

**STANDARD OPERATING PROCEDURES MANUAL  
OF THE  
MARROW DONOR PROGRAM BELGIUM**

**Marrow Donor Program Belgium  
Motstraat 40  
2800 Mechelen  
Tel: (32) - 15 44 33 96    Fax: (32) - 15 44 36 56**

**AUTHORS REVISION 2/2011**

<b>Responsible authors/review</b>	<b>Function</b>	<b>Function Board MDPB-R and MDPB-VZW/ASBL</b>	<b>Date</b>	<b>Signature</b>
Prof. Philippe Vandekerckhove	General Director Rode Kruis -Vlaanderen	Administrative director of the Red Cross		
Prof. Danielle Sondag	General Director Croix-Rouge de Belgique	Administrative director of the Red Cross		
Dominik Selleslag, MD	Medical Director of Transplant Center, AZ St Jan Brugge	Medical director transplant center		
Etienne Baudoux, MD	President MDPB-vzw/asbl Medical Director of CBB CHU Liège	Physician of tissue cell bank: cord blood bank		
Frederic Baron, MD	Transplant physician, CHU Liège	Medical director transplant center		
Micheline Lambermont, Pharm D	Vice Medical Director, Service du Sang, Donor Center	Medical director /substitute Red Cross		
Prof. Véronique Deneys, MD	Medical Director, Service du Sang – Croix-Rouge de Belgique	Medical director Red Cross		
Prof. Christian Demanet, MD	Medical Director of HLA typing lab , UZB	Medical director of typing lab		
Prof. Marie-Paule Emonds, MD	Medical Director of HLA typing lab, HILA	Medical director / substitute Red Cross		
Prof. Dominique Latinne, MD	Medical Director of CBB UCL St Luc	Medical director of typing lab		
Anne Vanhonselbrouck, MD	Director MDPB-R	Physician of medical team		
Hildegard Broos	Adjunct Director MDPB-R			

**APPROVED by GENERAL ASSEMBLY**

<b>GENERAL ASSEMBLY</b>		<b>Date</b>	<b>Signature</b>
Etienne Baudoux, MD	President MDPB- vzw/asbl		

**VERSION**

Approval General Assembly and date of implementation	Alterations to Document	Status
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Version 01/2010 23/09/2009 01/01/2010	SOP and FORMS	Approved
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**REVIEW AND UPDATE**

Every 3 years, a profound review of the SOP is necessary by the members of the MDPB-vzw/asbl and MDPB-R Board. If there are no major changes the SOP is prolonged annually.

New and revised policies and procedures shall be reviewed by the members of the MDPB-vzw/asbl and MDPB-R Board prior to implementation. This review is approved by the members in the General Assembly. This review shall be documented.

**SUMMARY OF MAJOR CHANGES : version 01/2010**

- FORMS: use of WMDA forms is introduced as these are used worldwide
- INDICATIONS for HSCT: the criteria of EMBT are used as recommendation
- Follow up of the donor until 5 years after donation of HPC

**SUMMARY OF MAJOR CHANGES : version 02/2011**

- INDICATIONS for HSCT : limitation MAC approval and clear overview for MAC notifications
- Update to WMDA standards

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## **1. INTRODUCTION**

The MDPB consists of the MDPB-Registry within the Belgian Red Cross and the MDPB-vzw/asbl, a non-profit corporation under Belgian law.

The MDPB-R is responsible for the administrative and financial management of the MDPB. The MDPB-vzw/asbl is responsible for the medical and scientific matters (issues). The medical advisory committee of the MDPB-vzw/asbl shall be consulted for any medical question/procedure not covered by the SOP.

This Standard Operating Procedures Manual (SOP) covers all procedures involving unrelated volunteer donors. The SOP intends to provide practical information to all Marrow Donor Program of Belgium (MDPB) users or coworkers. Deviation of procedures from these standards must be submitted in advance to the Board of the vzw/asbl of the MDPB.

The Medical Director of a participating Donor Center, Collection Center, or Transplant Center, is responsible for ensuring the Center's compliance with these standards.

A separate SOP covers procedures involving cord blood donations.

A separate Collaboration agreement covers the procedures to assure the proper functioning of (the software application) "SYRENAD", facilitating the search process for unrelated donors and cord blood units.

## 2. CRITERIA FOR PARTICIPATING CENTERS

### 2.1. Donor Centers

- 2.1.1. The Center must agree to abide by these standards, policies, and procedures of the MDPB-R. 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° 8271 as applicable, WMDA standards, (current version).
- 2.1.2. The Center must have demonstrated experience in donor management activities including counseling, confidentiality issues, and medical screening.
- 2.1.3. 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) shall be performed by laboratories accredited or licensed in accordance with applicable laws and regulations approved by the governmental authority.
  - Transfusion center for collection of autologous blood; the transfusion center must be authorized by the governmental authority.
- 2.1.4. Each Center is fully responsible for the effective management of its registered donors (regular contacts, calling for additional typing, checking availability, counseling,...)
- 2.1.5. It is the responsibility of the Donor Center to archive all donor informed consent forms. (Info consent for donor recruitment into to the Registry, info consent additional blood sample collection, HPC or TC donation). Please note that these are templates that can be adapted for local use in the Donor Center. The informed consent form consists of two parts: the information sheet and the consent certificate.
- 2.1.6. Each Center is connected with the MDPB-R that is in charge of centralizing data and searching for donors.
- 2.1.7. Each Center is responsible for regularly updating information on its donors, to check donor availability, to delete donors no longer available and for transmitting electronically consequently all available information to the MDPB-R.
- 2.1.8. Each donor is registered in the software application Syrenad.
- 2.1.9. **In no way**, the name of a donor and the name of a patient should appear together on the same document. This is mandatory to strictly respect the complete anonymity "donor/recipient".
- 2.1.10. The donor **must always be identified by her/his code number**.

