FACT-JACIE International Standards.

6.2.1 Procedure for donor management at time of extended typing or blood sample collection for verification typing

If a possible stem cell donor is found to be a good match for a recipient, the DC must provide the donor with appropriate information and material(s) and take steps to counsel the donor regarding the need for additional testing. To achieve a donor's full comprehension, this information must be provided in the national language. The DC must ensure he/she is making an informed decision, as is being asked of them.
At a minimum, the DC is expected to have a written policy that documents the following elements when counselling the donor:

- Anonymity of the donor and patient, the confidentiality of personal data

- Donation for any recipient in need, including an international patient
- Donation not being remunerated
- Requirement for further blood samples before donation
- Requirement for infectious disease and other testing (e.g. HLA), which testing will be performed, that results will be communicated to the TC, and the possibility that some sample may be retained for further testing
- Implications of transmission of infectious and other diseases from donor to patient
- Principles and risks of donation
- Possible duration of loss of time from normal activities
- Location of the collection
- Potential for collection of autologous blood
- Right to withdraw and consequences for the patient
- Details of insurance coverage
- Possible subsequent donations of hematopoietic stem cells or blood products
- Alternative collection methods and whether blood is reserved for research purposes

Information must be appropriately documented and retained according to local requirements.

6.2.2 Request for blood sample collection for verification/extended typing transmitted by the registry in _____ (specify year)

A DC is legally obligated to protect the confidentiality and security of donor and recipient identifying information. The DC must have a well-defined policy that preserves donor confidentiality, as the identity of the donor must be protected from disclosure. Centres should avoid the use of donor and recipient names in communications and solely use a donor unique identifier/GRID wherever possible. The DC must ensure that information is only accessible by authorised personnel.

The DC shall have a policy that provides direction for managing confidentiality compliance with all records and communications relating to donor and recipient. The communication between parties involved with donor information must be traceable on all pages of the

records and source documents. Personnel performing respective operational tasks must be identifiable and have documented training.

The DC is expected to describe how authorisation for access to computer systems and paper files is determined. In the unexpected event of staff absence or departure, designated individuals must have access to all donor records. For example, if staff maintain records in their locked desk cabinets, secondary keys must be accessible to designated personnel.

6.2.3 Medical questionnaire completed at time of verification/extended typing - verify current version is in use, current requirements included in the questionnaire, etc.

The medical questionnaire is used as part of the process to evaluate a donor ‘s suitability and eligibility status for donation. At the time of verification typing, the medical history questionnaire should provide information that evaluates a prospective donor’s suitability and eligibility status for donating stem cells. This includes donors that convert from peripheral donation to bone marrow harvest and vice-versa. Each questionnaire should target a specific reason for excluding or deferring the donor from donating. They should gather information about risk behaviours that may have exposed the donor to certain diseases. This is a critical aspect because discovery of new risk findings necessitates that the potential donor might require further evaluation or deferral. For example, since the bone marrow donation is a surgical procedure that requires an operating room, additional questions may be required for a donor response that indicates possible complications with anaesthesia from a previous procedure. Also, such information or other possible identified risks could impact product selection (marrow collection vs. apheresis) or the health of the patient, which the TC would need to be informed about at the VT stage.

The interview is one way to assess a donor’s risk for an infectious disease, however, it is mainly dependent on appropriate knowledge and tools for the interviewer, and the interviewee’s comprehension of the questions. It is essential that the DC accurately determines the donor ‘s health status to protect them from risk of damage to his/her own health for the donation and to protect the recipient from transmission of communicable diseases. It is especially important to identify potential risk for diseases and conditions for which there are no adequate laboratory tests or for which tests are unable to identify early

stage or window period infection. Assessing the risk of disease transmission may identify behaviours associated with risk of disease transmission. Positive responses on a screening questionnaire may lead to more in-depth donor evaluation and a thorough assessment of risk versus benefits, or donor deferral.

The DC must have a written process that details the administration of a medical history questionnaire to be used during the verification stage. The questionnaire should be controlled and regularly checked and updated as standards and regulations may change. Staff (and related DCs if applicable) should only access the current version of the document.

6.2.4 Accompanying documents for shipment of blood samples

The blood sample must be labelled according to national specifications, and at a minimum should include a donor identification number/GRID and information on the type of sample (e.g. anticoagulants/additives) and the collection date. However, the amount of information which can be included on a label is limited by space. Additional or more specific information, as well as patient and TC identification, may therefore be included in accompanying documents sent with the sample. This may also include additional forms used for traceability or documentation that the centre collecting the blood sample uses as distribution records.

