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MARROW DONOR PROGRAM BELGIUM

STANDARDS DONOR

APPROVAL

Governing Board of the MDPB-R	Function	Approval date + Signature
Prof. dr. Philippe Vandekerckhove	Director General Rode Kruis – Vlaanderen MDPB-R Governing Board	Digitally signed by Philippe Vandekerckhove (Signature) Date: 18/03/2024 15:38:15
Prof. dr. Pierre Zachée	Chair BHS-MDP-B Committee	Digitally signed by Zachée Pierre Gabrielle G Date: 19/03/2024 07:59:45

DISTRIBUTION

Function	Department - Institution
Contact person	Collection Center
Contact person	Donor Centers
Contact person	Transplant Center
Contact person	Hematopoietic Stem Cell Bank
Contact person	Cord Blood Bank
Members	MDPB-R Governing Board
Members	BHS-MDP-B Committee
Registry staff	MDPB-R
Contact person	WMDA
Contact person	Supporting services RKVL

VERSION CONTROL

Effective date	Version	Comment
01/04/2024	v7	Update according comments WMDA auditors.
01/11/2022	v6	Update to WMDA standards, update WMDA forms.
01/11/2021	v5	Update to WMDA standards, update WMDA forms. GDPR
01/07/2018	v4	Update to WMDA standards, update WMDA forms.
01/03/2017	v3	Update to WMDA standards, update WMDA forms.

27/06/2016	v2	New logo + address + fax number
01/09/2015	v1	Update to WMDA standards, update WMDA forms, Governing Board: details in summary of changes.
27/06/2014	v02/2011 addendum	Change of upper age limit of donors at registration
01/08/2011	v02/2011	SOP and forms
01/01/2010	v01/2010	SOP and forms
26/11/2002	v04/2002	SOP and forms

SUMMARY OF MAJOR CHANGES

Version	Comment
v7	- 3.3 + 4.11: subsequent donation - 4.2.5 + 4.2.7: additional testing - 4.4.3: donor reservation - 4.5.4: pregnancy test - 4.12.4 + 4.12.6
v6	- Changed “should” and “may” to “must” according to the latest WMDA standards - DC audit checklist - Affiliated centers: notify key changes - 4.4.5. + 5.3.1: new forms - 6.1.2.5: retention period - 6.1.2.6: donor removal - 7. Operational business continuity - 8. Strategy
v5	- Changed “shall” to “must” according to the latest WMDA standards - Changes to comply with GDPR - New information letters - GRID - BMDW is now Search & Match Service of WMDA - 4.1.2.1: donor transfer abroad - 5.1.2.8: invoicing of cancellations and postponements - 6.2.10 - 6.2.12: registry software info

v4	- 3.5.1: consultation HLA expert via MAC - 4.7.6.5: WBC count of HPC, A product - 4.9.2: WMDA transport guidelines - 5.1.1: inform significant changes via electronic mail - URL website WMDA and MDPB-R
v3	- Donor information letters - Informed consents – information letters - Medical questionnaires - Donor recruitment criteria - Donor reimbursement policy - Donor communication policy - Results health screening: implementation of C20 – C 30 WMDA forms - Ethnicity - Donation procedures - Quality assurance program - Donor patient – contact - Medical evaluation: F50 IDM testing to performed during workup - Rules of operation for international patients - QAC committee – MAC subcommittee - MAC approval
v2	- New logo + address + fax number
v1	- MDPB “SOP”: changed into MDPB “Standards”. - MDPB VZW: replaced by “BHS-MDP-B Committee”. - “Board” replaced by “Governing Board MDPB-R”. - Criteria and tasks participating center added: Hematopoietic Stem Cell Bank. - Accreditation requirements: reference to the JACIE standards. - Review disease categories. - SEARS/SPEARS procedure updated to the new WMDA reporting requirements. - Donor recruitment requirements specified. - Software “Syrenad” replaced by “Prometheus”. - Chapter 6. Information technology and information management: sections security management and management of changes added. - Update to WMDA forms where applicable. - New document numbering (document management system).

	- TC, Apheresis changed into MNC, Apheresis.
v02/2011 addendum	- Change of upper age limit of donors at registration.
v02/2011	- INDICATIONS for HSCT: limitation MAC approval and clear overview for MAC notifications. - Update to WMDA standards.
v01/2010	- FORMS: use of WMDA forms is introduced as these are used worldwide. - INDICATIONS for HSCT: the criteria of EBMT are used as recommendation. - Follow-up of the donor until 5 years after donation of HPC.

REVIEW AND UPDATE

Every 3 years, a profound review of the MDPB Standards is necessary: the medical and scientific regulations will be reviewed by the BHS-MDP-B Committee, the operational and procedural review by MDPB-R. The review also follows the timeline of the WMDA standards update, when WMDA procedures will be cross checked with the MDPB policies and procedures.

Updates are discussed and elaborated in the MDPB R BHS Staff meeting, proposals are further distributed for discussion and approval in the BHS-MDP-B Committee meeting and/or in working groups when necessary.

If there are no major changes, the MDPB Standards are prolonged annually. New and revised policies and procedures will be approved by the BHS-MDP-B Committee and the MDPB-R Governing Board the review must be documented. Final voting will be done by email and requires a 2/3's majority for approval.

Update requests must be sent to the MDPB-registry@rodekruis.be using the *MDPB FRM017 Update request MDPB Standards and forms*.

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1 INTRODUCTION

The Marrow Donor Program Belgium (MDPB) consists of the MDPB-registry (MDPB-R) within the Belgian Red Cross and the BHS-MDP-B Committee.

The MDPB-R is responsible for the administrative, financial and operational management of the MDPB. The BHS-MDP-B Committee is responsible for the medical and scientific matters (issues). The Medical Advisory Committee of the BHS-MDP-B Committee must be consulted for any medical question/procedure not covered by the MDPB Standards.

The Marrow Donor Program Standards cover all procedures involving unrelated donors. These standards intend to provide practical information to all MDPB users or coworkers. Deviation from these standards must be submitted in advance to the Governing Board of the MDPB-R.
The Medical Director of a participating Donor Center, Collection Center, Hematopoietic Stem Cell Bank or Transplant Center is responsible for ensuring compliance with these standards.
Each Collection Center and Transplant Center must appoint a certified Hematopoietic Stem Cell bank that will release products for transplantation, perform import/export operations and be the Registry's contact point for those operations.
The Marrow Donor Program Standards Cord Blood cover procedures involving cord blood requests.

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

After the WMDA qualification period is completed, the word "must" indicates that deviations are not acceptable. There will be no difference between WMDA bolded benchmark standards and non-bolded standards containing the words "must". The words "should", "might", and "may" are used for recommendations that are not mandatory.

A separate Collaboration agreement covers the procedures to assure the proper functioning of (the software application) "Prometheus", facilitating the search process for unrelated donors and cord blood units and sets out rights and obligations as regards to the processing of personal data in the scope of the MDPB.

Each institution must be GDPR compliant and appoint a Data Protection Officer.

2 CRITERIA FOR PARTICIPATING CENTERS

2.1 Donor Centers (DC)

The Center must agree to abide by these standards, policies, and procedures of the MDPB and FAGG/AFMPS (Federal agency for medicines and health products - www.fagg.be). The Center must also agree to abide by the standards, policies, and procedures of the JACIE standards (current edition), Belgian Standards of the HGR-CSS N° 8550 as applicable, WMDA standards (current version available on the WMDA website www.wmda.info), NMDP standards (current version), Anthony Nolanoperation and patient services User guide (current version).

Recruitment practices must meet relevant national laws and regulations. If governmental laws and regulations differ from WMDA standards, the requirement to meet local legal standards will be accepted as a valid cause of deviation from WMDA standards.

2.1.1 The Center must have demonstrated experience in donor management activities including counseling, confidentiality issues, and medical screening. Recruitment of donors must be performed under the supervision of individuals experienced in recruitment of donors and in donor management activities including education, consenting, counseling, confidentiality and medical screening. These individuals must receive relevant training and be appropriately qualified. The training and experience of these individuals must be documented.

2.1.2 The Center must have access, by reciprocal agreement, to the following facilities accredited, certified or licensed in accordance with governmental regulations:

- Histocompatibility Laboratory accredited by EFI and/or ASHI. The validity of the certificate may not be older than 6 months in the past.
- Laboratory testing of all donors (f.e. Infectious Disease Markers) must be performed by laboratories accredited or licensed in accordance with applicable laws and regulations.
- Transfusion center for collection of autologous blood: the transfusion center must be authorized by the governmental authority.

2.1.3 Center must have adequate staff, resources, space, equipment, communication links and supplies to support its donor management activities, including a private space for donor counseling sessions to maintain confidentiality.

2.1.4 Each Center must manage effectively its registered donors: regular contacts, calling for additional typing, checking availability, counseling...

2.1.5 Each Center must be connected with the MDPB-R, that is in charge of centralizing data and searching for donors.

2.1.6 Each Center must regularly update information on its donors, check donor availability and delete donors no longer available, and must transmit this information electronically to the MDPB-R.

2.1.7 Each Center must register all donors in the software application Prometheus or import the donors using the Prometheus interface.

2.1.8 **Each center must** strictly respect the complete anonymity "donor/recipient" **and may not use** the name of a donor and the name of a patient on the same document.

2.1.9 Each center **must always identify the donor by her/his GRID identifier** which must match international standards. The name and birth date of the donor may only be used in communications with the affiliated Collection Center.

2.1.10 Each donor prepared for HPC (Marrow or Apheresis), or MNC, A donation must benefit from a **disability life insurance** subscribed by the MDPB-R.

2.1.11 The Donor Center must be able to provide donor blood samples for testing, in compliance with national and international shipping standards.

2.1.12 Centers participating in human subject research must follow country specific regulations and policies, act in accordance with the applicable GDPR provisions and have a designated Institutional Review Board (IRB) or similar entity.
In case donor cells are intended for use in a research protocol, the protocol must be approved by the local IRB and necessary authorization must be obtained from the Registry or Center in charge with the donor.

2.1.13 Each center must have the necessary agreements in place with its data processors or third parties with whom it exchanges personal data in order to be compliant with GDPR.

2.1.14. Each center must have the following procedures, technical and organizational measures in place in order to be compliant with GDPR:

- There must be continuity in the performance of the role “DPO’ by the person designated by the organization. The DPO must have a backup with the required knowledge about GDPR legislation.
- The institution must have a register of processing activities.
- The institution must have a security policy and internal policies related to the retention of personal data, access control, permitted use, measures to be observed when using personal data. These procedures must be documented in a “WISP”: Written information security policy:
    - physical access control: to prevent unlawful or unauthorized processing of personal data, as well as to prevent accidental loss, destruction or damage to them or unauthorized disclosure or access to them.
    - electronic data protection, pass word management, access rights management.
    - infringement procedure, documentation of all infringements.
    - a communication security policy: the institution must have a policy to ensure that all communication and records about donors / patients are stored to ensure confidentiality.
    - the institution must have a procedure to deal with questions form a data subject.

- The Donor Center must have a procedure to notify the Marrow Donor Program Registry about key changes: address and contact information, change of staff, accreditation status, changes in affiliated facilities.

2.1.15. Each center will be audited based upon the WMDA Guidelines for Auditing of Donor Centers (ACC-9902-WGG-Guidelines DC Audit).

- The MDPB Donor Center Audit (MDPB FRM077) will be available and must be completed by the donor centers.
- The evaluation of the Audit will be part of the MDPB accreditation.
- Evaluation of the WMDA Key performance indicators for Registries are included in the Donor Center audit (Recommendation 20200820-WGQR-KPI 2020).
    - % of blood samples for verification (confirmatory) typing shipped within 14 calendar days of request. (target 92%)
    - % donor availability at verification (confirmatory) typing stage. (target 80%)
    - % donor availability at WU stage. (target 94%)

2.2 Collection Centers (CC)

The Center must agree to abide by the standards, policies and procedures of the MDPB, FAGG/AFMPS, JACIE standards (current edition) part C, Belgian Standards of the HGR-CSS N° 8550 as applicable, WMDA standards (current version, info available on the WMDA website : https://www.wmda.info/ and NMDP standards (current version).

2.2.1 The Collection Center must be linked to a FAGG/AFMPS certified Hematopoietic Stem Cell bank. The bank is responsible for product release conform to Belgian Law.

2.2.2 The Center must ensure that HPC (Marrow or Apheresis) or MNC, A products are collected by a team member of an MDPB accredited Collection Center.

2.2.3 For HPC, M collections, the hospital must provide a surgical operating room. All Collection Centers must have access to a medical intensive care unit.

2.2.4 The Collection Center must be able to provide donor blood samples for testing in compliance with national and international shipping standards.

2.2.5 The Collection Center must be formally accredited for the collection of HPC, M or HPC, A or both.

For accreditation as a HPC, M Collection Center:

- Valid JACIE certificate must include HPC, M.
- Part CM (Marrow collection facility standards) of JACIE standards for HPC, M collection apply.

For accreditation as HPC, A or MNC, A Collection Center:

- Valid JACIE certificate must include HPC, A or MNC, A.
- Part C of JACIE standards for the apheresis collection facility apply.

2.2.6 The hospital must have irradiated blood components available. If allogeneic blood is transfused to donors in situations of unexpected blood loss, this must be reported as a SEAR (see: reference documents).

2.2.7 The Collection Center must clearly define responsibilities for donor care before, during and after the procedure, which include at least the following:

- Obtain valid Informed consent.
- Document Fitness for donation (must be evaluated by or with a qualified anesthesiologist if applicable).
- Document Eligibility.
- Use of autologous blood and the number of units to be collected by Donor Center if indicated cfr 2.1.2.
- Document fitness for discharge as applicable.
- Donor follow-up according to a pre-defined schedule.
- Delivery of the product and accompanying documents (collection report, informed consent, donor eligibility) to the affiliated bank for release.

2.2.8 Centers participating in human subject research must follow country specific regulations and policies, act in accordance with the applicable GDPR provisions have a designated Institutional Review Board (IRB) or similar entity.
In case donor cells are intended for use in a research protocol, the protocol must be approved by the local IRB and necessary authorization must be obtained from the Registry or Center in charge with the donor.

2.2.9. Each center must have the necessary agreements in place with its data processors or third parties with whom it exchanges personal data in order to be compliant with GDPR.