- 2.1.11. Each donor prepared for HPC (marrow or Apheresis), or TC donation benefits from a disability life insurance subscribed by the MDPB-R.

## 2.2. Collection Centers

- 2.2.1. The Center must agree to abide by the standards, policies, and procedures of the MDPB, JACIE standards (current edition) part C, Belgian Standards of the HGR-CSS N° 8271 as applicable, WMDA standards, current version.

The collection center must be a FAGG/AFMPS certified hematopoietic stem cell bank. The bank is responsible for product release conform Belgian Law.

- 2.2.2. The HPC (marrow or Apheresis) or TC products must be collected by a team member of a MDPB accredited Collection Center. The Collection Center can be formally accredited for the collection of HPC, M or HPC, A or both.

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

- 2.2.4. For accreditation as a bone marrow Collection Center:

- The bone marrow collection team must consist of at least one responsible senior physician (minimum 2 years, and not a trainee physician) and at least one other trained ancillary person or physician who has the experience and the team must have the equipment for bone marrow collection and processing. All staff attending bone marrow collection will be adequately trained for the procedure.
- The team must be experienced and must collect bone marrow on a regular basis (5 over 5 years)
- The team must have performed at least 10 prior bone marrow collections for transplantation.
- Anesthesia must be provided under the supervision of a licensed, board-certified anesthesiologist.
- The team should obtain a bone marrow nucleated cell count as prescribed by the Transplant Center. This should be accomplished by withdrawing no more than 20 mL/kg of donor Body Weight or 1500 mL of bone marrow (total volume).
- If any processing of the bone marrow is necessary, it has to take place in a facility that complies with the Belgian HGR/CSS standards.

- 2.2.5. For accreditation as HPC, A or TC, A Collection Center:

- The HPC, A or TC, A collection team must consist of a responsible senior physician (not a physician in training) and at least one other trained ancillary person who have the experience and the equipment for the use of growth factors and leukapheresis.
- The team must be experienced (at least 2 years) and the team must have collected HPC, A or TC, A on a regular basis.
- The team must have performed at least 30 prior HPC collections for transplantation, performing at least 10 of them over the previous year.
- The team should obtain a CD34+/CD3+ cell count as prescribed in maximum 3 consecutive apheresis (HPC, A) and in maximum 2 consecutive apheresis (TC, A).

- 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 should 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 and shall include at least the following:
- Written Informed consent
  - Documented Fitness for donation (must be evaluated by or with a qualified anesthesiologist if applicable)
  - Documented Eligibility
  - The use of autologous blood and volume to be collected by Donor Center if indicated cfr 2.1.3.
  - Documented fitness for discharge as applicable
  - Donor follow up according to a pre-defined schedule

### 2.3. Transplant Centers

The Center must agree to abide by the standards, policies, and procedures of the MDPB, JACIE standards (current edition) part B, Belgian Standards of the HGR-CSS N° 8271 as applicable, WMDA standards, current version.

#### **2.3.1. EXPERIENCE**

2.3.1.1. HPC, M and HPC, A transplantations using unrelated, volunteer donors must be carried out only by Transplant Centers with adequate experience of sibling transplants. Such Transplant Centers must be formally accredited by EBMT 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 accreditation criteria of the EBMT.

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 and EBMT have formally approved this collaborative agreement.

#### **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. Laboratory testing of all donors shall be performed by a lab licensed in accordance with laws – regulations by the governmental authority.

2.3.2.3. There must be an air-handling system designed to prevent nosocomial infections disseminated from central heating and cooling systems.

2.3.2.4. There must be documented evidence of adequate blood component support, including irradiation of blood components and CMV testing.

- 2.3.2.5. There must be documented evidence that radiation therapy support is available if needed.
- 2.3.2.6. Research Protocols for unrelated donor hematopoietic stem cell transplants must have been approved by a local Institutional Review Board (Ethical Committee). (MDPB046 Request for unrelated donor to participate in a Research study v2 2011).
- 2.3.2.7. There must be a designated nursing unit for stem cell transplantation, in case of a program treating pediatric patients, nurses must have experience in the management of pediatric patients.

### 3. CRITERIA FOR CONSIDERING A PATIENT FOR AN UNRELATED DONOR TRANSPLANT

#### 3.1. Indications for initiating a search

A search may be initiated when:

- the potential recipient is aware of the risks of the procedure
- the potential recipient is registered on the waiting list of the RIZIV/INAMI (see 5.3. for additional criteria)

#### 3.2. Disease categories

The MDPB does not restrict access to its donors for patients in specific disease categories. It is the responsibility of the transplant physician to judge whether a patient is eligible for transplantation with an unrelated donor. However, recommendations should be based on these published according to the EBMT guidelines in bone marrow transplantation (reference see chapter 9/10? Standards). (Cfr. disease list in form MDPB001 preliminary search request (reference see chapter 11 Standards)

- 3.2.1. List of allogeneic transplantation for haematological diseases, solid tumours and immune diseases: definitions and current practice in Europe.

When GNR appears in the list (generally not recommended); the approval of the MAC is mandatory.

If the indication is *Developmental* and patient is included in a *protocol approved by the Ethical Committee (EC)* then no MAC approval is required. A copy of the EC approval should be provided at least for the first request for this protocol.

Categories are listed in the MDPB001 preliminary search request.