6.2.5 Process for updating donor status and HLA at VT

In order for the recipient to have the highest potential of a successful transplant, the donor's human leukocyte antigens (HLA) must be closely matched with the recipient. Preliminary searches may identify just a few or many potential matches. HLA matching depends on the level of DNA-based resolution typing (Low, Intermediate, High) and on which loci are tested. Once a donor is selected as a potential request for a specific recipient, the donor should become temporarily unavailable for other potential recipients and should not be represented on TC search reports, or alternatively be marked as reserved.

Additionally, upon receipt of the VT result, this needs to be compared to the previously listed donor HLA. Procedures should be in place for updating donor HLA according to the respective policy (e.g. how the DC deals with results at more loci and higher resolution).

Procedures also need to be in place for investigating any HLA discrepancies which may be detected after receiving results from the TC.

6.2.6 Infectious disease markers and blood group results sent with regards to blood samples to the transplant centre

The purpose of infectious disease marker (IDM) testing is to assess the donor's exposure to infectious diseases and the likelihood of transmitting a disease to the recipient. It indicates if an individual currently has, or previously had, an infectious disease that could be transferred to another person. Routine health care screening and personal history and physical examinations are not a comprehensive evaluation for hematopoietic cell donations.

There are numerous infectious agents that, if present in the donor, pose definite risk to the transplant recipient and are only detected via IDM testing. Testing must be performed to meet the minimum requirements of the WMDA. The geographical location or other local factors may require additional testing according to national requirements as well. WMDA Donor Medical Suitability provides additional information on testing at VT.

Policies need to be in place specifying which testing is to be done at VT and which information is transmitted by which means to the TC. It needs to be assured that all required testing according to WMDA standards and national requirements at a minimum are performed and transmitted accordingly. It must also be assured that policies are in place to inform donors and TCs accordingly if positive IDM results are detected which could have implications on donor or patient health.

6.3 Workup

6.3.1 General requirements

Unrelated donors are not patients requiring medical assistance. They are enrolled in the registry to donate for a person who they do not even know. This is a very special situation for them and they should be treated with respect and the understanding that they are doing something very remarkable. Donors are healthy persons who are acting completely altruistically and are willing to take some small risks in order to help others. Donors are volunteers and can withdraw from the process at any time. No undue

pressure should ever be applied. Therefore, they need to be treated differently than a patient, and they should be treated with consideration to make them feel special and well cared for during the entire workup and donation procedure.

The process toward the donation is very special for the donor as well as for their family and friends. Therefore, it is recommended that the staff at the DC and CC is prepared and handles them with appropriate sensitivity.

A policy that clearly establishes the responsibility and tasks of the DC and CC must be in place. The SOP must ensure the proper planning and coordination of appointments and communication with the TC during the whole workup procedure.

Procedures should also include a system of documentation, ensuring the appropriate version of the forms and documents are in use, signatures and dates are correct, and respect of anonymity of the donor.

WMDA standards and guidance are well detailed in describing the requirements for this very critical and important procedure, therefore they can be a valid reference for setting up an audit focused on recognition, documentation and appropriate action plans in relation to the workup process.

6.3.1 Workup process: from information session to product collection

The donor management at time of UD workup must be performed according to National laws, regulations, and WMDA Standards.

The DC should have a SOP in place to define the process of organising, together with the CC, the workup. These policies must include the process to verify the prescription, to inform and counsel the UD, and to test the UD, including medical history, physical exam, and laboratory tests in order to determine the UD's fitness to donate. Workup request forms of the registry are expected to include information such as dates of patient's conditioning and graft infusion, proposed collection dates, and donor clearance date.

The purpose of verification typing is to ensure that the individual being selected for donation is the same individual whose HLA typing was listed on the search report used to select the donor. Because of the likelihood that two random individuals share some HLA types, it is important to type several HLA loci spanning the HLA region. A process must be in place to ensure the DC receives and verifies as congruent the results of extended/verification typing before the activation of a workup. The verification typing must be performed at a minimum of HLA-A, -B, -C, -DRB1 and must comply with registry SOPs before processing the workup request.

There must be policy in place to confirm that prescription forms are detailed, comprehensive, include clear donor identification (donor unique identifier/GRID), patient status and degree of urgency.

According to WMDA standards and guidance there must be a policy to inform the TC/ registry of critical information pertaining to the donor which could impact the collection or transplant. For example if the donor cannot be reached in a reasonable number of days after workup request, or when some complications occur. There must also be a written policy that describes how the transplant centre is advised of donor preferences and other related issues, such as the release of products that are considered to have increased risk. Refer to WMDA guidance for further examples.