2.2.10. Each center must have the following procedures, technical and organizational measures in place in order to be compliant with GDPR:

- There must be continuity in the performance of the role “DPO’ by the person designated by the organization. The DPO must have a backup with the required knowledge about GDPR legislation.
- The institution must have a register of processing activities.
- The institution must have a security policy and internal policies related to the retention of personal data, access control, permitted use, measures to be observed when using personal data. These procedures must be documented in a “WISP”: Written information security policy:
    - physical access control: to prevent unlawful or unauthorized processing of personal data, as well as to prevent accidental loss, destruction or damage to them or unauthorized disclosure or access to them.
    - electronic data protection, pass word management, access rights management.
    - infringement procedure, documentation of all infringements.
    - a communication security policy: the institution must have a policy to ensure that all communication and records about donors / patients are stored to ensure confidentiality.
    - the institution must have a procedure to deal with questions form a data subject.

- The Collection Center must have a procedure to notify the Marrow Donor Program Registry about key changes: address and contact information, change of staff, accreditation status, changes in affiliated facilities.

2.3 Transplant Centers (TC)

The Center must agree to abide by the standards, policies, and procedures of the MDPB, FAGG/AFMPS, JACIE standards (current edition/version) part B, Belgian Standards of the HGR-CSS N° 8550 as applicable, WMDA standards (current version) and NMDP standards (current version).

The TC must have RIZIV/INAMI certification for allogeneic transplantation.

2.3.1 General requirements:

2.3.1.1 HPC, M and HPC, A transplantations using unrelated, donors must be carried out only by Transplant Centers with adequate experience in sibling transplants. Such Transplant Centers must be formally accredited by JACIE and listed on the Transplant Center list of the MDPB-R. They must be willing to report results and exchange information and materials as appropriate. Requests for a donor will only be handled if the recipient Center has **adequate experience**.

2.3.1.2 The definition of adequate experience is a Center that has been in operation for allogeneic transplantation for at least 5 years and where at least 10 new allogeneic transplants are performed annually in the past 2 years, according to the JACIE accreditation criteria.

2.3.1.3 An exception to this level of activity (10 new allogeneic transplants in past 2 years) can only be granted to pediatric centers sponsored by an accredited adult Transplant Center from the same Institution and after both the MDPB-R, the BHS-MDP-B Committee and JACIE have formally approved this collaborative agreement.

2.3.1.4 Part B - clinical program standards of JACIE apply.

2.3.1.5. Each center must have the necessary agreements in place with its data processors or third parties with whom it exchanges personal data in order to be compliant with GDPR.

2.3.1.6. Each center must have the following procedures, technical and organizational measures in place in order to be compliant with GDPR:

- There must be continuity in the performance of the role “DPO’ by the person designated by the organization. The DPO must have a backup with the required knowledge about GDPR legislation.
- The institution must have a register of processing activities.

- The institution must have a security policy and internal policies related to the retention of personal data, access control, permitted use, measures to be observed when using personal data. These procedures must be documented in a “WISP”: Written information security policy:
    - physical access control: to prevent unlawful or unauthorized processing of personal data, as well as to prevent accidental loss, destruction or damage to them or unauthorized disclosure or access to them.
    - electronic data protection, pass word management, access rights management.
    - infringement procedure, documentation of all infringements.
    - a communication security policy: the institution must have a policy to ensure that all communication and records about donors / patients are stored to ensure confidentiality.
    - the institution must have a procedure to deal with questions form a data subject.
- The Transplant center must have a procedure to notify the Marrow Donor Program Registry about key changes: address and contact information, change of staff, accreditation status, changes in affiliated facilities.

2.3.2 Supporting Services:

2.3.2.1 There must be documented evidence of collaboration with an HLA Laboratory accredited by EFI or ASHI.

2.3.2.2 The TC must work in cooperation with a Hematopoietic Stem Cell Bank, licensed by FAGG/AFMPS and JACIE accredited.

2.3.2.3 Research Protocols for unrelated donor hematopoietic stem cell transplants must have been approved by a local Institutional Review Board (Ethics Committee) by using the form *MDPB FRM010 Request for unrelated donor to participate in a research study*.
Centers participating in human subject research must follow country specific regulations and policies, act in accordance with the applicable GDPR provisions and have a designated Institutional Review Board (IRB) or similar entity.
In case donor cells are intended for use in a research protocol, the protocol must be approved by the local IRB and necessary authorization must be obtained from the Registry or Center in charge with the donor

2.4 Hematopoietic Stem Cell Bank (HSCB)

2.4.1 The Hematopoietic Stem Cell Bank must be certified by FAGG/AFMPS as a Hematopoietic Stem Cell Bank. In addition, the bank must comply with JACIE standards and be accredited for that part of the JACIE standards.

2.4.2 The Hematopoietic Stem Cell Bank must be affiliated with a Collection and/or Transplant Center and have the responsibility for product release conform Belgian Law for these centers.

2.4.3 The Hematopoietic Stem Cell Bank must be responsible for:

- Processing, conditioning and storage of cellular products.
- Release of cellular products.
- Import of cellular products, including conformity with national regulation and (re)testing of IDMs by a EU certified lab.
- Traceability of donor and recipient.
- Export.

2.4.4 Centers participating in human subject research must follow country specific regulations and policies, act in accordance with the applicable GDPR provisions and have a designated Institutional Review Board (IRB) or similar entity. In case donor cells are intended for use in a research protocol, the protocol must be approved by the local IRB and necessary authorization must be obtained from the Registry or Center in charge with the donor.

2.4.5. Each center must have the necessary agreements in place with its data processors or third parties with whom it exchanges personal data in order to be compliant with GDPR.

2.4.6. Each center must have the following procedures, technical and organizational measures in place in order to be compliant with GDPR:

- There must be continuity in the performance of the role “DPO’ by the person designated by the organization. The DPO must have a backup with the required knowledge about GDPR legislation.
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- The institution must have a security policy and internal policies related to the retention of personal data, access control, permitted use, measures to be observed when using personal data. These procedures must be documented in a “WISP”: Written information security policy:
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    - electronic data protection, pass word management, access rights management.
    - infringement procedure, documentation of all infringements.
    - a communication security policy: the institution must have a policy to ensure that all communication and records about donors / patients are stored to ensure confidentiality.
    - the institution must have a procedure to deal with questions form a data subject.
- The Hematopoietic Stem Cell Bank must have a procedure to notify the Marrow Donor Program Registry about key changes: address and contact information, change of staff, accreditation status, changes in affiliated facilities.

3 CRITERIA FOR CONSIDERING A PATIENT FOR AN UNRELATED DONOR TRANSPLANT

3.1 Prerequisite for initiating a search

A search may only be initiated after the potential recipient has been registered on the waiting list of the RIZIV/INAMI (see 3.5 for additional criteria). Each patient must be provided with a written document (MDPB STD017 Information letter patient NL, MDPB STD018 FR, MDPB STD019 EN, MDPB STD020 DE) containing specific information on the global search for a suitable stem cell donor and on the processing of his personal data.

3.2 Disease categories

The MDPB does restrict access to its donors for patients in specific disease categories. These categories are based on those published according to the EBMT guidelines in bone marrow transplantation. The criteria of EBMT are used as recommendation for MDPB. Access to donors must apply with applicable Belgian law.

3.2.1 List of allogeneic transplantation for hematological diseases, solid tumors and immune diseases:

If the indication is stated GNR (generally not recommended) a MAC is required.

If the indication is *Developmental* and patient is included in a *protocol approved by the Ethics Committee (EC)* then no MAC (Medical Advisory Committee) approval is required. A copy of the EC approval must be provided on request. In the other case of Developmental indication, a MAC is required.

For international patients, eligibility is assessed according to EBMT guidelines when the workup stage is initiated.

3.3 Subsequent donations

3.3.1 Subsequent donations from abroad donors

Second donations from abroad donors are acceptable without prior MAC approval. Requests go through specific procedures in donor registries abroad.

3.3.2 Subsequent donations from Belgian donors for the same patient

1. Unstimulated apheresis (MNC, A) requires no prior approval by MAC.
2. HPC, M or HPC, A after mobilization with growth factors require prior approval by MAC.

3.4 Request for approval by Medical Advisory Committee (MAC)

3.4.1 For patients not fulfilling the eligibility criteria as described above (3.2.1- 3.3) as well as for any request not clearly covered by the MDPB Standards the Registry must contact all MAC members (a minimum of 5 MAC members) individually by email. The members of the MAC must reply within 1 week (48

hours if urgent). A minimum of 50% of the members have to approve the request prior to proceeding. A MAC member cannot vote on a request from his/her own center.
The decision will be considered final. In general, deviations from the standards will only be accepted in exceptional situations. Requests for MAC approval must be sent to the MDPB-R by completing the *MDPB FRM038 MAC request for review* form. MAC approval will be notified through the *MDPB FRM039 MAC approval* form.

If a colleague MAC Member opposed to a MAC request, the complete MAC team must be informed about his/her opinion. (In both cases, approval or not approval of the MAC request.)

In case of a MAC approval with a minority of rejections, a second round will be organized to study and discuss the argumentation of the rejection between the MAC members.

A backup pool must be available during holiday periods, and must be informed to the MDPB-R.

3.4.2 In case of a MAC approval request for a Belgian donor request, the MAC approval request must be sent to all MAC Members without exclusion. In case of a rejection, the decision will be considered final and the Donor Center may not proceed with the request. In case of approval, the final decision is the responsibility of the Donor Center.

3.5 Initial search request at MDPB-R

3.5.1 Donor searches can be requested by a Belgian accredited Transplant Center, any International Registry (HUB) or any European EBMT accredited Transplant Center (if no HUB available in that country) or by an accredited US Transplant Center. If no HUB is available in that country the request must be approved by the Medical Advisory Committee. A search cannot be initiated if the patient is not accepted on the waiting list of an accredited Transplant Center.
A donor search by a Belgian Transplant Center must include the search of the Belgian donor registry. A donor search by an international non EMDIS Registry or Transplant Center must be initiated by an initial search form of the applicable Registry or the WMDA *S10 Preliminary search request* form. The MDPB-R will register the patient in the Prometheus software.

In case a suitable donor is not found, the Transplant center can submit a MAC Request to ask to the MAC committee if there is an alternative therapy for the patient. The Medical Advisory Committee can also ask a consultation of a HLA expert to help the transplant center.

3.5.2 Each Belgian initial search request can be initiated in Prometheus by the Transplant Center. A request cannot be validated if information is missing. (The Blood group and CMV testing are not mandatory.)
For registries not connected to the EMDIS network, the Transplant Center can use the *MDPB FRM002 Non EMDIS search request* to initiate the search request.

3.5.3 The HLA typing of the patient must be COMPLETE, i.e. HLA-A, B, C (at least 2 digits), DRB1 (4 digits – at least intermediate resolution) and preferably

DQB1. The HLA typing must be confirmed on a second sample or by family HLA typing. No search will be initiated if the above typing level is not available. It is the responsibility of the Transplant Center to check which Registries will be searched by consulting the WMDA Search & Match Service.

3.5.4 The Transplant Center must cancel the search if the patient is no longer eligible for transplantation (medical reasons) or if a transplant is no longer considered. If at a later time the decision is made to resume the search, the search must be reactivated. Patients can also be temporarily suspended and reactivated by the Transplant Center. The Transplant Center must follow up the status of the patient's search in the application Prometheus. A suspended status means that the patient is not in an active state, but the pending requests will be further processed. The repeat search program will be stopped for this patient. The Transplant Center must follow up the patient's activity and check on a regular basis the active searches: patients with no activity for 6 months must be suspended or cancelled.

3.5.5 Following the registration of the patient a search report on unrelated donors and cord bloods is sent to the requesting Transplant Center via Prometheus (EMDIS search results). The Registry will send the Transplant Center the "Notification of unrelated donor search by the Registry" to confirm the URD search in the MDPB-R for RIZIV/INAMI purposes (*MDPB FRM022 RIZIV/INAMI doc*).
For international searches requested by the Transplant Center, an electronic search result list will be sent via Prometheus (EMDIS search results); for non EMDIS countries, the search result list will be sent via email (via TLS encryption).

On the search report of the Prometheus software appear the number of donors and codes of (depending on the selected parameters):
6/6 Allele Matched donors
6/6 Potential (Allele) Matched donors
6/6 Antigen Match (Allele Mismatch) donors
5/6 Antigen Matched donors
4/6 Antigen Matched donors
4/4 AB Antigen Matched donors
3/4 AB Antigen Matched donors

3.5.6 Following the submission of an initial search request for a patient at MDPB-R, a search report on Cord Blood Units of the Belgian Cord Blood Bank is sent to the requesting Transplant Center via Prometheus (EMDIS). International cord search results of EMDIS connected countries will be sent via Prometheus (EMDIS) if requested by the Transplant Center, cord search results of non EMDIS countries will be sent via email.

On the cord search report of the Prometheus software appear the number of cord bloods and codes of (depending on the selected parameters):
6/6 allele Matched cord bloods
6/6 Potential (Allele) Matched cord bloods
6/6 Antigen Match (Allele Mismatch) cord bloods
5/6 Antigen Match cord bloods
4/6 Antigen Match cord bloods
4/4 AB Antigen Match cord bloods
3/4 AB Antigen Match cord bloods

4 PROCEDURES

4.1 Recruitment of donors

4.1.1 Each candidate donor must be, at a first stage, provided with a written document (MDPB STD013 Information letter donor registration NL, MDPB STD014 FR, MDPB STD015 EN, MDPB STD016 DE) containing specific information on HPC, M and/or HPC, A donation and on the processing of his personal data. (This document must be approved by the Registry.)

4.1.2 Each donor **MUST** be a **VOLUNTEER**.

4.1.3 To be able to be registered within the MDPB-R, donors must have passed their 18th birthday but must not have passed their 40th birthday. Information on donor age, gender and ethnic background must be collected at the time of recruitment.

4.1.4 *RECOMMENDATION:*
Taking into account the characteristics of donors selected for donation, it is recommended that young males with a diverse genetic background are recruited.

4.1.5 A medical questionnaire must be obtained on time of registration in conformity with :

Each recruited donor must sign an initial informed consent form to document that he has received all necessary information and a medical questionnaire must be obtained. Each recruited donor must also give its explicit written consent as regards to the processing of his personal data as meant in clause 7 GDPR.

(MDPB FRM048 Info consent for donor recruitment into the Registry NL, MDPB FRM049 FR, MDPB FRM050 EN, MDPB FRM051 DE).

(MDPB FRM068 Medical questionnaire donor recruitment and blood sample collection SFS NL, MDPB FRM069 FR, MDPB FRM070 EN, MDPB FRM071 DE).