General rule: indications are divided in 3 categories:

1. Recommended indications: NO MAC
2. Development indications are acceptable if patient is included in an approved protocol: NO MAC  
For patients who are included in a protocol documentation must be available at the center on request of the Registry.
3. Indications generally not recommended: MAC

The indication list provided in the form will be revised annually by the Board.

### 3.3 Second donations

#### 3.3.1. Second donations from abroad donors: NO MAC

Requests go through specific procedures in donor registries abroad.

#### 3.3.2. Second donations from Belgian donors:

1. Unstimulated apheresis (TC,A): NO MAC.
2. HPC, M or HPC, A after mobilization with growth factors:  
MAC APPROVAL always required.

### 3.4 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 SOPs, the Registry must contact all 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 has 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 SOPs will only be accepted in exceptional situations. Requests for MAC approval must be sent to the MDPB-R by completing the "MDPB038 mac request for review v2 2011" form. Mac approval will be notified through the "MDPB039 mac approval" form.

### 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. A search cannot be initiated if the patient is not accepted on the waiting list of an accredited Transplant Center. A patient older than 65 years, is considered as a non-standard indication for HPC, A or HPC, M transplantation in other Registries, therefore submission of the IRB approved research protocol synopsis and the patient's Karnofsky performance scale at the time of registration are requested.

- 3.5.2. Each initial search request has to be sent on a specific form (MDPB001 prelim search request v2 2011) except for requests from International registries sent through EMDIS. On this form, all items have to be filled in. A request will not be accepted if information is missing. (The Blood group and CMV testing are not mandatory). Please submit the IRB approved research protocol synopsis and the patient's Karnofsky rating if the patient is older than 65.

- 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), DQB1 is highly recommended. The HLA typing must be at least confirmed on a second sample or segregated in a family. 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 BMDW search program..

3.5.4. The Transplant Center has to cancel the search if the patient is no longer eligible for transplantation (medical reasons) or a transplant is no longer considered . If at a later time the decision is made to proceed with transplant, a reactivation should be requested. Patients can also be temporary suspended and reactivated by the Transplant Center.

3.5.5. Following the submission of an initial search request for a patient at MDPB-R, a search report on unrelated volunteer donors of the MDPB-R is sent to the requesting Transplant Center via Syrenad. 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. (MDPB022 RIZIV INAMI v2 2011)

For international searches, requested by the Transplant Center, an electronic search result list will be sent via Syrenad, for non Emdis countries, the search result list will be sent via email. The type of search (national – Emdis – non Emdis will be based upon the specifications of the preliminary search request)

On the report appear:

- the number and codes of HLA AB DR identical donors.
- the number and codes of HLA AB split identical donors.
- the number and codes of HLA AB broad identical 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 Syrenad. International cord search results of Emdis connected countries will be sent via Syrenad, if requested by the Transplant Center, cord search results of non Emdis countries will be sent via email. The type of search (national – Emdis – non Emdis will be based upon the specifications of the preliminary search request).

On the report appear:

- the number and codes of 0 mismatch CB units.
- the number and codes of 1 mismatch CB units.
- the number and codes of 2 mismatch CB units (upon request).

3.5.7. If the initial search request by a Belgian Transplant Center includes a request for search for a cord blood unit, both a BMDW CB report and a search report on the Netcord inventory of cord blood units is sent to the requesting Transplant Center on which appear:

- the number, codes, HLA typing and number of NC of 0 mismatch CB units.
- the number, codes, HLA typing and number of NC of 1 mismatch CB units.
- the number, codes, HLA typing and number of NC of 2 mismatch CB units.

## 4. PROCEDURES

### 4.1. Recruitment of donors

- 4.1.1. Each potential volunteer donor should be, at a first stage, provided with a written document containing specific information on HPC, M and/or HPC, A donation. (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 50th birthday.
- 4.1.4. Each recruited donor has to sign an initial informed consent form to document that he has received all necessary information. This document should 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 possible risks related to general anesthesia, HPC, A collection after mobilization with growth factors, bone marrow collection, lymphocyte and blood donation
  - the duration of hospitalization and temporarily cessation of activity following HPC, M harvesting or HPC, A collection
  - the importance of keeping the donation **ANONYMOUS** and **VOLUNTARY**
  - the possibility and associated risks of second donations
- 4.1.5. **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.
- 4.1.6. All prospective donors must be given educational materials regarding the risks of infectious diseases transmitted by a stem cell transplant. These materials must include detailed information on risk groups for transmission of HIV (human immunodeficiency virus). The donor must acknowledge in writing that he or she read and understood the educational material, has been given the opportunity to ask questions, has had those questions answered to his or her satisfaction, and has provided accurate information to his or her best ability.
- 4.1.7. A history of positive confirmed 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 antibody shall be ground for cancellation the donor.
- 4.1.8. Through medical history and examination, the following risks shall be evaluated:
  - Donor safety
  - Cellular product quality
  - Recipient safety
  - Collection and Processing Staff safety

- 4.1.9. A pregnant donor must be temporary suspended from the Registry's database file during the entire time of her pregnancy and up to a period of six months after delivery when requested for a typing request or blood sample request.
- 4.1.10. A volunteer 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 cancelled from the Registry's database by the Donor Center.
- 4.1.11. All typings done on a newly recruited donor must be done with molecular methods. All new donors must be at least HLA-A, B and Cw typed in low resolution (2 digits) and DRB1 typed in high resolution (4 digits). This typing should be fully reported to MDPB-R. The donors then appear in the national file of the MDPB-R under an unique code number.
- 4.1.12. The Donor Center is responsible for ensuring 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 according to the applicable laws.  
Donors of the UK are an exception to blood donation exclusion criteria and can be used through an exceptional release procedure.
- 4.1.13. All staff members (Donor and Collection Center, Registry) involved in donor recruitment, collection, administration shall follow the rule of donor and recipient confidentiality.
- 4.1.14. The donor's HLA typing data shall not be used to commit the donor to programs for which he or she has not given explicit written consent.
- 4.1.15. 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.
- 4.1.16. When blood or tissues are obtained for research purposes, specific written consent must be obtained from the donor. Informed consent must be approved by an ethical committee if donor blood or other biological material information is stored or used for the purpose of an especially approved research project.