A policy must be in place to verify together with CC the workup request and prescription and the timing to send back the signed and accepted prescription form (verification of prescription/cell product).

6.3.2 Pre-donation informative session and informed donation consent form

A written policy must be in place to obtain a valid signed informed consent from the donor. According to WMDA Standards the informed consent form must be written according to the national laws and regulations and must adhere to WMDA standards and registry SOPs.

The DC responsible physician or their designee, in accordance with the CC responsible physician, must explain the procedure in a language and terms the donor can clearly understand, and at a minimum the information session must cover the topics as listed in WMDA standards and guidance.

A SOP must be in place to verify, together with CC, the identity of the volunteer donor, at a minimum at workup and at collection, by the qualified staff signing the consent form. The responsible DC physician or their designee must be aware of the fact, that the UD can decline the donation process at any time; and training should be provided for handling this situation, comprehensive of the policy to inform the TC/ requesting registry immediately after the UD has refused to donate.

A policy must be in place to storeconsent documents signed by volunteer donors in a secure way to protect confidentiality. They must be promptly available for review by individuals designated by the registry or national authorities to evaluate the registry.

6.3.3 Collecting pre-collection samples

As per the WMDA standards, DCs must have the capability of shipping samples, if requested, to the facility indicated by the TC if required for further testing. The sample must be appropriate for the testing required. A policy should be available which outlines how and when to collect a pre-collection sample. In particular, the donor must sign the informed consent form before any pre-collection samples can be collected, and the DC must ensure the identity of the donor in an appropriate way before collecting the samples (e.g. photo ID).

The samples must be prepared for shipping according to the international safety recommendations, national rules and laws and according to the shipping instructions given on the workup forms

The samples must be labelled according to national regulations, WMDA standards and accreditation of the facility. National requirements as well as the registry's policies concerning the maximum volume of peripheral blood at the time of PE from a UD must

be followed. In case there is more blood requested from the UD than usual, the responsible DC or CC physician or their designee can decide to decline additional blood collection for donor safety reasons. This decision should be reported to the TC / requesting registry immediately.

6.3.4 Medical assessment and unrelated donor eligibility

If a registry relies on an independent collection centre for the collection of donor haematopoietic 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 in these areas. Detailed requirements are reported in the WMDA guidance.

The DC together with CC must plan the medical assessment of the UD. It must be performed according to the national standards. WMDA Standards should also be applied at a minimum. The DC together with CC must ensure the medical and physical examination of the donor is completed and recorded. This examination must be performed or supervised by a physician who is not a member of a team who has cared for the patient. The DC must have a plan to select a different physician or CC in order to comply with this requirement

The communication policy must include any issues, which may have a possible impact on the collection schedule, and they must be reported to the TC immediately.

SOP should be in place to cover the following

1. Possible need for central venous access
2. Mobilisation therapy for collection of HSC and apheresis
3. Anaesthesia and HSC BM collection
4. Pregnancy assessment for all female UDs according to national standards and regulations, and WMDA standard infectious disease markers (IDMs) must be tested within 30 days prior to the HSC collection or according to the applicable law and national requirement as well as to WMDA standards. If country-specific

IDMs are required (by applicable law and/or regulations), the UD must be tested for evidence of clinically relevant infections accordingly. IDM testing must be carried out in a manner to ensure the safety and accuracy of the data by laboratories that meet national requirements and standards (as well as international lab standards if applicable), and using diagnostic tests approved by the government or prevailing authority in the relevant community for performing these services. Additional tests must be performed as required to assess the possibility of transmission of other infectious or non-infectious diseases. UDs, which have recently travelled outside their country, should be evaluated for infectious agents prevalent in the areas of travel. The DC must have a SOP to counsel the UD in case of positive disease results.**Unrelated donor final clearance**

After having collected all required information about the UD's health, the responsible DC and CC physicians or their designee decides if the UD is suitable for the requested collection procedure and this decision must be documented on the final clearance form according to the WMDA standards and guidance. The DC and/or CC physician or their designee is responsible for completing and signing the clearance form prior to collection. If not required by national laws or requirements, then the subsequent review by a second person is strongly recommended. The donor final clearance must be communicated in writing to the TC before commencement of patient conditioning and before the UD begins the mobilisation regimen. Internal policy must also ensure that the DC /CC clearly communicates the expected hour for end of collection, pick up address for the product and collection centre contact information.

The donor final clearance and the detailed results of the medical assessment as well as the signed informed consent form from the UD must be added and stored with the donor's records for at least 30 years.