The document used for informing the donor must contain at least:

- The duration of his registration in MDPB-R (until the age of 60).
- Willingness to donate for ANY patient either in Belgium or abroad.
- The importance of the reliability of his act (availability towards all convocations).
- The importance of keeping the donation **ANONYMOUS** and **VOLUNTARY**. *(Ref: MDPB STD004 Donor expenses and anonymous communication NL, MDPB STD005 FR, MDPB STD006 EN, MDPB STD 007 DE)*
- The possible risks related to general anesthesia for HPC, M collection. The possible risks related to collection after mobilization with growth factors for HPC, A collection. The possible risks related to MNC, A collection and blood donation.
- In case of failed mobilization, the donor will be asked to donate HPC, M. The information letter *(MDPB STD009 Information letter blood sample*

collection and HPC, A - HPC, M - MNC, A donation NL, MDPB STD010 FR, MDPB STD011 EN, MDPB STD012 DE) explains that a failure of HPC,A mobilization can occur in less than 1 % of the cases and in this rare situation, the donor can be asked to donate HPC, M. The consent form includes the possibility for the donor to refuse this second donation. In this case, the Transplant Center will be notified in advance that a HPC, M donation in case of mobilization failure is refused by the donor and the Transplant Center will be requested to confirm if it is willing to continue with the same donor.

- The information letter also explains that in some clinical situations, as poor engraftment, life threatening viral infections, or poor transplant residual disease or early relapse, a subsequent immobilized collection of lymphocytes (MNC, A) can be asked from the donor. The consent form includes the possibility for the donor to refuse this potential subsequent donation of MNC, A. In this case the Transplant Center will be notified in advance that a subsequent MNC, A donation is refused by the donor and the Transplant Center will be requested to confirm is it is willing to continue with the same donor.
- In case of excess of cells, the cells must be destroyed cfr Belgian Law. If applicable, the information letter will explain the donor the benefice for the collecting center of using a small clinically insignificant amount of cells for research purpose according to a specific project approved by an Ethics Committee. The consent form will offer the donor the possibility to accept or refuse the use of his cells for research purposes.
- The donor will be informed that according to the Belgian law, the excess of collected cells are kept for the intend recipient and only for him until his death. Approval to freeze the cells must be requested and obtained via a MAC request. After the recipient's death it is required by law to discard the remaining donor cells. The cells cannot be kept to be used for the donor himself.
- All information required for informing the donor of the processing of his personal data in accordance with GDPR.

4.1.6 Each recruited donor understands the different donation procedures as well as the recovery and follow-up, and the duration of hospitalization and temporarily cessation of activity.

4.1.6.1. Donation procedures

There are 2 methods of stem cell donation: HPC, M and HPC, A.
The patient's physician will express a preference for a certain donation type which is best for the patient, but it is the donor's total freedom to decide which method of donation he accepts or refuses.

HPC, A donation is a non-surgical procedure. For 4-5 days leading up to donation, the donor will be given G-CSF injections, a medication that increases the number of blood-forming cells in the bloodstream. On the day of donation, the donor's blood is drawn through a needle on one arm and passed through a machine that separates out the blood-forming cells. The remaining blood is returned to the donor through the other arm.

HPC, M donation is a surgical procedure that takes place in a hospital operating room. Needles are used to withdraw liquid marrow from the back

and front of the pelvic bone and/or from the sternum. Donors receive anesthesia and feel no pain during the donation.

4.1.6.2. Duration of hospitalization and temporary cessation of activity: Recovery and follow-up.

The donation procedure, the risk, the follow-up and the recovery is explained in the donor information letter.

The time it takes for a donor to recover from stem cell donation varies. It depends on the person and type of donation. Most donors are able to return to work, school and other activities within 1 to 7 days after donation. This work incapacity can be covered by social security depending of the donor's employment status but is not at the charge of the MDPB or the Transplant Center. In case of a temporary sick leave, the donor will not beneficiate of temporary disability compensations from the Registry or the Transplant Center. In case of an unexpected side effect in term of duration (more than 2 weeks) or type (e.g. severe puncture point infection, severe prolonged anemia), the insurance of the MDPB intervenes on the request of the collecting physician responsible for the donor.

HPC, M donation.

The most serious risk associated with donating HPC, M involves the use and effects of anesthesia during surgery. After the surgery, the donor might feel tired or weak and have trouble walking for a few days. The area of prelevation of the HPC, M might feel sore for a few days. The donor can take pain medication to relieve the discomfort. The donor will likely be able to get back to his normal routine within a couple of days, but it may take a couple of weeks before the donor feels fully recovered. Common side effects of HPC, M donation reported 2 days after donation are: Back or hip pain (84% of the donors), fatigue (61% of the donors), throat pain (32% of the donors), muscle pain (24%), insomnia (15%), headache (14%), vertigo (10%), loss of appetite (10%), nausea (9% of the donors).

The median time to full recovery for a HPC, M donation is 20 days. Recovery after HPC, M donation: < 2 days for 5% of the donors, <7 days for 18%, <30 days for 71%, <180 days for 97%, <1 year for 99% of the donors.

HPC, A donation.

The risks associated with this type of stem cell donation are minimal. Before the donation, the donor will get G-CSF injections to increase the number of stem cells in his blood. G-CSF injections can cause side effects, such as bone pain (80% of donors), muscle aches, headache, fatigue, nausea and vomiting. These usually disappear within a couple of days after the last injection. Pain medication can be taken to relieve the discomfort. During the donation, the donor will have a catheter (thin, plastic tube) placed in a vein in the arm. If the veins in the arms are too small or have thin walls, he may need to have a catheter put in a larger vein in his neck, chest or groin. This rarely causes side effects, but complications that can occur include pneumothorax, bleeding and infection. During the donation, the donor might feel lightheaded or have chills,

numbness or a tingling feeling around the mouth, and cramping in the hands. These will go away after the donation. The median time to full recovery after a HPC-A donation is one week (seven days).

4.1.7 **There must never be any pressure on any potential donor, at any stage.** The prospective donor must be given ample opportunity to ask questions and to consider the decision. The donor must be assured of the right to decline or to withdraw at any time without prejudice.

4.1.8 All prospective donors must be given educational material regarding the risks of transmitting infectious diseases by a stem cell transplant. This material must include detailed information on risk groups for transmission of HIV (human immunodeficiency virus). The donor must acknowledge in writing that he or she has read and understood the educational material, has been given the opportunity to ask questions and has had those questions answered to his or her satisfaction, and has provided accurate information to his or her best ability.

4.1.9 A history of confirmed positive tests for hepatitis B surface antigen (HBs Ag), anti-human immunodeficiency virus type 1 and 2 (HIV1-2 antibodies), anti-hepatitis C virus (HCV) or anti-syphilis antibodies must be ground for cancelling the donor.

4.1.10 Through medical history and examination, the following risks must be evaluated:

- Donor safety.
- Cellular product quality.
- Recipient safety.
- Collection and Processing Staff safety.

4.1.11 If a pregnant donor is requested for typing/blood sample/donation, she must be suspended for the entire time of her pregnancy and up to a period of six months after delivery or end of breastfeeding.

4.1.12 A donor must be prevented from donating again (unless he or she donates for the same recipient and according to the same rules as defined above). After donation the donor must be removed from the Registry's database by the Donor Center. A donor that has already donated for a relative doesn't qualify for registration as an unrelated donor.

4.1.13 HLA typing performed on a newly recruited donor must be by sequencing exon 2 and 3 for HLA A, B and C and exon 2 for HLA DR, DQ. This typing must be fully reported to MDPB-R. The donors then appear in the national file of the MDPB-R under a unique GRID identifier.
ABO-D and CMV status should be communicated to the Registry if available.

4.1.14 The Donor Center must ensure that the donor (at least at time of Verification Typing or additional typing request) responds in writing to a medical history questionnaire that meets the blood donation criteria except for: (Reference WMDA wiki for exclusion criteria) according to the applicable laws.
https://share.wmda.info/display/DMSR/Prion-associated+disease
https://share.wmda.info/display/DMSR/High+risk+sexual+behaviour
https://share.wmda.info/display/DMSR/Hepatitis+B+infection+-+past

The criteria for blood donors and candidate stem cell donors must be specified in the guidelines of Rode Kruis-Vlaanderen and la Croix- Rouge de Belgique Service du Sang.

4.1.15 All staff members (Donor and Collection Center, Registry) involved in donor recruitment, collection, and administration must preserve donor and recipient confidentiality.

4.1.16 The donor's HLA typing data must not be used to commit the donor to programs for which he or she has not given explicit written consent.

4.1.17 Donors who have not previously been offered the option of being a blood donor may be asked whether they are willing to participate in a blood component donation program.

4.1.18 When blood or tissues are obtained for research purposes, specific written consent must be obtained from the donor. The Informed consent form must be approved by an Ethics Committee and must be in accordance with all GDPR requirements.

4.1.19 Related donors, not compatible for the related patient but willing to donate for unrelated patients must pass the registration process as an unrelated donor. Related donors living abroad are allowed to register as an unrelated donor in the foreign country if accepted by the International Registry of this country. Further activations and workup will be initiated as a regular UD search.
In the event of a related donor residing in Belgium for a recipient living abroad, the Registry may organize donor registration, workup and collection on the same conditions as a MUD.

4.1.20 Registration of international donors moved to Belgium must not fulfill the Belgian donor registration requirements for HLA typing and age. A medical interview/questionnaire must be done by the Belgian DC, but typing doesn't need to be re-done (an official lab report of the HLA Typing is a prerequisite).
REMARK UK donors: Donors moving from the UK can be registered in Belgium and later donate cells through an exceptional release. A person living in Belgium who resided in the UK between 1980 and 1996 for a period of 6 months or longer (not yet registered in the UK) cannot register in Belgium as a donor.

4.1.21 When Belgian donors move abroad, the donor must be informed to get in contact directly with the international Registry. In case of a donor transfer during CT or Workup the MDPB will intervene to accelerate the process.

4.2 Additional testing when a potential donor has been identified

4.2.1 Upon specific request the following tests will be performed: A B C DR DQ DP by low or high resolution. (Request via Prometheus for Belgian and international donors or via form *S20 Request For Extended Donor HLA Typing* for international non EMDIS donors).

4.2.2 A blood sample for Verification Typing (Confirmatory Typing) can be sent to the Transplant Center upon request via Prometheus for Belgian or

international EMDIS donors or using a specific form *S40 Blood sample request for verification typing* for international non EMDIS donors.

4.2.3 In case of a significant mismatch (cfr. Seattle Criteria), the request for further testing has to be submitted to the Medical Advisory Committee (MAC) of the MDPB, before continuing with transplantation (the IRB approved protocol to be provided to the Registry upon request).

4.2.4 **Informed consent** and medical questionnaire must be obtained from the donor to provide a blood sample for further tests (additional typing and Verification Typing (Confirmatory Typing)).

(MDPB FRM052 Info consent blood sample collection NL, MDPB FRM053 FR, MDPB FRM054 EN, MDPB FRM055 DE).

(MDPB FRM068 Medical questionnaire donor recruitment and blood sample collection SFS NL, MDPB FRM069 FR, MDPB FRM070 EN, MDPB FRM071 DE).

4.2.5 The Donor Center, when requested for blood from the donor for Verification Typing (Confirmatory Typing) must perform the following tests:

infectious disease markers (IDM)

Syphilis	
HBs Ag	
HBcore antibody	
Anti-HIV1-2 antibodies	
Anti-CMV antibodies	
Anti-hepatitis C virus (anti-HCV) antibodies	
Other tests	
ABO and Rh typing	if not already performed

The IDM results must be entered in Prometheus including the test date.

The number of previous pregnancies and/or transfusions must be recorded.

Laboratory testing of all donors must be performed by a lab licensed in accordance with laws – current regulations by the governmental authority. The Donor Center must be able to provide on request the test methods and reagents used in the laboratory.

4.2.6 If the results of the blood test do not comply with donor requirements, the donor will not be accepted. If such a donor must be used, prior approval from the MAC is mandatory. This MAC approval is only applicable for Belgian donors. This is not the case for international donors, the Donor Center is responsible and will take the final decision.

4.2.7 The HLA typing of any donor selected for stem cell donation **must be confirmed by the Transplant Center (to the resolution level required by the Transplant Center of the patient)**. Notification of the results of the HLA typing performed (minimum requirement HLA-A/B/C and DRB1 typing at high resolution, including additional loci if required by the transplant center) by the

Transplant Center must be sent to the Donor Center via Prometheus (Belgian donors and international EMDIS donors). For non EMDIS donors the form *S60 Donor HLA verification typing results* must be sent to the Registry. Decisions on donor acceptability must be made promptly, so that unsuitable donors be released and suitable donors be informed on the further procedure.

4.2.8 The ABO blood group and Rh factor testing of donors must be performed at the time of Verification Typing if the donor's blood group has not been previously determined.

4.2.9 When the Transplant Center finds discrepancies when performing the Verification Typing tests, the discrepancy must be reported using the *S70 Discrepant typing report*. The Transplant Center finding the discrepant type must complete section A, the Donor Center must complete section B and return via the Registry to the Transplant Center specifying the type of error: clerical error or technical error. The Registry must report the discrepancies of Belgian donors to WMDA annually.

4.2.10 Invoices concerning additional HLA typing are sent by the MDPB-R to the requesting International Registries (HUBs).
In case of a search cancellation at the stage of additional typing, the emission of an invoice can occur within the next 4 weeks following the cancellation.
Invoices for blood sample collection, IDM testing, pre-collection samples and shipment are invoiced by the Donor Centers or Collection Centers to the MDPB-R (the form *MDPB FRM012 Additional info invoice donor sample transport* must be attached). The MDPB-R will not send order forms. Billing should occur within 40 days of service completion. The MDPB-R will re-bill to destination of the International Registry and follow up settlement of payments by sending regular statements of account.
Due to international policies, invoices won't be accepted over 4 months after service completion.

4.3 Donor information - intent to donate

4.3.1 Upon completion of Verification (Confirmatory) Typing, the Transplant Center must select the donor for donation using *F10 Formal request and prescription for HPC, M; HPC, A or MNC, A*. Results of the Verification Typing as well as the suggested transplant date (on F10) must be provided by the Transplant Center through *F30 Final compatibility test results*.

4.3.2 The HLA matching between donor and patient must comply with the Seattle criteria:

The Seattle criteria for acceptable mismatches are:

9/10 match : One allelic mismatch
One antigenic mismatch
at HLA-A or -B or -C or -DRB1 or –DQB

8/10 match: Two allelic mismatches
One antigenic mismatch ± 1 allelic mismatch
at HLA-A or -B or -C or -DRB1 or -DQB1

One antigenic mismatch at -DQB1 and
one other antigenic mismatch at HLA-A or -B or -C or -DRB1

4.3.3 Once the donor has been selected, he/she must be counseled by the Donor Center and/or the Collection Center as follows:

- He/she must be given detailed information on further tests to be done, the procedure of HPC, M or HPC, A donation, potential discomfort and risks related to donation, incl. anesthesia, the period of time for which he or she may have to commit, the reimbursement of reasonable costs.
- It is strongly recommended to include the spouse or other trusted confidant of the donor in this process.
- The donor must be reminded of his or her right to withdraw at any time for the HPA, A collection and up to induction of anesthesia for the HPC, M collection. However they must also be informed of the serious risk for the recipient must the donor withdraw after the beginning of the recipient's conditioning regimen.