#### 4.2. Further tests when a potential donor has been identified

- 4.2.1. Upon specific request the following tests will be performed : A B C DR DQ by low or high resolution. (DP on special request) (Request via Syrenad for Belgian and international donors or via Form "MDPB002 DNA typing request v2 2011" for international non Emdis donors).
- 4.2.2. A blood sample for verification (confirmatory typing) can be sent to the Transplant Center upon request via Syrenad for Belgian or international Emdis donors or using a specific form "MDPB003 Verification typing sample request v2 2011" 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).
- 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). (“MDPB027 info consent blood sample collection NL v2 2011”, “MDPB028 info consent blood sample collection FR v2 2011”)
- 4.2.5. The Donor Center, while taking blood from the donor for verification typing (confirmatory typing) will perform the following tests:

<b>infectious disease markers IDM</b>	
Syphilis	
HBs Ag	
HBcore antibody	
Anti-HIV1-2 antibodies	
Anti-CMV antibodies	
Anti-hepatitis C virus (anti-HCV) antibodies	
<b>Other tests</b>	
ABO and Rh typing	if not already performed

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

Laboratory testing of all donors shall 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. (Also applies for 2.3.2.2.)

- 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 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 by the Transplant Center must be sent to the Donor Center via Syrenad (Belgian donors and international Emdis donors). For non Emdis donors the form “MDPB005 verification typing results v2 2011“ must be sent to the Registry. Decisions on donor acceptability should be made promptly, so that donors who are inappropriate for that patient may be released and appropriate donor be informed on the further procedure.
- 4.2.8. When the transplant center finds discrepancies when performing the verification typing tests, the discrepancy must be reported using the “MDPB004 discrepant typing v2 2011”. 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.

- 4.2.9. Invoices concerning additional HLA typing are sent by the MDPB-R to the requesting Transplant Centers or 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 and shipment are invoiced by the Donor Centers to the MDPB-R (the "FORM MDPB045 sample transport invoice must be attached). 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 monthly statements of account.

### 4.3. Donor information - intent to donate

- 4.3.1. Upon completion of verification (confirmatory) typing, a Transplant Center may select a matched donor for donation using the "MDPB006 formal request for stem cell collection v2 2011" or in case of Lymphocytes the "MDPB007 formal request for lympho collection v2 2011". Results of the verification typing as well as the suggested transplant date should be provided by the Transplant Center "MDPB009 final compatibility test results v2 2011".

- 4.3.2. The HLA matching between donor and patient must comply to 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 a donor has been selected for a certain patient, he/she must be counseled by the Donor Center and/or the collection center as follows:
- He/she must be given more detailed information about 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 costs.
  - It is strongly recommended that the spouse or other trusted confidant of the donor would be included in this discussion.
  - again mention his or her right to withdraw at any time up to induction of anesthesia for the bone marrow collection. However they should also be informed of the risk of death of the recipient should the donor withdraw after the beginning of the recipient's conditioning regimen.

- 4.3.4. The following points should be considered:
- Emphasis on anonymity between donor and patient
  - Requirement for the blood samples before donation (where Registry policy permits)
  - Patient's need for a transplant and chance of success expressed in general terms.
  - Possibility of second donation for the same patient (including treatment with haematopoietic growth factors or leukapheresis).
  - Emphasis on donation as a gift without remuneration. 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. Once a donor has been found eligible to donate in the collection or Donor 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). The Donor 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.

#### 4.4. Donor reservation - Pre-collection communication

- 4.4.1. A prescription form for collection of HPC (Marrow or Apheresis) or of TC, A must be completed and signed by the responsible transplant physician and transmitted via the Donor Center to the Collection Center using the "MDPB010 prescription v2 2011" or "MDPB011 prescription HPC, A v2 2011" or "MDPB012 prescription TC, A v2 2011".
- 4.4.2. The Donor Center will, after having received the Prescription Form then contact its donor in collaboration with the Collection Center and schedule with him/her a date for medical evaluation (see 4.5) and then agree on a date for HPC (Marrow or Apheresis) or of TC, A collection according to the specifications by the transplant physician.
- 4.4.3. A donor selected for a specific patient must be placed on a "reserved" status in Syrenad from the time of the verification typing until the donation date is reached. ONLY if a precise date or period of time (not exceeding 3 months from the initial request) has been determined by the transfer physician. If this is not the case, the donor can be recruited for any other.
- 4.4.4. The Donor Center, Collection Center, and Transplant Center must agree on the date of collection as well as the volume and cell count of HPC (Marrow or Apheresis) or of TC, 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 "MDPB013 verification HPC, M v2 2011" or "MDPB014 verification HPC, A v2 2011" or "MDPB015 verification TC, A v2 2011". For characteristics of the collected HPC, M, see § 2.2.4., for characteristics of the collected HPC, A and TC, A, see § 2.2.5.