6.3.6 Medical ineligibility

A policy must be in place which clearly states what to do in case of a medical ineligibility of the UD for the requested collection procedure. The registry standards and

national regulations must be followed; additionally, WMDA donor suitability as well as registry-specific medical eligibility criteria lists can be consulted for general recommendations (WMDA Donor Medical Suitability Recommendations). The DC/ CC must have a procedure in place to inform the TC immediately about medical ineligibility of the UD. Additionally, this information must be forwarded to the registry in writing using WMDA forms or an equivalent.

When a potential risk for the recipient is identified, there might be a need to declare the UD as ineligible for the recipient according to national requirements and laws. The TC needs to be informed about this fact via the responsible registry according to the applicable data protection laws and requirements using the WMDA form (or equivalent). Additionally, some country-specific requirements have to be fulfilled (e.g. DUMN, declaration of ineligibility). These documents must be added to the donor's records and provided to the responsible registry. UD's eligibility can only be confirmed once TC has confirmed that the risk has been evaluated and is acceptable for the TC. Additional information about the health situation of the UD that might be relevant for the TC, but does not have a direct impact on the UD's eligibility, can be added to the WMDA form or equivalent as comments.

6.3.7 Insurance coverage for the donor

A policy should be in place to inform the donor about extra expenses and insurance. Check if material is given to the donor with information about disability and death benefits for all volunteer donors.

6.4 Follow-up

6.4.1 General requirements

The registry must have policies and procedures for the follow-up and care of donors for conditions related to the HPC donation. Donors must be provided a mechanism to contact the registry to report related medical concerns. The registry should ensure that the follow-up on the donor is done for a minimum of 10 years, starting with the first follow-up immediately after the HPC donation. Auditors should check that policies and

procedures are in place and are compliant with WMDA and registry requirements. Auditors can check for examples like questionnaires, forms, lab results and the documentation of attempts to proceed with the follow-up (in cases where donors do not show up for follow-up appointments, or do not fill out the questionnaire).

6.5 SAR/SAE

6.5.1 General requirements

Donors are healthy persons who voluntarily donate for a patient and are accepting some small risks in order to help others. They undergo thorough medical exams prior to donating to protect their health as well as the health of the recipient. Therefore, although the risks for both parties are clarified before donation/transplantation and are generally minor, it is still important to monitor the health and well-being of the donor not only during the collection procedure, but also afterwards.

According to WMDA standards, a serious adverse event (SAE) is defined as:

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

By contrast, a serious adverse reaction (SAR) is defined as:

"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."

The intent of the standards is to assure that measures are in place to assist in detection and reporting of the occurrence of an SAE/SAR, and that should a SAE or SAR occur, that the donor can be monitored and treated appropriately, and that all

parties involved are suitably informed so that also the transplant centre can care for the patient appropriately, if necessary.

Additionally, the WMDA reporting system (S(P)EAR) can assimilate long-term data on possible risks associated with the donation process, as well as assist in the (rapid) distribution of SAE-/SAR-related information to registries and their partners to assist in the prevention of the recurrence of such events.

The focus of the audit is, therefore, recognition, documentation and appropriate action plans in relation to SAEs and SARs, examples of documentation and investigation of SAR/SAE, and initiation of necessary remedial and/or corrective action

Both SAEs affecting a cellular product intended for a specific patient as well as SARs affecting donors undergoing collection of HPC and/or cellular product must be identified, documented, investigated and remedial and/or corrective action taken. There must be policies in place, which require monitoring of the donor during procurement. Should an event occur during donation, the donor must be suitably treated. Any possible effects the event may have on product quality, and thus the recipient, need to be documented. This also includes short-term monitoring and testing of the donor after donation (e.g. within a week, month or year). Long-term contact with the donor may also be necessary. Thus, procedures should outline when and in what form donors need to be contacted for over a year after donation.

Procedures should also include the system of documentation of cases and corrective action, and may also describe who processes and reviews cases.

6.5.2 Example of communication of SAR/SAE (if any) to the registry, as well as the TC and other organisations as applicable

The WMDA provides examples of cases, which need to be reported. There should be a procedure in place, which describes how and when cases are reported to the registry or directly to the WMDA.

Additionally, for cases which may involve transmission of communicable or other diseases to the patient, or which affect the quality of the product provided for treatment of the patient, a process must be implemented to assure that this information is provided to the transplant centre.

6.5.3 Example of documentation of an SAR and corresponding reports to WMDA covered by two points above

A policy should be available which outlines how and when cases are reported to assure they are submitted to the S(P)EAR program for documentation by the WMDA. The period of 15 working days, or 3 days for fatal cases, as prescribed by the WMDA, should be followed.