4.3.4 The following points must be discussed with the donor:

- The anonymity between donor and patient.
- The requirement for blood samples before donation (where Registry policy permits).
- The patient's need for a transplant and the chances of success expressed in general terms.
- The possibility of second donation for the same patient (including treatment with hematopoietic growth factors or leukapheresis).
- The financial issues:
  - a gift without remuneration, reimbursements of cost of donation.
  - details of the insurance coverage.

4.3.5 After counseling, the donor must express the willingness to continue the process before the medical evaluation may be scheduled.

4.3.6 In case of abnormal donor finding, urgent medical need must be documented in order to proceed. The Collection Center must inform the Transplant Center using the *C20 Abnormal donor finding letter* form.

4.3.7 If the donor is medically not able to proceed with the donation as scheduled the Collection Center must inform the Transplant Center using the *C30 Notification unable to clear the donor.*

Once a donor has been found eligible to donate in the Collection Center, he/she must give informed consent expressing his or her willingness to continue the process (specific informed consent forms for HPC, M or HPC, A donation respectively: *MDPB FRM056 Info consent HPC, Apheresis, HPC, Marrow donation NL, MDPB FRM057 FR, MDPB FRM058 EN, MDPB FRM059 DE, MDPB FRM060 Info consent, MNC, Apheresis NL, MDPB FRM061 FR, MDPB FRM062 EN, MDPB FRM063 DE) and* a medical questionnaire must be obtained *(MDPB FRM072 Medical questionnaire workup NL, MDPB FRM073 FR, MDPB FRM074 EN, MDPB FRM075 DE).*

4.3.8 The Collection Center must notify the MDPB-R and the Transplant Center that the donor has been found eligible for donation.

A signed copy of the informed consent must be available in the Donor and Collection Center and must be archived after donation in the Hematopoietic Stem Cell Bank.

4.4 Donor reservation - Pre-collection communication

4.4.1 A prescription form for collection of HPC (Marrow or Apheresis) or MNC, A must be completed and signed by the responsible transplant physician and transmitted via the Donor Center to the Collection Center using the form *F10 Formal request and prescription for HPC, M; HPC, A or MNC, A*.

4.4.2 After having received the Prescription Form, the Donor Center will contact its donor in collaboration with the Collection Center and agree on the date for medical evaluation (see 4.5) and subsequently agree on a date for HPC (Marrow or Apheresis) or MNC, A collection according to the specifications by the transplant physician.

4.4.3 In the search process, upon receiving a typing request, the donor must be reserved for 60 days, after the transmission of the HLA test results the reservation must be extended with 60 days.

In case of a blood sample request for verification typing, after receiving the blood sample request, the donor must be reserved for 60 days, after dispatching the sample, the reservation must be extended with 60 days.
After receiving the confirmatory typing results and in case the transplant center is interested in the donor, the reservation must be extended with 60 days.

ONLY if a precise date or period of time (not exceeding 3 months from the initial reservation request) has been determined by the transplant physician, the donor must be placed on a “reserved” status in Prometheus from the time of the Verification Typing until the donation date is reached. If this is not the case, the donor can be recruited for any other. Requests for extensions of the period of 3 months must be accompanied with a reasonable argument.

4.4.4 The Donor Center, Collection Center, the Hematopoietic Stem Cell Bank and Transplant Center must agree on the date of collection as well as the volume and cell count of HPC (Marrow or Apheresis) or MNC, A to be collected from the donor as soon as possible after selection of the donor but no later than 2 working days prior to initiation of the preparative regimen for the recipient. This must be done in writing using the *F70 Verification of cell product*. Section A of the form must be completed by the Donor Center.

For characteristics of the collected HPC, M and for characteristics of the collected HPC, A and MNC, A, see § 2.2.5.

4.4.5 Once the harvesting date is scheduled, this date cannot be changed, except for specific and important reasons. The Collection Center provides the MDPB FRM078 Workup Schedule and the FRM079 Courier instructions to be confirmed by the Transplant center.

4.4.6 Pre-harvesting and harvesting costs are invoiced centrally by MDPB-R to the International Registry. All costs, related to the HPC (Marrow or Apheresis) or the MNC, A donation are included in the collection fee that is invoiced by the MDPB-R to the requesting International Registry or Transplant Center, except for pre-collection samples.

4.4.7 Should a cancellation take place before HPC (Marrow or Apheresis) or MNC, A collection, a cancellation fee will be charged to the Transplant Center considering the services performed.

- after medical examination of the adult donor.
- before the medical examination of the adult donor.

4.4.8 Should a transplant be postponed (e.g. the patient's disease progresses or a medical complication occurs), a new collection date shall be established as soon as possible.

If an official request of donor workup or formal recruitment has been received and the transplant is postponed a fee will be charged considering the services already performed:

- after medical examination of the adult donor.
- before the medical examination of the adult donor.

4.4.9 If the donor withdraws or is not found eligible to donate at the stage of a pre-donation check-up, no fee will be charged to the Transplant Center.

4.4.10 The HPC (Marrow or Apheresis) or MNC, A harvesting of a Belgian donor must take place in Belgium, wherever the location of the Transplant Center is.

4.4.11 The HPC (Marrow or Apheresis) or MNC, A collection always takes place in an accredited Collection Center, preferably located in the area where the donor is living.

4.4.12 A disability life insurance is systematically subscribed by MDPB-R for each donor to be harvested via *MDPB FRM023 Donor insurance request*.

4.4.13 It is the policy of the Marrow Donor Program Belgian Registry (MDPB-R) that the donation must remain completely **ANONYMOUS**. The country of the patient may never be disclosed to the donor, the country of the donor may never be disclosed to the patient

Indirect, anonymous communication in the form of letters or cards, between donor and recipient is allowed post-donation and may not contain any reference to the sender’s identity or location. Therefore all communication needs to be in English. Donor and recipient must not be allowed to exchange direct correspondence. All correspondence, if any, will go through the MDPB-R and must be censured by the Donor Center or the transplant physician. Items received should be sent to the other party within 1 month from date of receipt.

When receiving anonymous communication from a donor or recipient it is the responsibility of the Donor Center or Transplant Center to screen the content to ensure donor and patient anonymity is maintained. Unacceptable content within the correspondence or gift must be removed prior to forwarding to the MDPB-R. A Donor Center or Transplant Center can decide not forwarding the message or present (in its whole or partially) if they judge it more appropriate considering the circumstances.

Screening cards, letters and Gifts for Anonymity:

Type	Accepted	Not accepted
Donor, patient names		Not accepted.
Country of donor or patient		Not accepted.
Transplant and donor center information		Not accepted.
Contact details (telephone numbers,…)		Not accepted.
Gender	Accepted.	
Age	Accepted.	
Disease	Mostly accepted.	No genetic diseases
Professions	General professions acceptable.	No specific professions.
Food		Not accepted.
Gift cards, DVD's, CD's		Not accepted.
Photos		No personal photos with people in the picture.

4.4.14 Donor and recipient may not be hospitalized in the same unit of the hospital.

4.4.15 The donor may need sick leave immediately after harvesting of HPC (Marrow or Apheresis) for medical reasons. No financial compensation is offered by MDPB-R or by any other party.

4.4.16 Any patient undergoing an unrelated donor transplant has to sign an informed consent prior to the workup of the donor to inform him/her about the source of stem cells (Belgian or international unrelated donor) and the need for data exchange. The patient must give its prior written consent for the processing of his personal data in this regard.

4.4.17 A donor must be informed when he is requested as a backup donor.
A MAC approval is required and the requesting Registry must provide a stringent justification for the simultaneous workup.

4.4.18 The donor has a right to receive the results of his/her health screening. The donor or his/her physician must receive any abnormal result which may affect his/her health status. The donor center must have a policy how the donor is informed.

4.4.19 After receiving a workup request, the Registry will assure that the requesting Transplant Center is informed of the donor's availability within 5 working days.

4.5 Medical evaluation of the matched prospective donor (Collection Team's responsibility)

4.5.1 A physician, member of the Collection Team, has the primary responsibility for protecting the safety of the donor and for delineating conditions in the donor that may be transmissible by blood or HPC, M.
A licensed physician must perform and evaluate a complete medical history and physical examination to assess fitness for donation, and must evaluate the results of the tests according to current good practices.

NAT testing (HIV, HCV, HBV) is mandatory. The Collection Center will use the *F50 IDM testing to be performed during donor workup* to inform the Transplant Center regarding the infectious disease markers that will be tested and those that may be available upon request.

After 30 days repeat testing must be done.

Allogeneic donors must be tested for ABO and Rh type using 2 independently collected samples.

4.5.1.1 For international donors it is the responsibility of the Hematopoietic Stem Cell Bank to ensure that all mandatory testing has been performed:

- All standard tests must be performed in compliance to the Belgian law, f.i. HBV NAT.
- Donors coming from endemic areas may have to be tested for additional infectious agents (e.g. Malaria, HTLV-1,…).
- Donors from non-EU countries must be tested in a laboratory in conformity with applicable Belgian laws and regulations.

Reference: current JACIE standards.

4.5.2 The physician responsible for donor suitability must not be the treating physician.

4.5.3 This physician must report the results of the medical examination as well as the infectious disease screening results using the form *F80 Notification of donor clearance* to the MDPB-R.
In addition, the physician must report in writing the presence of the following conditions:

- Number of previous pregnancies and/or transfusions.
- Recent vaccinations: HPC (Marrow or Apheresis) or MNC, A harvest must be deferred for 4 weeks after inoculation of attenuated virus vaccines (rubella).
- Whether there are any contraindications to anesthesia or to HPC (Marrow or Apheresis) or MNC, A donation.

4.5.4 Female adult donors of childbearing age must have a pregnancy test performed during the workup stage. The blood pregnancy test must be performed 7 days prior to starting the donor mobilization regimen and, as applicable, within 7 days prior to the initiation of the recipient's preparative regimen. For MNC, A, the blood pregnancy test must be performed 7 days prior to the collection.
Female donors of childbearing potential must have a pregnancy test and be counselled to avoid pregnancy during the workup stage before use of

mobilizing agents, collection or initiation of the recipient's preparative regimen, whichever occurs first.

4.5.5 Final clearance of a donor must not be given until the Collection Team has determined that the donor meets its criteria (WMDA) for stem cell collection and is fully committed to proceeding.

https://share.wmda.info/display/DMSR/WMDA+Donor+Medical+Suitability+Recommendations+Main+page

4.5.6 If more than 8 weeks have elapsed since the complete physical examination, the stem cell collection physician must take an interval history and perform an appropriate physical examination including IDM testing.

4.5.7 Donors with abnormal findings:

- Any abnormal finding in the prospective donor must be reported by the Collection Center to the MDPB-R and the Transplant Center and the Donor Center, while respecting donor and recipient confidentiality.

- Any abnormal findings during workup must be reported to the donor, who is appropriately counseled as to the potential impact of the abnormality(ies). Written documentation of counseling must be maintained at the Donor Center.

- Abnormal donor findings that may increase risk to the donor:

  The Donor Center's Medical Director, the Collection Center's Medical Director, or the examining physician may determine that the abnormal findings constitute unacceptable risk(s) to the donor.

- Abnormal findings that may increase risk to the HPC (Marrow or Apheresis) or MNC, A recipient:

  The Transplant Center must determine whether HPC (Marrow or Apheresis) or MNC, A from a donor with abnormal findings poses unacceptable risks to the recipient.

- Abnormal findings must be reported to the recipient, who is appropriately counseled as to the potential impact of the abnormality(ies). Written documentation of counseling must be maintained at the Transplant Center.

4.6 Pre-collection donor blood samples

4.6.1 The volume of pre-collection donor samples and of blood samples collected for medical evaluation must be limited.

4.6.2 These blood samples may be obtained to:
- Evaluate the need of removing erythrocytes or plasma from the HPC (Marrow or Apheresis) product.
- Store the biological samples necessary for retrospective analysis.

- Repeat infectious disease marker testing when previous testing is outdated (more than 30 days before expected donation date).

4.7 Hematopoietic Stem Cell collection and processing

4.7.1 Choice of HPC, M versus HPC, A as cell source

The Transplant Center may request either HPC, M or HPC, A collection. Both options will be presented to the donor with appropriate information on the advantages and disadvantages of both procedures, as well as on the Transplant Center preference. The final decision will be left to the donor, after proper counseling and a written consent will be proposed. The collection team agree and inform the Transplant Center.
It is required that every Donor/Collection Center has a policy for the administration of growth factors. That policy must cover the risk assessment for the administration of growth factors for a specific donor.

In a donor who already donated HPC, M, and who is foreseen for second donation, HPC, A collection after proper counseling and written consent will be obtained.

4.7.2 HPC, M collection

4.7.2.1 HPC, M must preferably be collected under general anesthesia.

4.7.2.2 Transplant and Collection Centers must agree on the media and additives used for collection and transportation of HPC, M. Anticoagulation should be achieved with ACD (in a ratio of 1 part to 9 parts HPC, M). Heparin (minimum 10 U/mL) is optional. It is optimal to use ACD or HEP depending on the technique you use.

4.7.2.3 Syringes and needles used to aspirate the HPC, M must be rinsed with the same medium.

4.7.2.4 The number of HPC, M nucleated cells collected must be precisely determined before the end of anesthesia to ensure that they meet the quantity agreed upon by the collection and Transplant Centers.

4.7.2.5 This must be accomplished by withdrawing no more than 1500 mL of HPC, M.

4.7.2.6 The collected HPC, M must be transferred to the hematopoietic stem cell bank where it must be filtered if necessary and undergo final conditioning and labeling.

4.7.2.7 The HPC, M collection shall be transferred into a minimum of two sealed plastic bags before transportation. The cells must be divided into approximately equal portions and placed into at least two hermetically sealed plastic bags, each with ports that can be entered aseptically.

4.7.2.8 For storage -Temperature range refer to 4.9.11.

4.7.2.9 The total hospital stay will not be less than 24 hours in a unit inside a Collection Center/hospital that is accredited by MDPB to perform HPC, M harvesting.

4.7.2.10 Appropriate deep venous thrombosis prevention will be given (i.e. adequate amounts of subcutaneous LMW Heparin) to the donor.

4.7.2.11 During or after HPC, M harvesting, no pre deposit should be performed as long as hemoglobin levels and risk factors have been checked normal. Systematic iron supplements can be given if needed from time of physical examination to 3 months post harvesting.
The use of blood (allogenic or autologous) in unrelated donors must be reported as a SEAR.