- 4.4.5. Once the harvesting date is scheduled, this date cannot be changed, except for very specific and important reasons.
- 4.4.6. Pre-harvesting and harvesting costs are invoiced centrally by MDPB-R to the Transplant Center. All costs, related to the HPC (Marrow or Apheresis) or of TC, A donation, are included in the collection fee that is invoiced by the MDPB-R to the requesting International Registry or Transplant Center.
- 4.4.7. Should a cancellation take place three weeks or less before HPC (Marrow or Apheresis) or TC, A collection, and when the donor has already undergone physical and biological examinations a cancellation fee will be charged to the Transplant Center.
- 4.4.8. Should a transplant be postponed (e.g. the patient's disease progresses or a medical complication occurs), a new collection date must immediately be established to occur within 3 months of the original collection date. In that case the donor will not be released, and the cancellation fee will not be charged. MDPB-R will only charge the physical and/or biological examinations performed.
- 4.4.9. If the donor withdraws, or is not found eligible to donate, at the stage of a pre-transplant check-up, no fee will be charged to the Transplant Center.
- 4.4.10. The HPC (Marrow or Apheresis) or TC, A harvesting of a Belgian donor should take place in Belgium, wherever the location of the Transplant Center is.
- 4.4.11. The HPC (Marrow or Apheresis) or TC, A collection always takes place in an accredited Collection Center, if possible, 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 ("MDPB023 donor insurance request v2 2011").
- 4.4.13. The donation must remain completely **ANONYMOUS**. Indirect, anonymous communication between donor and recipient is allowed post-donation. In **NO CASE**, donor and recipient shall be allowed to exchange direct correspondence. Correspondence, if any, will go through and must be censured by the Donor Center, the transplant physician, or by MDPB-R.
- 4.4.14. In **NO CASE**, donor and recipient shall be hospitalized in the same unit of the hospital.
- 4.4.15. The donor might 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 work-up of the donor to inform him/her about the source of stem cells (Belgian or International unrelated donor) and the need for data exchange.

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 bone marrow.  
A licensed physician must perform and evaluate a complete medical history and physical examination to assess fitness to donation, and must evaluate the results of the following tests:

Full blood count and differential count
Glycaemia
Electrolytes
Either urea nitrogen or creatinin
Bilirubin
Serum total protein plus albumin or serum protein electrophoresis
Haemostatic check-up
Liver function tests (SGOT, SGPT, $\gamma$ -GT)
Pregnancy test in all female donor with childbearing potential (less than 7 days prior to collection)
Electrocardiogram
Chest X-ray
Other tests may be foreseen depending on donor's medical history or on Transplant Center's request

NAT testing (HIV, HCV, HBV) is mandatory.

After 30 days repeat testing must be done.

- 4.5.1.1. For international donors it is the responsibility of the Transplant center to proceed to mandatory testing:
- a. all standard tests must be performed in compliance to the Belgian law, f.i. HEP B NAT.
  - b. donors coming from endemic areas may have to be tested for additional infectious agents. (e.g. Malaria, HTLV-1,....)
- 4.5.2. This physician should not be a member of the Transplant Team of the Center performing the transplantation.
- 4.5.3. This physician must report the results of the medical examination as well as the infectious disease screening results using the form "MDPB016 donor clearance v2 2011" to the MDPB-R .  
In addition, the physician shall report in writing the presence of the following conditions:
- Number of previous pregnancies and/or transfusions
  - Recent vaccinations: HPC (Marrow or Apheresis) or TC, A harvest should 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 TC, A.

- 4.5.4. Female adult volunteer donors of childbearing years must have a pregnancy test performed during the work-up stage.
- 4.5.5. Final confirmation of a donor shall not be done until the Collection Team is satisfied that the donor meets its criteria for stem cell collection and is fully committed to proceeding.
- 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.

#### **Donors with abnormal findings**

- 4.5.7. 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, with respect to the protection of donor and recipient confidentiality.
- 4.5.8. Any abnormal findings during work-up 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.
- 4.5.9. 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.

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

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

- 4.5.11. 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 must be done if results date back to testing more than 30 days.

## 4.7. Haematopoietic Stem Cell collection and processing

### 4.7.1. **Samples to be obtained at time of first collection:**

Blood for ABO and Rh type : a test for ABO group and Rh type shall be performed on blood obtained from the donor at the time of the first collection (or on the first product collected)

### 4.7.2. **Choice of bone marrow versus peripheral blood 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 must 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 bone marrow, and who is foreseen for second donation, HPC, A collection after proper counseling and written consent will be obtained.

### 4.7.3. **Bone marrow Collection**

4.7.3.1. Bone marrow should preferably be collected under general anesthesia.

4.7.3.2. 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 bone marrow). Heparin (minimum 10 U/mL) is optional

4.7.3.3. Syringes and needles used to aspirate the bone marrow should be rinsed with the same medium.

4.7.3.4. The number of bone marrow 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.

4.7.3.5. This should be accomplished by withdrawing no more than 1500 mL of bone marrow. § 2.2.4 applies.

4.7.3.6. The collected bone marrow must be filtered

4.7.3.7. The bone marrow collection should be transferred into a minimum of two sealed plastic bags before transportation.

4.7.3.8. For storage -Temperature range refer to cfr. 4.9.11

4.7.3.9. 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 bone marrow harvesting.

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

4.7.3.11. During or after bone marrow harvesting, one to three bags of previously collected autologous blood may be transfused to the donor. Administration of blood transfusion should only be allowed after proper evaluation of risks and benefits for the donor.

WMDA recommends the use of allogenic blood instead of autologous blood, but risks and benefits of autologous blood should be evaluated on a case by case basis.

The WMDA also recommends that the use of blood (allogenic or autologous) in unrelated donors should be reported as a SEAR.

4.7.3.12. There must be documented follow-up by a physician of donors after donation. This should 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 or Donor 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.

#### 4.7.4. **Peripheral blood progenitor cell collection**

##### 4.7.4.1. Mobilization

Donors will begin treatment with G-CSF at a dose of 10 µg/kg/day by subcutaneous injection for 4 or 5 consecutive days (days 1-4/5).