Indicative schedule for autologous blood collections (NMDP verification of HPC, Marrow request document number F00070):

Total Nucleated cells	< 132 x 10^8	132-263 x 10^8	264-395 x 10^8	>395 x 10¨^8
NMDP recommendation	None	One	Two	Three

4.7.2.12 There must be documented follow-up of donors after donation by a physician. This must be performed as a minimum immediately after donation and a few days later, plus after 1 month, 1 year and 5 years (by the Collection Center) to screen for potential complications. This may be achieved by a visit of the donor to the Collection Center physician or telephone between the donor and the Collection Center physician or through a questionnaire completed by a physician visiting the donor or via email.

4.7.3 <u>HPC, A collection:</u>

4.7.3.1 Mobilization

Donor mobilization must be conducted in compliance with JACIE Standards. WMDA and EBMT standards don't recommend biosimilars for use in unrelated donors, due to insufficient long term safety data.
Indicative schedule for G-SCF stimulation of unrelated donors:

Step	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
GCSF 10 µg/Kg/day (option 1)	X	X	X	X	X	(X)
GCSF 2x5 µg/Kg/day (option 2)	X | X	X | X	X | X	X | X	X | (X)	(X) | (X)
Apheresis					X	(X)

Option 1:
If injected <u>once daily</u>, G-CSF should normally be administered at approximately the same time each day:

- very early in the morning for G-CSF
- late in the evening for glycosylated G-CSF

Option 2:
If injected twice daily, G-CSF should be administered at approximately 12-hour intervals.

4.7.3.2 Leukapheresis

Prior to leukapheresis, the donor will require adequate venous access. Every effort must be made to avoid placing a central venous line. The collection center must have a policy concerning the use of Central Venous Catheter in donors to ensure that a Central Venous Catheter is only used in exceptional circumstances. Those circumstances must be documented.
One or two leukapheresis procedures will be undertaken, for example in the morning of day 5 and optionally day 6 (corresponding to day -1 and day 0 of the recipient) of G-CSF treatment using an automated continuous-flow blood cell separator. Each CC must use a properly validated collection method and the best moment to start the procedure must be based on the optimal CD34 pre-count. Normally, around 10-12 liters of whole blood are processed during each leukapheresis procedure, using ACD-A in a ratio of 1:9 as anticoagulant in the collection bag.
In centers where large volume apheresis are performed >15 liters up to 20 liters may be treated. In that case, heparine may be added to the anticoagulant solution so that lower ACD-A/Blood ratios are possible to avoid causing hypocalcemia. No full heparinization of the donor is allowed.
As soon as the day 5 leukapheresis procedure has been completed, an aliquot must be taken for Total Nucleated Cell count (TNC) and CD34+ assays. If the target number of CD34+ cells agreed upon by the Collection and Transplant Center is not achieved with this leukapheresis, the donor must receive an additional dose of G-CSF on day 5 and undergo a second leukapheresis on day 6. If the target number is not achieved with two leukapheresis, further G-CSF treatment and additional apheresis have to be discussed formally between the Transplant Center, Collection Center and the Donor Center.

4.7.3.3 Storage

The leukapheresis products must be transported to the Hematopoietic Stem Cell Bank and stored in the original collection bag according to the temperature requirements specified in 4.9.11. The product may be diluted for optimal cell survival during storage.

4.7.4 MNC, A collection:

4.7.4.1 Donor lymphocytes from the same donor may be requested by the Transplant Center in case of relapse, EBV lymphoma or graft rejection of a previously grafted patient or within a protocol for pre-emptive DLI. The request must be discussed with the donor and informed consent documented in writing.

4.7.4.2 Donor lymphocytes are collected by apheresis without growth factor stimulation. Repeat collection with growth factor stimulation are considered second donation.

4.7.4.3 Prior to lymphocyte collection, donor workup must be performed as described in previous chapters and written informed consent must be obtained.

4.7.4.4 The Collection and Transplant Centers must agree on the number of nucleated (or CD3+) cells required on *F70 verification of stem cell product* form.

4.7.4.5 Prior to leukapheresis, the donor will require adequate venous access. Every effort must be made to avoid placing a central venous line.
One or 2 leukapheresis procedures will be undertaken, usually on consecutive days, using an automated cell separator and according to best current practices. Indicative parameters are 10-12 liters of whole blood being processed during each leukapheresis, using ACD-A in a ratio of 1:9 as the anticoagulant
As soon as the first leukapheresis is completed, an aliquot must be taken for nucleated cell count and CD3+ assay. If the target number of cells is not achieved a second leukapheresis must be carried out the next day. If the target number is still not reached, further leukapheresis will be at the discretion of the physician at the Collection Center.

4.7.4.6 Storage

Leukapheresis products must be transported to the Hematopoietic Stem Cell Bank and stored in the original collection bag according the temperature requirements specified in 4.9.11 without further manipulation until transportation. The product may be diluted for optimal cell survival during storage.

4.7.5 Cell processing

4.7.5.1 If any processing outside of the prescription is foreseen, a formal agreement between Collection and Transplant Center must be obtained in advance, with clear definition of respective duties and responsibilities. In that case, the Registry must be informed of the ongoing processing.

4.7.5.2 The cells of a donor must always be transfused as soon as possible to the patient.
Cryopreservation of HPC, M or HPC, A is not recommended and should not be done, except for very specific cases and MAC approval is mandatory (not applicable to MNC, A) for Belgian donors.

In case of cryopreservation the Donor Registry must be contacted (as informed consent from the donor is necessary for disposal in case of no infusion).

Planned cryopreservation
A formal agreement between Transplant Center and the Registry must be obtained by MAC approval. The Registry will contact the Donor Center with the motivated decision of the MAC.

Unexpected cryopreservation
This situation must remain exceptional, and necessitates immediate information of MAC/Registry and Donor Registry and expected date of transplantation.

In both cases: final decision lies with the Donor Center.

4.7.5.3 Additional processing, such as the removal of T cells, incompatible red cells, or plasma, must be performed by the Hematopoietic Stem Cell Bank associated with the Transplant Center or in another Hematopoietic Stem Cell Bank designated by the Transplant Center.

4.7.5.4 No processing of cells must be done by the Hematopoietic stem cell bank associated with the Collection Center without specific request by the Transplant Center.

4.7.5.5 The concentration of WBC count in the HPC, A product must be verified. The concentration may not be more than 300.000/µL when it leaves the Collection Center. It may not exceed 200.000/µL before infusion except if infused within 4 to 6 hours; if the concentration is > 200.000/µl the stem cell product must be diluted with a plasma protein solution in the Hematopoietic Stem Cell Bank designated by the Collection Center.

4.7.5.6 The cells collected from a voluntary donor must not be used for research purposes without research protocol approved by an Ethics Committee and the MAC.

4.8 Labeling bags

4.8.1 On completion of collection, the collection bags must bear information in English as described in appendix 1 of JACIE Standards.

4.8.2 If the primary container is capable of bearing only a partial label, it must show at a minimum the proper name of the component, the unique identifier of the component, the MDPB-R unique GRID identifier, the name of the intended recipient. The rest of the information must be securely attached to the primary container using the sticker label posted on a sheet of paper.

4.8.3 The Hematopoietic Stem Cell Bank is responsible for product conditioning and release. This includes a check of ABO and Rh, check of donor IDM, collection report, donor suitability report and quality controls on product (TNC, CD34 numbers), and conformity with the request form of the Transplant Center. All information on labels and on documents and containers must be checked by at least two staff members before the cells leave the HSCB.

4.8.4 In the event the product is not conform with the Transplant Center request, the Transplant Center will be informed and asked to agree with exceptional release.

4.9 Transportation of cells

The TC is responsible for transport (unless otherwise decided), the responsibility of the HSCB ends when product is handed to the courier. The HSCB must identify the courier and make sure he is associated with the Transplant Center.

4.9.1 The collected cells must be infused prior to the expiration date, which is on the label.

4.9.2 The cells must be hand-carried by a single, designated courier. Any change in the transport plan should be communicated and agreed on beforehand between the TC and the courier company.

In case the TC takes care of transport to the TC, the following applies:
The designated courier must be a nurse, medical laboratory technician, doctor or other person of appropriate training and member of the Transplant Center; exceptionally the courier might be a member of the collection team, or a qualified person from a contracting company. This company should have sufficient experience in hand carrying sensitive medical material. The Transplant Center must have a formal written agreement with the contracting company and must have an insurance for the transportation of cells.
The transport must meet the WMDA transport guidelines. (20210609-EQ-P.Courier Guidelines).

4.9.3 Details of the courier identity and itinerary must be sent by the Transplant Center to the Registry at least 72 hours before collection of donor cells, using the *T10 Courier & emergency contact information during stem cell transportation*.

4.9.4 The courier must arrive in the Collection Center country the day prior to the planned harvest if required by the International Registry. Once at the destination (hotel in the Collection Center country), the courier must telephone the contact person at the HSCB to announce safe arrival.
On the day of harvest, the courier must arrive at the HSCB at or before the earliest estimated time at which the cells will be available.

4.9.5 The cells must stay with the courier at all times. In the plane, the cells must remain in the passenger compartment as a carryon luggage.

4.9.6 Airplane or other reservations must be confirmed in due time.

4.9.7 There must be a back-up plan for alternative transport in case of an emergency.

4.9.8 Full details on the nature of the transport, identification of the courier and the flights must be transmitted to the Belgian airport authorities by the MDPB-R 1-2 days prior to the transport (*T40 Courier letter*).

4.9.9 The cells must not be passed through X-ray irradiation devices designed to detect metallic objects.

4.9.10 The container used to transport HPC (Marrow or Apheresis) or MNC, A must meet the following criteria:

- Each bag must be placed in an outer bag, which is also sealed to prevent leakage.
- The bags must be enclosed in a rigid container with insulating properties and adequate to withstand conditions incident to ordinary handling in transportation (leakage of content, shocks, pressure changes).

- Adequate material must be present inside the transport container to maintain the expected temperature range until the cells reach the destination lab/center. Adequate temperature monitoring checking the external display or use of data loggers will be performed during transportation between centers.

4.9.11 Temperature specifications

Temperature range and transport conditions are under the responsibility of the TC.

Indicative transport conditions:

HPC, M

- Product must be transported with a minimum of delay.
- During transport the temperature must be between 2-24°C for periods not exceeding 12 hours.
- If transported for a period exceeding 12 hours the HPC, M must be brought below 10°C, within 4 hours and then subsequently transported and stored between 2-10°C.
- Once below 10°C the HPC, M must be maintained between 2-10°C for the remainder of the journey.

HPC, A - MNC, A.

- Product must be transported with a minimum of delay.
- During transport the temperature must be between 2-24°C for periods not exceeding 12 hours.
- If transported for a period exceeding 12 hours the HPC, A must be brought below 10°C, within 4 hours and then subsequently transported and stored between 2-10°C.
- Once below 10°C the HPC, A must be maintained between 2-10°C for the remainder of the journey.

4.9.12 Documents accompanying the cells must include

- Accompanying documents as applicable to the requirements of the destination Transplant Center.
- “Label for HPC (Marrow or Apheresis) or MNC, A” form which accompanies the bag(s) if the bag itself does not bear all required information on the sticker label.
- The T30 *Transport of stem cell product audit* form which is given to the courier by the Collection Center (to be completed and signed by the Collection Center and the courier at product pickup and to be completed and signed by the Transplant Center and courier on arrival at Transplant Center). The form has to be sent back to the MDPB-R.
- The Transplant center must have a procedure how records of transport are stored and how copies of a transport from a past delivery can be obtained.

4.9.13 Import/export of **products**: HPC (Marrow or Apheresis) or MNC, A

The import/export of cells is under the responsibility of the responsible physician of the HSCB. The HSCB must ensure that imported products meet the same standards of quality, safety and ethical standards as applicable in

Belgium. This implies that the donor criteria, donor testing and microbial testing must be conform Belgian Law. In addition, the importing bank is responsible for traceability up to 3 years after transplantation.

4.9.14 Import/export of **patient specimen shipments**: any human biological sample including blood, DNA, serum must be performed in compliance with IATA packing instructions 650.

4.10 Quality control of cell collections

4.10.1 The number of nucleated cells in the collected HPC (Marrow or Apheresis) or MNC, A and in the peripheral blood of the donor must be counted in each bag. The number of HPC, M nucleated cells, corrected for peripheral blood nucleated cells, should aim to be higher than 2 x 10^8/kg of recipient body weight and approach the dose requested by the Transplant Center.

4.10.2 The number of CD34+ cells in the collected HPC, A must be counted in each bag. The total number should aim to be higher than 4x10^6/kg of recipient body weight.

4.10.3 The number of CD3+ cells in the collected MNC, A must be counted in each bag. This number must approach the dose requested by the Transplant Center.

4.10.4 Transplant Centers may require higher numbers, depending on the recipient's diagnosis and treatment and on any intended further processing of the cells. The request must be acknowledged by the Collection Center.

4.10.5 Bacterial (aerobic and anaerobic), yeast and fungal cultures must be performed at the Collection Center or HSCB, with timely reports to the Donor Registry.

According to Belgian law: microbial culture must be done (also on international collections). If result is not available the center receiving the cells must do the final control. It is the importing bank's responsibility to verify the microbiological cultures.

4.10.6 A sample from each bag must be placed into culture for bacteria (aerobic and anaerobic), yeasts and fungi at the HSCB.

4.10.7 The Collection Center/HSCB must retain an appropriate record of the collection procedure and transmit a copy to the MDPB-R using the *MDPB FRM019 Collection report BM (HPC, Marrow)* or the *MDPB FRM020 Collection report PBSC (HPC, Apheresis)* or *MDPB FRM021 Collection report lympho (MNC, Apheresis)* signed by the collecting physician.

This includes:

- Type, lot number and expiration date of any reagent or collection bag used.
- Volume of HPC (Marrow or Apheresis) or MNC, A as well as the volume of additive used.
- Any incident occurring during or after the collection.

- Nucleated cell count; the CD34+ cell count for HPC (Marrow or Apheresis), the CD3+ cell count for MNC, A.
- Results of bacterial and fungal cultures as soon as available.

4.10.8 It is the responsibility of the HSCB to know the final destinations of the delivered stem cell product using the MDPB FRM080 Transplant report.

4.11 Subsequent donation for a same patient from the same donor

4.11.1 Any request for a subsequent donation has to be made by submission of a specific form (*F20 Previous transplant history*) to the MDPB-R who will forward the request to the Donor Center for discussion with the donor.

4.11.2 Each request for subsequent donation of HPC (Marrow or Apheresis) (see 3.3) has to be submitted to the Medical Advisory Committee. The donor must not be approached before the Committee has given its approval. The Committee must give its decision within 5 working days (48 hours if urgent) of being asked. The request must be approved by the donor, the Donor Center and the MAC. This MAC approval is only applicable for Belgian donors (not for international donors).

4.11.3 The Donor Center must give the donor a general explanation of the reason for and expected results of second donation, the procedure involved and associated risks. The donor must be given ample time to make his/her free decision. There must be no pressure on the donor at any time.

4.11.4 A second donation may involve HPC (Marrow or Apheresis) or MNC, A. It is generally not recommended to perform a second HPC, M collection before 6 months after initial collection. (See chapter 3.3.2)

4.11.5 Donor workup for a second donation must be handled similarly to a first donation (see 4.5 through 4.12). Every effort must be made to speed up the process whenever the patient's medical condition requires it.

4.12 Donor (Collection Center) and patient follow-up (Transplant Center) – reporting of incidents

Risk management of the MDPB is based upon the follow up and reporting of incidents to mitigate against risks, and processes. The quality assurance program (Chapter 4.13) will revise and secure MDPB accreditation.

4.12.1 After transplantation of a patient with cells from an unrelated donor provided through the MDPB-R, the Transplant Center must report post-transplant clinical outcome by completing the EBMT data collection forms.

The Transplant Center will submit outcome data to EBMT. The Belgian Cancer Registry will prepare outcome analysis for the MDPB Quality Assurance based on the EBMT reporting (donors and cord bloods). The MDPB Registry will yearly share the list of transplanted patients with the Belgian Cancer Registry to check on completeness of EBMT reporting.

Missing reporting will be reminded to the Belgian Transplant Centers by the MDPB Registry, and will be reported to the Quality Assurance Committee.

4.12.2 The Collection Center is responsible for ensuring adequate follow-up of the donor up to at least 1 year after collection of any type of cells. Follow-up visits must be done within 1 week of collection, around 30 days (*MDPB FRM025 Donor follow-up report 30 days),* 1 year and 5 years after collection (*MDPB FRM026 donor follow-up report 1-5 years*). It is recommended that such visits be performed at the collection facility itself. The follow up in the hospital is done by the physician or nurses under supervision of the physician. If this is not feasible, follow-up information can be obtained through home physicians, direct telephone interviews or via email. However in case of HPC, M donation, a physician of the collection team (or nurse under supervision of the physician) must do the first follow-up visit within 1 week after collection.
It is also recommended that follow-up includes complete blood counts within 1 week as well as at 30 days, 1 year, 5 years after collection.
Follow-up information must be sent to the MDPB-R by completing the Donor follow-up report forms emailed to the MDPB-R around 30 days and 1 year after collection.
The collection center must have a mechanism for the donor to contact the collection center to report related medical concerns for a minimum of 10 years after donation: during the 30 days follow up the collection center will inform and request the donor to contact the collection center about any conditions that occur which they feel might relate to donation, this until 10-year after the collection took place.

4.12.3 All donors who have commenced the donation procedure (at least a single dose of growth factor administered) must be followed.

4.12.4 <u>Reporting Serious Adverse Events and Reactions to the WMDA:</u>

Serious Adverse Events (SAE) and Serious Adverse Reaction (SAR) must be identified, documented, and investigated and remedial and/or corrective action must be taken and submitted to the WMDA S(P)EAR Committee. The WMDA collects and analyzes information on recipient and donor serious adverse events and reactions which affect donors and/or products from all WMDA stem cell donor registries and cord blood banks.

This reporting applies to MDPB-R and affiliated centers.

All MDPB collaborative centers must have established processes and procedures to promptly identify, investigate, report and prevent quality incidents and adverse events.

The center must report the incident in the WMDA online reporting system in accordance with the requirements outlined in the WMDA Standards, reporting Serious Events and Reactions to the WMDA (participating is compulsory for WMDA qualified and accredited registries). The procedure and an electronic link for reporting S(P)EAR are available on the WMDA website.

The Registry has a designated individual responsible for S(P)EAR reporting, who will approve reports from the affiliated centers and submit to WMDA in the online reporting system.

The Registry follows up the reporting of adverse events in a national reporting database and assures that causes of adverse events are investigated and that steps to prevent another from occurring are taken.

Information pertaining to adverse events, must be communicated through the MDPB-R to the donor's or patient's Registry or center:

- In case of an adverse event or reaction involving a patient or product, the donor's registry must be notified if the information might impact or signify the donor health issue.
- The patient's registry must be notified if the adverse event may have an impact to the patient's health.

4.12.5 Incident reporting, quality deviations

Incidents not to be reported in the WMDA online tool and any other quality issues, have to reported by the *MDPB FRM013 Quality incident report* and will be logged in the MDPB-R QMS reporting database by the Registry staff.

Each incident or quality deviation must be investigated and closed with corrective actions taken if applicable.

4.12.6 The center must comply with governmental regulations including requirements to report such adverse events to the regulatory agency FAGG/AFMPS (provide the incident number to the Registry).

4.12.7 Missing status report

If any report of the above chapters has not been provided after 3 reminders by the staff of the MDPB-R, the file will be closed. In case the information cannot be provided, the form *MDPB FRM037 Notification of missing status report* must be completed.

The form will be evaluated by the Quality Assurance Committee.

4.13 Quality Assurance Program

4.13.1 The MDPB must have a regularly updated Quality Assurance Program.

4.13.2 This program must include formal accreditation of Donor, Collection, Transplant Centers and Hematopoietic Stem Cell Banks by the BHS-MDP-B Committee and Governing Board of the MDPB-R on a regular basis.

- The criteria for accreditation of Donor, Collection, Transplant Centers and Hematopoïetic Stem Cell Banks are listed in the MDPB Standards.
- The accreditation must be granted for a minimum of 1 year and a maximum of 3 years. Towards the end of the previous accreditation period, the BHS-MDP-B Committee and Governing Board of the MDPB-R must decide the duration of the next accreditation period.
- The MDPB-R must review the status of each Donor, Collection and Transplant Center and Hematopoietic Stem Cell Bank before expiration of the current period of accreditation. This review must include compliance with the MDPB Standards and verification of all accreditation criteria as listed in the MDPB standards. If necessary, the BHS-MDP-B

Committee and Governing Board of the MDPB-R may decide to perform on-site visits.

- The MDPB-R then prepares a list of centers proposed for accreditation approved by the BHS-MDP-B Committee and the Governing Board of the MDPB-R takes the final decision on that list of accredited centers.

4.13.3 The Quality Assurance Program must include a formal annual review of recipient outcome analysis (via the Belgian Cancer Registry), donor follow-up report forms, and HPC (Marrow or Apheresis) or MNC, A collection report forms. This review must be performed by the Quality Assurance Committee (QAC) of the BHS-MDP-B Committee. The annual report of the QAC must be approved by the BHS- MDP-B Committee.

4.13.4 In case a center does not comply with the Standards, the Governing Board of the MDPB will take all necessary steps to ensure further compliance with the MDPB standards. This may include temporary suspension of the MDPB accreditation approved by the BHS-MDP-B Committee, the Governing Board of the MDPB-R takes final decision.

4.13.5 If the Center does not take appropriate corrective action to ensure compliance with the Standards, the Governing Board of the MDPB-R and the BHS-MDP-B Committee may decide to remove the accreditation of that Donor, Collection or Transplant Center or Hematopoïetic Stem Cell Banks by the MDPB.

4.13.6 It is the responsibility of the MDPB-R to review annually the Center's compliance with the Standards. The certificates of accreditation by MDPB-R (Donor Center, Collection Center, Transplant Center, Hematopoietic Stem Cell Bank) include all MDPB standards criteria and the Quality Assurance Review to comply to for annual accreditation.

5 TASKS/RESPONSABILITIES OF EACH CENTER, THE MDPB-R AND THE BHS-MDP-B COMMITTEE

5.1 MDPB-R

5.1.1 Criteria:

The MDPB-R is responsible for the operational management of the MDPB.

The Governing Board is responsible for the management of the MDPB Standards assigned to the MDPB-R, is responsible for the budgets and financial annual reports for approval by the national council of the Belgian Red Cross and is responsible for the official representation of the MDPB-R.

The Management Committee is responsible for the daily operation of the MDPB-R.

The MDPB-R takes all necessary steps to ensure compliance of participating Centers with the MDPB Standards. This may include temporary suspension or removal of accreditation approved by the BHS-MDP-B Committee and must be confirmed by the Governing Board of the MDPB-R.

Upon proposal of the MDP-B Committee, the Governing Board decides on the list of Centers that will be accepted as Donor, Collection and Transplant Center.

The MDPB-R complies to the following WMDA requirements:

- The MDPB-R must be a legal entity that guarantees administrative and financial operation with a fixed physical location to ensure that all work can be carried out in an environment designed to minimize errors, reduce risks to health and safety, and maintain confidentiality.

- The Director or key Registry personnel must have the necessary skill in this field of activity documented by education and experience. At least one of this individuals must be a physician.

- The MDPB-R must maintain records of its activities and maintain a database of donor information. All patient and donor records must be stored to ensure confidentiality according to WMDA Standards: donor and patient identity must remain confidential during the search process. The access to donor and patient data information as well as the transmission must be organized so that unauthorized access is prevented – confidentiality is guaranteed.

- MDPB-R must have a quality management system that comprises Standard Operating Procedures (SOPs), staff training and education and guarantees compliance with the Standards.

- Changes to the status of the Registry that may affect WMDA accreditation must be brought to the attention of the WMDA in a timely fashion. The Registry coordinator must inform the WMDA Office about significant changes to the general organization by electronic mail.

- MDPB-R must be a WMDA organizational member. The Registry must participate in the WMDA Global Trends report.

- The operational and regulatory information must be available on the WMDA share. These requirements must be reviewed by the Registry at least annually and must be updated as significant changes occur.

- The Registry must have established standards for Transplant Centers that must be readily accessible to health care professionals involved in hematopoietic stem cell transplantation.

- The Registry must have a policy to be aware of new WMDA recommendations and to crosscheck them with the Registry policy and procedures. The Registry does not have to comply with the recommendations and adopt them, but it needs to consider the recommendations and adopt them, if appropriate. Medical and scientific procedures will be cross-checked by the BHS-MDP-B Committee, operational procedures by the MDPB-R staff and will be adopted in the MDPB Standards.

- The Registry must have a program of Collection Center/Cord Blood Bank audits to demonstrate compliance with WMDA standards. The registry must have a policy or procedure that describes the audits and provide blank audit forms.

- The Registry must update the contact list of all collaborative centers *MDPB LST005 Belgian contact list*.
  All MDPB and WMDA forms must be signed (digital signature is valid). Who signs the form is the responsibility of the center.
  The centers must inform the Registry about staff changes and all other significant changes and changes to the status of the center that may affect the applicable accreditations by electronic email to the Registry coordinator.

5.1.2 Tasks:

Administrative and financial management of the Belgian donor program.

5.1.2.1 Management of the HPC (Marrow or Apheresis) donor database. The Governing Board of the MDPB-R defines which equipment to be used in line with the international procedures. The coordinators act as the Belgian representatives at international meetings of the registries.

5.1.2.2 Searches for patients from Belgium and abroad: consultation of the database of the MDPB-R (incl. Belgian Cord Blood Bank) and all registries connected through EMDIS.

5.1.2.3 Transmission of requests from Transplant Centers abroad or other registries to Belgian Donor Centers for either:
- DR typing of a Belgian donor;
- DNA typing of a Belgian donor;
- Blood sample shipment for Verification Typing.

5.1.2.4 Transmission of requests from Belgian Transplant Centers to registries abroad for either:

- DR typing of a foreign donor;
- DNA typing of a foreign donor;
- Blood sample shipment for Verification Typing.

5.1.2.5 Once a donor has been selected by the Transplant Center, the Registry is coordinating the workup of that donor:

- Transmission of documents required for reservation of the donor, infectious disease marker testing, and medical exam of donor.
- Transmission of documents detailing the transport of HPC, A or HPC,M or MNC, A by courier.
- Transmission of the HPC, A or HPC,M or MNC, A prescription form.
- Notification of the insurance company.
- Notification of customs at the airport.
- EU donors: identity and license of the sending Hematopoietic Stem Cell Bank/agreement that they collect, release products according to EU legislation.
- Non-EU donors: request copy of informed consent, anamnesis, clinical findings, IDM, collection report, donor identity.

5.1.2.6 After delivery of the cells to the Hematopoietic Stem Cell Bank, the Registry will check if the Transplant Center completed the HPC, A or HPC,M or MNC, A delivery report and forward the document to the Collection Center.

5.1.2.7 Invoices for international patients are made by the Registry and sent to the requesting Registry for

- Typing requests;
- HPC, M or HPC, A or MNC, A collections;
- Workup Cancellations or postponements of Belgian donors.

Prices are defined by the Board of the Registry. Changes in the fee schedule (MDPB047 Fee schedule donor) must be provided to the interested parties 30 days prior to implementation. Billing should occur within 60 calendar days of service completion.
Payments are made to the Registry. The Registry will then distribute a fee as agreed between the different parties involved after receiving an invoice from the Collection Centers; Donor Centers, HLA labs and Cord Blood Banks.
(The Registry will send order forms to the involved centers for all services described above). The Registry is not responsible if invoices are not paid.

Any cost not standardized, or, for any reason, not accessible through such a schedule must be estimated and communicated in advance to the requesting Registry and/or Transplant Center.

5.1.2.8 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 30 calendar days of the cancellation date.

Invoicing of cancellations and postponements is done based on the services performed (before or after medical examination). The transplant

center will be charged for the portions of the workup that have been completed at the time of cancellation.

5.1.2.9 Invoices from registries/centers abroad are re-invoiced to the Transplant Centers that initiated the request. The Transplant center validates the received invoices. Payment to the MDPB-R must be made in the foreign currency for the full amount invoice, free of bank charges within 30 days. The Registry regularly sends statements of account and requests to pay outstanding invoices. The Registry settles the international invoices in 60 days.

5.1.2.10 The Registry is responsible for the financial management of the donor recruitment, cfr agreement RIZIV/INAMI, current version. The Registry sends periodically global invoices for the new donor registrations to the RIZIV/INAMI. The Registry will send periodically order forms to the labs for the typing of the new donor registrations.

5.1.2.11 The Registry settles national and international invoices in 60 days.

5.1.2.12 Statistics: the Registry collects monthly updates on the activities of the Registry.

5.1.2.13 Primary contact with the insurance company concerning the policy/contract for the Belgian donors and requests for reimbursement in case of complications post donation.

5.1.2.14 Maintain an updated list of participating Hematopoietic Stem Cell Banks/Transplant/Donor/Collection/HLA Typing Centers.

Posting of standards, forms, user documentation and other relevant information on the MDPB website https://www.stemcelldonor.be.