If injected once daily, G-CSF should normally be administered at approximately the same time each day (ideally very early in the morning for unglycosylated G-CSF or late in the evening for glycosylated G-CSF).

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

HPC, A harvesting will take place on day 5, and optionally on day 6. (on Day -1 and Day 0 of the recipient (for overseas recipients collections may take place on Day -2 and -1) and start after 4-6 days of G-CSF stimulation.

##### 4.7.4.2. Leukapheresis

Prior to leukapheresis, the donor will require adequate venous access. Every effort should be made to avoid placing a central venous line.

One or two leukapheresis procedures will be undertaken, 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. At least 10-12 liters of whole blood should be 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 should 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 should 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 leukaphereses, further G-CSF treatment and additional apheresis have to be

discussed formally between the Transplant Center, Collection Center and the Donor Center.

#### 4.7.4.3. Storage

The leukapheresis products shall be stored according to the temperature requirements specified in 4.9.11 in the original collection bag without further manipulation until transportation.

#### 4.7.5. **Lymphocyte collection:**

4.7.5.1 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 should be discussed with the donor and informed consent documented in writing.

4.7.5.2. This chapter only covers apheresis without growth factor stimulation. Repeat collection with growth factor stimulation are seen as second donation.

4.7.5.3. Prior to lymphocyte collection, donor workup shall be performed as described in § 4.6 and written informed consent obtained.

4.7.5.4. The Collection and Transplant Centers should agree on the number of nucleated (or CD3+) cells required ("confirmation of leukapheresis prescription" form). If the requested number of cells is sufficiently low, a bag of whole blood may be requested instead of a leukapheresis product.

4.7.5.5. Prior to leukapheresis, the donor will require adequate venous access. Every effort should 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; 10-12 liters of whole blood should be 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 should be taken for nucleated cell count and CD3+ assay. If the target number of cells is not achieved a second leukapheresis should be carried out the next day. If the target number is still not reached, further leukaphereses will be at the discretion of the physician at the Collection Center.

4.7.5.6 Storage:

Leukapheresis products shall be stored according the temperature requirements specified in 4.9.11 in the original collection bag without further manipulation until transportation.

#### 4.7.6. **Cell processing**

4.7.6.1. 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.

4.7.6.2. The cells of a voluntary 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 TC,A)

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 registry 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.

- 4.7.6.3. Additional processing, such as the removal of T cells, incompatible red cells, or plasma, should be done at the Transplant Center or in a laboratory designated by the Transplant Center.
- 4.7.6.4. No processing of cells shall be done by the Collection Center without specific request by the Transplant Center.
- 4.7.6.5 The concentration of WBC count in the HPC(A) product must be verified and should not exceed 200.000/ $\mu$ L except if infused within 4 or 6 hours; if the concentration is  $> 200.000/\mu$ l the stem cell product should be diluted with a plasma protein solution in the cell processing laboratory designated by the Collection Center.
- 4.7.6.6. In NO CASE, the cells collected from a voluntary donor should be used for laboratory research purposes. This procedure requires a research protocol and approval by an ethical committee and the MAC.
- 4.7.6.7. When 2 collections are needed, the cells for a single patient should be divided in at least 2 different bags, each with ports that can be entered aseptically.

#### **4.8. Labeling bags**

- 4.8.1. On completion of collection, the collection bag(s) (primary container) should bear the following information on the sticker label:
  - Identification of the FAGG/AFMPS certified bank
  - The proper name of the component: HPC, Bone marrow or HPC, Apheresis or TC, Apheresis
  - The component's unique numeric or alphanumeric identifier
  - Intended recipient's name and ID
  - Donor's unique MDPB-R code (not name)
  - Name and address of Collection Center; name and telephone number of contact person
  - Name and address of Transplant Center; name and telephone number of contact person
  - Date and time of collection

- Approximate volume of the component
- Type and volume of any additives (anticoagulant, medium)
- ABO and Rh type of donor
- Warnings:
  - properly identified intended recipient and component
  - do not X-ray and do not irradiate
  - this product may transmit infectious agents
- Type of any method used for hematopoietic progenitor cell manipulation
- Recommended storage temperature range
- Component's white blood cell count

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

4.8.3. The bank is responsible for product release. This includes a check of ABO and Rh check of donor and collection, collection report, donor suitability report and quality controls on product (TNC, CD34 numbers). All information on labels and on documents and containers shall be checked by at least two staff members before the cells leave the Collection Center or processing unit.

#### 4.9. Transportation of cells

4.9.1. Whenever feasible, every effort must be made to ensure that the collected cells arrive at the Transplant site within 12 hours of collection and that the cells are infused within 24 hours of collection. When 2 leukaphereses are performed on 2 consecutive days, the cells should be infused within 48 hours of the first collection.

4.9.2. The cells must be hand-carried by a designated courier. The designated courier should 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 should have a formal written agreement with the contracting company and should have an insurance for the transportation of cells.

He/she should meet the following requirements:

- a) He/she should not be related to donor or patient.
- b) He/she must be an experienced international traveler.
- c) He/she must have no other obligations until after the cells are delivered.
- d) He/she must be a major credit card holder with a reasonable limit.
- e) He/she should be covered by an insurance from the Transplant Center.