5.1.2.15 Day to day contact with the Belgian and foreign centers in accordance to the national SOPs, the MDPB Standards and the international guidelines. Consults with the BHS-MDP-B Committee for any medical/scientific question for which no procedures have been defined during previous board meetings to obtain a consensus.

5.1.2.16 The MDPB-R is not responsible for the medical management of donors at Donor or Collection Centers, or of patients at Transplant Centers. It is not responsible for problems of quality with the collection, transport and transplantation of cell products.

5.2 Donor Centers

Day to day management of the donors enrolled in the individual center according to the national SOPs.

5.2.1 Each Donor Center is connected with MDPB-R, which is in charge of centralizing data and searching for patients.

5.2.2 Each Donor Center is responsible for updating information on its donors and for transmitting consequently all available information to MDPB-R.

5.2.3 The Donor Center is responsible for adequate typing of their donors in an accredited HLA Typing Center.

5.2.4 The Donor Center is responsible for the management of their donors including:

- Counseling.
- Obtaining informed consent.
- Correct registration and initial typing.
- Contact for further DR typing and subsequent typing.
- Contact for DNA typing and subsequent typing.
- Contact for Verification Typing sample drawing.
- Checking donor's availability (delete donor from Registry database if unavailable).
- Collaborating with the Collection Center.
- Ensuring the donor receives no invoices post-donation.

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

5.2.6 Invoices for shipment of blood samples and IDM testing are sent to the MDPB-R within 40 days of service completion.

5.3 Collection Centers

Collection of HPC (Marrow or Apheresis) or MNC, A in accordance with the national SOPs.

5.3.1 The Collection Center is fully responsible for

- Ensuring the donor is a fit candidate for donating either HPC (Marrow or Apheresis) or MNC, A.
- Arranging infectious disease marker testing (repeat if > 30 days since last screening).
- Arranging medical exam prior to HPC (Marrow or Apheresis) or MNC, A collection.
- Ensuring that an adequate number of autologous blood unit has been stored prior to bone marrow collection if indicated.
- Ensuring that the required forms for HPC (Marrow or Apheresis) or MNC, A collection are completed and forwarded to the Registry.
- Agreeing with the Transplant Center on how to collect the cells (HPC (Marrow or Apheresis) or MNC, A, number of cells, anticoagulant, medium, etc).
- Providing the MDPB FRM078 Workup Schedule and the FRM079 Courier instructions to the Transplant center.
- Informing the Registry for arranging insurance coverage.
- Completing the cell delivery forms.
- Ensuring that the donor's health is appropriate for discharge.
- Providing a sick leave attest to the donor at discharge.
- Ensuring that the donor receives no invoices post-donation.
- Medical follow-up of the donor after donation.
- Informing the Registry if complications occur after donation.

- Transfer of the donation, the donor file (copy of informed consent, collection report, IDM, anamnesis, clinical findings) and the collection report forms to the associated local Hematopoietic Stem Cell Bank.

5.3.2 The Collection Center is requested to invoice the Registry for the HPC (Marrow or Apheresis) or MNC, A collection.

5.3.3 The Collection Center is fully responsible for ensuring the medical well-being of the donor before, during and after the collection for all aspects related to the cell donation.

5.3.4 The Collection Center is fully responsible for ensuring the quality of the cell collections in accordance with the SOP. This includes providing their HPC (Marrow or Apheresis) or MNC, A collection reports and the donor follow-up report forms in a timely fashion.

5.3.5 The Collection Center is responsible for the administrative follow-up of the donor post-donation.

5.4 Transplant Centers

5.4.1 The Transplant Center is fully responsible for the search/selection of a donor for their patients, including Verification Typing of the prospective donor at the Transplant Center. The Registry only forwards the requests and incoming results.

5.4.2 Once a donor has been selected the Transplant Center is fully responsible for completing all the necessary forms such as donor reservation (request for further workup of the donor), HPC (Marrow or Apheresis) or MNC, A prescription form, details on the courier, etc.

5.5 Hematopoietic Stem Cell Banks

5.5.1 Hematopoietic Stem Cell Banks must be licensed by FAGG/AFMPS for banking of hematopoietic stem cells and donor lymphocytes for infusion for the full time period covering their activities.

Rationale: A Collection Center must transfer the collected product to a Hematopoietic Stem Cell Bank. Although, legally, a Collection Center can provide the HPC (Marrow or Apheresis) or MNC, A directly to any Hematopoietic Stem Cell Bank within the EU such as the Hematopoietic Stem Cell Bank associated with the Transplant Center, the BHS-MDP-B advises, for conformity, that all collections are delivered first to the local Hematopoietic Stem Cell Bank. The local Hematopoietic Stem Cell Bank is therefore responsible for the quality of the donation, donor suitability, the labeling, traceability, confidentiality, etc.

Similarly, legally, a Transplant Center can order and receive HPC (Marrow or Apheresis) or MNC, A from any Hematopoietic Stem Cell Bank within the EU, however, the BHS-MDP-B advises, for conformity, that all collections are first “cleared” by the local (destination) Hematopoietic Stem Cell Bank and from there, are transferred to the Transplant Center.

For import and export of cells from non-EU countries, this workflow is legally required.

The responsibility of the local Hematopoietic Stem Cell Bank for outgoing collections is to ensure the quality and infectious safety of the product, and to make the necessary arrangements with the foreign partner (Transplant Center or Hematopoietic Stem Cell Bank) to ensure full traceability, full conformity with informed consent, etc.

The responsibility of the local Hematopoietic Stem Cell Bank for incoming collections is to ensure the conformity of the product with Belgian legislation and to make the necessary arrangements with the foreign partner (Collection Center or Hematopoietic Stem Cell Bank) to ensure full traceability, etc.

These workflows have the advantage that quarantined HPC (Marrow or Apheresis) or MNC, A that are not (yet) released for administration cannot reach the transplant unit and be administered inadvertently.

5.5.2 <u>For collections performed by associated local Collection Centers (outgoing products)</u>

The Hematopoietic Stem Cell Bank must receive the HPC (Marrow or Apheresis) or MNC, A from the Collection Center.

The Hematopoietic Stem Cell Bank must receive and archive for minimum 30 years (maximum 50 years) : donor identity, anamnesis, clinical findings, IDM, informed consent, donor suitability (HLA matching, CMV status, gender).

The Hematopoietic Stem Cell Bank must ensure traceability from donor to recipient and critical materials including documents related to transportation (minimum 30 years – maximum 50 years).

The Hematopoietic Stem Cell Bank must ensure donor confidentiality.

The Hematopoietic Stem Cell Bank must label the HPC (Marrow or Apheresis) or MNC, A with an ISBT conform label (required by JACIE).

The Hematopoietic Stem Cell Bank must make the necessary arrangements with the Transplant Center/Hematopoietic Stem Cell Bank to ensure that the manipulation and use of the HPC (Marrow or Apheresis) or MNC, A is in agreement with the signed informed consent.

The Hematopoietic Stem Cell Bank must ensure the quality of the HPC (Marrow or Apheresis) or MNC, A and the proper storage, if applicable (section 4.10).

The Hematopoietic Stem Cell Bank must release the cells for administration (donor identity, donor selection criteria, IDM, informed consent, collection report). In addition, the Hematopoietic Stem Cell Bank must make sure that the requested quantities (TNC, CD34, volume), transportation conditions, requested blood and requested documents are transferred. In case the requested quantities are not reached, the Hematopoietic Stem Cell Bank must makes sure, via MDPB-R, that the Transplant Center is informed.

The Hematopoietic Stem Cell Bank must ensure microbial testing of collected product and send results to receiving Transplant Center, via MDPB-R in due time.

The Hematopoietic Stem Cell Bank must store retention samples for repeat IDM.

When applicable the Hematopoietic Stem Cell Bank must release and document using the exceptional release procedure (considering donor and patient conditions).

After release, the Hematopoietic Stem Cell Bank must transfer the cells to the courier contracted by the receiving Transplant Center/Hematopoietic Stem Cell Bank (transport is responsibility of receiving Hematopoietic Stem Cell Bank).

5.5.3 <u>For collections performed by non-EU, EU or Belgian Collection Centers associated with another Hematopoietic Stem Cell Bank (incoming products)</u>

The Hematopoietic Stem Cell Bank must make the necessary arrangements with the Collection Center/Hematopoietic Stem Cell Bank to ensure that the HPC (Marrow or Apheresis) or MNC, A and donor selection criteria are conform Belgian legislation (non-EU, EU).

<u>Import of cellular therapy products (HPC, Apheresis, HPC, Marrow, HPC, Cord Blood, MNC, Apheresis), collections performed by non-EU Centers:</u>

The import of HBM from a specific donor is the decision of the transplant physician, and function of complex criteria to determine the transplant that fits the recipient the best. It depends on the indication and emergency level. The importing cell bank shall comply with requirements of applicable standards and legislations.

In the conditions of working of cell banks affiliated to MDPB, import conditions correspond to the legal definition of exceptional import.

- Recipient known by importing establishment and by the provider in a third party country.
- Import normally happens only once for each recipient. If more than one import has to take place, they would be part of distinct and complete processes with respect to donor selection, evaluation as well as for HBM import.
- Import of HBM necessitates the checking of the WMDA accreditation status of the donor's registry of origin, and/or FACT-NetCord or AABB accreditation status of the Cord Blood Bank. WMDA, AABB and FACT-NetCord standards foresee that requirements of the Royal Decree on HBM imports are fulfilled in the following areas:
  - Selection/evaluation of donor
  - Infectious safety
  - Traceability

Consequently, the imported HBM from a WMDA accredited or qualified for accreditation registry (on time of donor formal reservation), or from a FACT or AABB accredited cord blood bank (on time of CB formal reservation) may be seen as being of equivalent quality level compared to the requirements of applicable legislation.

- The necessary checks shall be documented by the importing cell bank
- If the origin of the imported HBM does not allow to guarantee conditions foreseen by applicable law, the bank director takes necessary measures to bring the imported HBM to conformity and/or to apply exceptional distribution measures.

References:

- Royal decree (RD) on Human Bodily Material (HBM) imports of 31/07/2017: http://www.ejustice.just.fgov.be/eli/arrete/2017/07/31/2017031030/moniteur
- List of Unrelated Donor registries and accreditation by the World Marrow Donor Association (WMDA), with detailed characteristics of donor registries and cord blood banks: https://share.wmda.info/x/4gdcAQ
- WMDA Standards: https://share.wmda.info/x/0wB7Cw
- List of cord blood banks with FACT-NetCord accreditation: http://accredited.factwebsite.org/?_sft_category=cord-blood
- List of cord blood banks with accreditation of the American Association of Blood banks (AABB):

  http://www.aabb.org/sa/facilities/celltherapy/Pages/CordBloodAccrFac.aspx
- List of JACIE accredited centres: https://www.ebmt.org/jacie-accredited-centres

The Hematopoietic Stem Cell Bank must ensure timely transportation and define and ensure transport conditions as defined in section 4.9 (transport is responsibility of receiving Hematopoietic Stem Cell Bank).

Make the necessary arrangements with the Collection Center/Hematopoietic Stem Cell Bank to ensure traceability of donor-recipient and critical materials for minimum 30 – maximum 50 years after transplantation.

Check that the IDMs were performed by a lab certified by an EU authority. In the event that the IDMs were performed in a non-EU certified lab, the receiving Hematopoietic Stem Cell Bank must repeat the IDMs before transplantation.

The Hematopoietic Stem Cell Bank must receive the product.

The Hematopoietic Stem Cell Bank must produce and store retention samples for IDMs.

The Hematopoietic Stem Cell Bank must perform all requested processing and storage.

The Hematopoietic Stem Cell Bank must ensure microbial testing is performed on starting and final product.

The Hematopoietic Stem Cell Bank must release the product for infusion:

- Identity of the donor is usually not provided, make sure you know the establishment that has the identity of the donor.
- Informed consent: idem.
- Donor selection criteria: see above.
- IDMs: see above.

The Hematopoietic Stem Cell Bank must, if applicable, release by Exceptional release (considering donor and patient conditions).

The Hematopoietic Stem Cell Bank must transfer the cells to Transplant Center.

5.5.4 The Hematopoietic Stem Cell Bank must report serious adverse events to the FAGG/AFMPS.

5.5.5 The Hematopoietic Stem Cell Bank must inform the donor in the event analyses were performed on the donor material which contain relevant information for the health condition of the donor.

5.6 BHS-MDP-B Committee - Scientific Committee

5.6.1 The BHS-MDP-B Committee is responsible for general medical/scientific supervision of the MDPB Standards.

5.6.2 The BHS-MDP-B Committee provides medical/scientific support to its members.

5.6.3 The BHS-MDP-B Committee is responsible for the medical revision of the MDPB Standards: design, regular reviews and amendments (distribution by the Registry). The board may incorporate urgent amendments into the MDPB Standards but all changes must be approved by the Governing Board.

5.6.4 The BHS-MDP-B Committee supports information campaigns in relation to stem cell transplantation in general and unrelated donor actions and provides the scientific content of the brochures/leaflets. Registry staff oversees recruitment initiatives. (Central inventory of all actions is needed for WMDA.)

5.6.5 The BHS-MDP-B Committee elects the chair and co-chairs of the BHS-MDP-B- Committee every 3 years.

5.6.6 The BHS-MDP-B Committee designates the members (6 members and 6 substitutes) of the Medical Advisory Committee (MAC) for a term of 3 years. The MAC is a sub Committee from the QAC. The MAC must be consulted for any medical question/procedure not covered by the standards and must be referred to for any ethical question.
This Committee will take the final decision and motivate the answer.

5.6.7 The BHS-MDP-B Committee designates the members (5 members) of the Quality Assurance Committee (QAC) for a term of 3 years. The QAC is responsible for the annual review of all patient follow-up report forms, donor

follow-up report forms, HPC (Marrow or Apheresis) or MNC, A collection report forms. The annual report of the QAC must be reviewed and approved by the BHS-MDP-B Committee. The Chair of the BHS-MDP-B is the president of the QAC, the Co-Chair is the secretary of the QAC. The president is member of the MDPB-R medical quality meetings.

5.6.8 Upon proposal by the BHS Committee, the Governing Board decides on the list of centers that will be accepted as Donor - Collection - Transplant Center – Hematopoietic Stem Cell Bank and Cord Blood Bank.
All affiliated centers must assign representative(s) and deputy(ies). One representative may represent TC, CC, DC, HSCB, CBB together.
Each representative and deputy must be a member of the BHS-MDP-B Committee.

5.6.9 The Governing Board of the MDPB-R takes all necessary steps to ensure compliance of participating centers with the MDPB standards. This may include temporary suspension of accreditation or removal of the accreditation of that center approved by the BHS-MDP-B Committee and confirmed by the Governing Board of the MDPB-R.