4.9.3. Details of the courier identity and itinerary should be sent by the Transplant Center to the Collection Center at least 72 hours before collection of donor cells, using the "MDPB017 courier information v2 2011"

- 4.9.4 The courier should have arrived in the foreign country by the day prior to the planned harvest if required by the international Registry. Once at the destination (hotel in the foreign country), the courier should telephone the contact person at the Collection Center to announce safe arrival. On the day of harvest, the courier should arrive at the Collection Center 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 should 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 should 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 should be transmitted to the Belgian airport authorities by the MDPB-R 1-2 days prior to the transport. (MDPB037 customs form v2 2011)
- 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 TC, A must meet the following criteria:
- 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.
  - Each bag should be placed in an outer bag, which is also sealed to prevent leakage.
  - The bags should 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

**HPC, M**

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

**HPC, A**

- Product should be transported with a minimum of delay

- During transport the temperature shall be between 2-24°C for periods not exceeding 12 hours
- If transported for a period exceeding 12 hours the HPC, A shall 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 should 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 TC, A” form which accompanies the bag(s) if the bag itself does not bear all information needed on the sticker label
- “MDPB018 transport audit v2 2011” form which is given to the courier by the Collection Center (to be completed and signed by the Collection Center and the courier – and to be completed and signed by The transplant center and courier on arrival at Transplant center). The form has to be faxed back to the MDPB-R.

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

The import/export of cells is under the responsibility of the responsible physician of the tissue bank/establishment. The import/export is only authorized if the tissue establishments are authorized for the procurement, collection, processing, storage, transplantation of cells in the other country and shall meet the same standards of quality, safety and ethical standards as applicable in Belgium.

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 TC, A and in the peripheral blood of the donor must be counted in each bag. The number of bone marrow nucleated cells, corrected for peripheral blood nucleated cells, should exceed  $2 \times 10^8$ / 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 exceed  $4 \times 10^6$ /kg of recipient body weight.
- 4.10.3. The number of CD3+ cells in the collected TC, A must be counted in each bag. This number should 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 shall be performed at the Collection Center, with timely reports to the Transplant Center in case of positive culture.
- 4.10.6. A sample from each bag should be placed into culture for bacteria (aerobic and anaerobic), yeasts and fungi at the Transplant Center.
- 4.10.7. The Collection Center must retain an appropriate record of the collection procedure and transmit a copy to the MDPB-R using the "MDPB019 collection report v2 2011" or the "MDPB020 collection report HPC, A v2 2011" or "MDPB021 collection report TC, A v2 2011" form 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 TC, 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 TC, A
- results of bacterial and fungal cultures as soon as available

#### 4.11. Second donation for a same patient from the same donor

- 4.11.1. Any request for a second donation has to be made by submission of a specific form ("MDPB008 second donation request v2 2011") to the MDPB-R who will forward the request to the Donor Center for discussion with the donor.
- 4.11.2. Each request for second donation of HPC (Marrow or Apheresis) (see 3.3) has to be submitted to the medical advisory committee. The donor shall not be approached before the committee has given its approval. The committee shall 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 shall 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 TC, A. It is generally not recommended to perform a second bone marrow collection before 6 months after initial collection.
- 4.11.5. Donor work-up for a second donation must be handled similarly to a first donation (see 4.5 through 4.12). Every effort should 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)

- 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 to the MDPB-R at regular intervals. This is done by completing form “MDPB024 patient follow up report v2 2011” at 100 days, 1 year, after transplantation.

- 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 donor follow up (“MDPB025 donor follow up report 30 days v2 2011”) and 1 year, 5 years after collection (“MDPB026 donor follow up report 1-5- years v2 2011”) ; it is recommended that such visits be performed at the collection facility or at the Donor Center itself. If this is not feasible, follow-up information can be obtained through home physicians or direct telephone interviews. However in case of bone marrow donation, a physician of the collection team 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” form emailed to the MDPB-R around 30 days and 1 year after collection.

- 4.12.3. Serious events and adverse reactions (SEAR) (to be reported by collection center)

When a serious event or adverse reaction has occurred in relation to stem cell donation by unrelated donors, the report “Sear form” has to be completed for the central reporting system of Serious events and Adverse Effects Registry of WMDA. (international database recording adverse events occurring during procurement of hematopoietic stem cells that have or may have resulted in harm to an unrelated donor and the outcome of any investigation to determine the cause of the event). (See reference documents)

The Collection Center must send to the MDPB-R and a copy to the Donor Center.

General issues:

Any event that results in death or is in the opinion of the reporting Registry:

1. Is life threatening
2. Requires in-patient hospitalization or significant prolongation of existing hospitalization or transfusion.
3. Results in persistent or significant disability/incapacity.

Specific issues which should be reported:

- Any serious potential risk during anesthesia
- Any serious cardiac complication
- Any serious infection
- Any serious mechanical injury
- Any serious incident in haemostasis
- Any serious (late) effect of HPC (Marrow or Apheresis) donation

- 4.12.4. Serious product events and adverse effects Registry (SPEAR) (to be reported by collection center)

When a serious event or adverse effect has occurred in relation to stem cell harvest and processing from unrelated donors, the report “Spear form” has to

be completed for the central reporting system of Serious events and Adverse Effects Registry of WMDA. (see reference documents)  
The Collection Center center must send to the MDPB-R.

General issues:

The general principles request that events likely to result from a defect in the stem cell product should be reported if they lead to one or more of the following outcomes in the recipient:

1. Death
2. Life-threatening disease
3. Unexpected hospitalization or considerable prolongation of existing hospitalization.
4. Persistent of significant disability/incapacity.

Specific issues related to products HPC (Marrow or Apheresis) or TC, A which should be reported:

- Inadequate cell dose
- Any serious impairment of the quality of the stem cell product including coagulation and contamination
- Serious problems in transportation
- Serious problems with product identification/labeling
- Wrong stem cell product transfused
- Any serious unpredicted transmissible infection
- Any serious unpredicted non-infectious transmissible disease

4.12.5. Incident report (to be reported by transplant center).

The incident report must be completed by the transplant center and sent to the MDPB-registry using the “MDPB049 Incident report V2 2011”.