5.6.10 The BHS-MDP-B Committee is not responsible for the medical management of donors at Donor or Collection Centers, or of patients at Transplant Centers. It is not responsible for problems of quality with the collection, transport and transplantation of cell products.

5.7 Service level agreement between MDPB-R and its cooperative centers

A service level agreement will be signed between the MDPB-R and its collaborative centers to delineate their respective medical, operational, GDPR and financial responsibilities.
This agreement will be signed by 2 representatives of the Governing Board of the MDPB-R on one hand and by the Medical director and the Financial director of the hospital or other institution as appropriate on the other hand.

6 INFORMATION TECHNOLOGY AND INFORMATION MANAGEMENT

6.1 General information management

Appropriately interpreted, the regulations in this section apply likewise to electronic, paper based or otherwise manual processes.

6.1.1 The Registry must maintain records of its activities and must maintain a database of donor and/or cord blood unit information.

6.1.2 All patient and donor/cord blood communications and records must be stored to ensure confidentiality and to allow for traceability of the donors/cord blood units from recruitment through the donation process long term.

6.1.2.1 The Registry must assign a unique and anonymous identifier to each donor record. The organization listing adult donors must use GRID to issue donor identifiers at the time that WMDA makes GRID mandatory. This identifier must be used to track the donor with their associated data and biological material and their participation in the donation process long term.

6.1.2.2 The Registry's documentation must describe the rules for handling information pertaining to patients, donors and search processes.

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

6.1.2.4 The access to personal donor and patient data information in the Registry as well as the transmission of these data between organisations must be coordinated in a way that accidental or unauthorized access, destruction or modification is prevented and confidentiality is guaranteed.

6.1.2.5 Records must be maintained for an appropriate period of time, at least as dictated by national laws or standards. Key documents related to donor traceability must be maintained at a minimum for thirty (30) years and a maximum of fifty (50) years following donation. Data storage may be on paper or in electronic form.

The retention period is a minimum of 30 years and a maximum of 50 years (Article 6.&3 of the Royal Decree of 28 September 2009).

The Registry will use a term of 50 years (donors can register at the age of 18 and stay in the database until the age of 60). When the voluntary stem cell donor reaches the age of 60, he or she will be automatically deleted from the MDPB database.

6.1.2.6 A donor wishes to be removed from the Registry database:

- When the donor explicitly requests deletion of his personal data, the donor data will be deleted in case the donor was never requested for a patient (i.e. Verification typing, Confirmatory typing, Workup, IDM, etc…). In this case the donor file will be set to status "deleted" in Prometheus by the donor center, and the donor data must be pseudomised.
- When the donor was activated for a patient (i.e. Verification typing,…) the status of the donor will be set to deleted without pseudonimising.

6.2 System administration

6.2.1 The 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.

6.2.2 Electronic connection and communication between organizations must be coordinated and performed with the greatest possible care, minimizing vulnerabilities and exploitation risks.

6.2.3 Redundant, reliable software and hardware architecture must be used to minimize the probability of failure or data loss and the possible length of a down time.

6.2.4 Backup of all systems and data must be performed regularly at Backup reasonable intervals. These activities must be documented.

6.2.5 The overall documentation system must provide all information necessary for trained and skilled staff to keep the IT systems operational.

6.2.6 Any such system installed must be accompanied with adequate documentation for its maintenance (in particular detail if developed in-house), administration and operation.

6.2.7 System modifications must be managed through a documented change management process.

6.2.8 Reliance on any one individual must be minimized and critical technical components should be made redundant wherever possible.

6.2.9 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 for the functions they are providing. Responsibilities of both parties must be described in writing.

6.2.10 Registry information technology systems must be maintained to ensure that the used software is up to date that the used software is up to date to minimize security risks and to make sure that all systems are running properly.

6.2.11 The Registry software is developed by a third partie, which follows a documented software development process. This process covers all the important steps in a software lifecycle process (planning, analyses, design, implementation, testing and integration, maintenance).

6.2.12 When transferring data between organisations, the transfer of data is validated by the EMDIS protocol.

6.3 Essential Functionality of IT Systems

6.3.1 Search algorithms must provide lists of suitably matched donors/cord blood in a reasonable time frame.

6.3.2 Each printed report must be dated.

6.3.3 Each step in the search process (e. g. patient registration and any request, result or update) must be documented with all relevant attributes, including a date and a time stamp.

6.3.4 The information history of relevant data must be recorded.

6.4 Software application Prometheus

The software application Prometheus facilitates the search process for unrelated donors and Cord Blood Units for the benefit of patients in need of a stem cell transplantation. Prometheus provides a link with international registries (connected to the EMDIS network) and operates in accordance with international procedures and in compliance with the Standards (Collaboration agreement between the participating parties). Prometheus User documentation will be posted on the MDPB website: https://www.stemcelldonor.be/professionals.

In case of a new software or major update, training is given or coordinated by the staff of the MDPB to the users of the cooperative centers. Minor changes are explained in the updated Prometheus manuals for the users. Minor changes are explained in the updated Prometheus manuals for the users.

The updates of Prometheus are in accordance with the implemented EMDIS updates.

6.5 Security management

A formal access request must be completed and be approved by the user's supervisor. Use the *MDPB FRM042 Password authorization* to request for authorization to Prometheus, please fill out the fields and fax or mail it to the MDPB-R. Personal data of the user must be completed in section A, the level of access granted to information and systems is described in the user roles in section B. The user will not be given user authorization if fields or signatures are missing in the form.

The personal access data will be sent to the personal email address. Login is only possible after receiving a password to avoid unauthorized access. A password is used for personal authentication, and must be kept secret for others, an account may never be shared. The user must avoid unattended user equipment.

RKVL-domain users will use their windows account to login to the Citrix Web interface. Users outside the RKVL domain need to install the "rkvl.cer" certificate to be able to log in to Citrix, and will therefore receive an additional password.

The Prometheus password you receive from the MDPB-registry must be changed when logging in for the first time, at the latest the day you receive the email.

When logging in to Prometheus, you have 3 attempts to enter the right password. When the third attempt in a row fails, the user account will be locked. The user has to ask the Registry to unlock the account.

Changes must be communicated to the system owner: access rights of users who have changed their job function, roles, responsibilities, users who left the organization must immediately be reported by the form *MDPB FRM042 Password authorization*.
To disable an account, the supervisor must complete section C of the *MDPB FRM042 Password authorization* and send it to the MDPB-registry@rodekruis.be

The user accounts must be reviewed to maintain effective control over access to data and the information system: formal review reports will be maintained

The Prometheus password must be changed at regular interval: the password must be changed every 90 days.

6.6 Protection personal data

6.6.1 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.

6.6.2 The name and contact information of the security role is posted on the Registry's information profiles posted on the WMDA share (Organisations Information Profiles).

6.6.3 A Written Information Security Policy (WISP) is included in the MDPB quality manual.

6.6.4 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 must be encrypted before it is copied to removable or portable media, or transmitted using unsecured channels.

6.6.5 Evidence of compliance to the requirements for data protection will be maintained for a minimum of six (6) years.

6.7 Management of changes

This procedure describes the process to be followed for the management of changes: that is, how changes are initiated, carried out, approved, implemented and documented. The procedure is applicable to the Prometheus software and applies to all participating centers of the Marrow Donor Program Belgium, to the MDPB-registry and the RKVL departments of the Dienst voor het Bloed (ICT department, Quality department, etc.).

6.7.1 Change request form

All requests for changes must be submitted in timely matter and must follow the standard Change Request Procedure outlined in this chapter.
The *MDPB FRM014 Change request form* must be completed and sent to the Registry coordinator for approval. The requestor must complete **section A: change request description**. Change requests must be assigned a change priority classification - critical, priority, normal - to define whether needs are to

be fixed in current production or in a future version. The type and reason of change and complete description must be completed in the form. The impact of the change request will be evaluated in section B by the Registry, Approval or non-approval of the change request will be notified in section C.

6.7.2 Change review, Evaluation and approval

The Registry coordinator will evaluate all change requests and evaluate the impact of the proposed change. The change requests will be listed in the *MDPB FRM015 Change request list*, change priority and classification will be evaluated. When a new version is being planned, all pending change requests will be reviewed to be included in the new release

Change requests or new developments related to EMDIS requirements will be evaluated by the EMDIS User Group, responsible for the definition of new EMDIS requirements and revisions.

After evaluation, the Registry coordinator will complete **section B: impact assessment** of the *MDPB FRM014 Change request form* to comment on estimated impact to budget, work effort and time schedule.

After evaluation the proposed list of change requests will be approved by the members of the Governing Board and signed by a representative of the Governing Board.

New change requests are submitted in the Steiner helpdesk tool, bug fixing and handling of urgent changes will be given priority and submitted immediately.

6.7.3 Project setup after change request approval

After the change request approval: the Registry coordinator will complete **section C: project management approval** of the *MDPB FRM014 Change request form* and send a copy to the requesting center.

The Registry coordinator will complete the *MDPB FRM016 Change request implementation plan* form and outline what the project will be delivering eventually, including fallback plan, validation, necessary training sessions, documentation to be adapted, risk management.

7 OPERATIONAL BUSINESS CONTINUITY

During crisis situations mutual assistance in international transport and regulations is necessary. Information on national documents will be provided to national border security agencies and other authorities. The WMDA board has approved the establishment of an international emergency task force to support communication and cooperation among registries in times of crises.

Emergency contact information for WMDA members is available on the WMDA website.

The MDPB STD021 indicates the action plan for emergency cases and follow up in case of illness or decease of the MDPB R search coordination team.

8 STRATEGY

The strategy and the objectives of the Marrow Donor Program Belgium are defined in the service level between the BHS-MDP-B committee and the MDPB-R.

The common goal of the MDPB-R and the MDPB cooperative centers is to strive for continuous WMDA accreditation. WMDA promotes product quality and global collaboration, and is an indication that high quality hematopoietic stem cell products are efficiently provided and donor safety is ensured.

9 ABBREVIATIONS AND TERMINOLOGY

The following abbreviations cover terms used in these Standards:

ABO, Rh	Major human blood groups (A, B, O) / Rh refers to Rh D antigen
ACD-A	Anticoagulant Citrate Dextrose-Solution A
AIDS	Acquired immune deficiency syndrome
Anti-HIV-1,2	Anti-human immunodeficiency virus 1 and 2 antibodies
ASHI	American Society for Histocompatibility and Immunogenetics
CB	Cord Blood
CC	Collection Center
DC	Donor Center
DLI	Donor Lymphocyte Infusion
DPO	Data protection officer
EBV	Epstein Barr Virus (family of herpes virus)

EFI	European Federation for Immunogenetics
EMDIS	European Marrow Donor Information System
G-CSF	Granulocyte-Colony Stimulating Factors results in mobilization of stem cells
GDPR	General Data Protection Regulation (GDPR)
Global registration identifier for donors (GRID)	The global registration identifier for donors provides format for registries and donor centers that issue donor identifiers. The GRID assures that every donor is assigned a globally unique identifier.
HBM	Human Bodily Material
HbsAg	Hepatitis B surface antigen
HCV	Hepatitis C virus
HGR/CSS	Hoge Gezondheidsraad/Conseil supérieur de la Santé
HLA	Human Leucocyte Antigen
HPC	Hematopoietic Progenitor Cells
HPC, A	HPC, Apheresis
HPC, CB	HPC, Cord Blood
HPC, M	HPC, Marrow
HSCB	Hematopoietic Stem Cell bank
IDM	Infectious Disease Markers
IRB	Institutional Review Board or independent Ethics Committee or ethical review board
JACIE	Joint Accreditation Committee – ISCT and EBMT
MAC	Medical Advisory Committee
MDPB-R	Marrow Donor Program Belgium Registry
MUD	Matched unrelated donor
MNC, A	MNC, Apheresis
NAT	Nucleic Acid Testing
NC	Nucleated cells
NMDP	National Marrow Donor Program
PROMETHEUS	Prometheus is the information system for stem cell donor registries. It covers all key business processes of the registry daily work, including donor management, upload to the WMDA submission platform, patient and search management.
QAC	Quality Assurance Committee

SAE	Serious adverse event: Any untoward occurrence associated with the procurement, testing, processing, storage and distribution of tissues and cells that might lead to the transmission of an infectious disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalization of morbidity.
SAR	Serious adverse reaction: an unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement of human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalization or morbidity.
SEAR	Serious events and adverse reactions
SOP	Standard Operating Procedures
SPEAR	Serious product events and adverse reactions
TLS encryption	Transport layer Security: secure tunnel over the internet between the sender and the recipient, the message is protected in transit.
TC	Transplant Center
TNC	Total Nucleated Cell Count
URD	Unrelated Donor
Verification Typing	This typing includes the tests carried out on a fresh sample of a specific donor or on a attached segment of a cord blood unit with the purpose of verifying the identity and concordance of an existing HLA assignment. This stage may also be referred to as “Confirmatory Typing (CT)”. When in case of emergency situations a donor swab kit is sent to the lab of the transplant center, this will count towards verification typing in case of further workup.

10 REFERENCE DOCUMENTS

Report of Serious (Product) Events and Adverse Reactions	www.WMDA.info WMDA Committees and working groups – S(P)EAR Committee
Donor suitability criteria	www.WMDA.info - Working groups - Medical

11 STANDARDS

The Centers must agree to abide by the standards, policies, and procedures of the (current version):

EFI STANDARDS	European Federation of Immunogenetics standards.
BELGIAN STANDARDS	HGR/CSS standards Nr 8550 (Hoge Gezondheidsraad / Conseil supérieur de la Santé) (Revision version 2 July 2008) https://portal.health.fgov.be
SEATTLE CRITERIA	BLOOD, 15 December 2007, Vol 110, number 13
EUROPEAN DIRECTIVES	2004/23/EC of 31 March 2004 (standards of quality, safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells) 2006/17/EC of 8 February 2006 (Technical requirements for the donation, procurement and testing of human tissues and cells) 2008/86/EC of 24 October 2008 (Implementation of 2004/23/EC as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells. http://ec.europa.eu/health/ph_threats/human_substance/legal_tissues_cells_en.htm
JACIE	International standards for cellular therapy product collection, processing and administration. www.JACIE.org
WMDA standards	World Marrow Donor Association International standards for unrelated hematopoietic stem cell donor registries. https://www.wmda.info/
EBMT	European Group for Blood and Marrow Transplantation Operational Manual (2004 Revised Edition) EBMT Transplant guidelines and accreditation Indications for unrelated HSCT transplantation : “Bone Marrow Transplantation : special report 2006, 37, 439-449 : allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: definitions and current practice in Europe”. P.Ljungman et al.” www.ebmt.org

12 ADDENDUM

See *MDPB LST008 Addendum standards*.