Donor centers, collection centers and cord blood banks use the WMDA SEAR (serious events and adverse reactions) and SPEAR (serious product events and adverse effects) forms to report incidents.

4.12.6. The Registry must comply with governmental regulations including requirements to report such adverse events to a regulatory agency. (copy to the Registry). Reports of adverse events affecting a donation must be submitted to the Registry involved in the transplantation if the event might affect an initial or subsequent donation.

Donor health issues post-donation potentially affecting the health of a patient having received a hematopoietic stem cell donation from that donor must be reported to the Transplant center.

Adverse events affecting donors undergoing harvest of hematopoietic stem cells and occurring long term as a consequence of the donation must be defined, identified, documented, investigated and corrective action taken. Similar actions must be taken for adverse events occurring due to Registry operations and impacting the health and safety of donors or patients. Donors are entitled to receive at least minimal information how the patient for whom they provided stem cells is doing, as the donation is performed voluntarily and not remunerated. This is a way to “reward” the donor.

#### 4.12.7. Missing status report

If any report of the above chapters has not been provided after 5 reminders by the staff of the MDPB-R, the file will be closed off. In case the information cannot be provided, the form "MDPB048 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 shall have a regularly updated quality assurance program.

4.13.2. This program shall include formal accreditation of Donor, Collection and Transplant Centers by the MDPB-vzw/asbl on a regular basis.

- The criteria for accreditation of Donor, Collection and Transplant Centers are listed in the SOP.
- The accreditation shall be granted for a minimum of 1 year and a maximum of 3 years. Towards the end of the previous accreditation period, the board of the MDPB-vzw/asbl shall decide the duration of the next accreditation period.
- The board of the MDPB-vzw/asbl shall review the status of each donor, collection and Transplant Center before expiration of the current period of accreditation. This review shall include compliance with the SOP and verification of all accreditation criteria as listed in the SOP. If necessary, the board may decide to perform on-site visits.
- The board of the MDPB-vzw/asbl then prepares a list of centers proposed for accreditation. The general assembly of the MDPB-vzw/asbl takes the final decision on that list of accredited centers.

4.13.3 The quality assurance program shall include a formal annual review of all patient follow-up report forms, donor follow-up report forms, and HPC (Marrow or Apheresis) or TC, A collection report forms. This review shall be performed by the Quality Assurance Committee (QAC) of the MDPB-vzw/asbl. The annual report of the QAC shall be reviewed by the board of the MDPB-vzw/asbl and then submitted for final approval to the General Assembly of the MDPB-vzw/asbl.

4.13.4. In case a center does not comply with the SOP, the board of the MDPB-vzw/asbl will take all necessary steps to ensure further compliance with the SOP. This may include temporary suspension of the accreditation of that center by the MDPB-vzw/asbl. This temporary suspension must be confirmed by the next General Assembly of the MDPB-vzw/asbl.

4.13.5. If the center does not take appropriate corrective action to ensure compliance with the SOP, the General Assembly of the MDPB-vzw/asbl may decide to remove the accreditation of that donor, collection or Transplant Center by the MDPB.

4.13.6. It is the responsibility of the MDPB-R to review annually the centers' compliance with the SOP. The certificates of accreditation by MDPB-R (Donor Center, Collection Center, Transplant Center) include all SOP criteria and the Quality assurance review to comply to for annual accreditation.

## 5. OFFICIAL FORMS

MDPB001 preliminary search request v2 2011  
MDPB001a preliminary search request - international patient v2 2011  
MDPB002 DNA typing request v2 2011  
MDPB003 blood sample request for verification (confirmatory) typing v2 2011  
MDPB004 discrepant typing v2 2011  
MDPB005 verification (confirmatory) typing results v2 2011  
MDPB006 formal request for stem cell collection (HPC, Marrow or HPC, Apheresis)  
v2 2011  
MDPB007 formal request for lympho collection (TC, Apheresis) v2 2011  
MDPB008 second donation request v2 2011  
MDPB009 final compatibility test results v2 2011  
MDPB010 prescription BM (HPC, Marrow) v2 2011  
MDPB011 prescription PBSC (HPC, Apheresis) v2 2011  
MDPB012 prescription lympho (TC, Apheresis) v2 2011  
MDPB013 verification BM (HPC, Marrow) v2 2011  
MDPB014 verification PBSC (HPC, Apheresis) v2 2011  
MDPB015 verification lympho (TC, Apheresis) v2 2011  
MDPB016 donor final clearance v2 2011  
MDPB017 courier information v2 2011  
MDPB018 transport audit v2 2011  
MDPB019 collection report BM (HPC, Marrow) v2 2011  
MDPB020 collection report PBSC (HPC, Apheresis) v2 2011  
MDPB021 collection report lympho (TC, Apheresis) v2 2011  
MDPB022 RIZIV/INAMI doc v2 2011  
MDPB023 donor insurance request v2 2011  
MDPB024 patient follow up report v2 2011  
MDPB025 donor follow up report 30 days v2 2011  
MDPB026 donor follow up report 1-5 year v2 2011  
MDPB027 info consent blood sample collection NL v2 2011  
MDPB028 info consent blood sample collection FR v2 2011  
MDPB029 info consent for donor recruitment into the Registry NL v2 2011  
MDPB030 info consent BM donation NL v2 2011  
MDPB031 info consent PBSC donation NL v2 2011  
MDPB032 info consent lympho donation NL v2 2011  
MDPB033 info consent for donor recruitment into the Registry FR v2 2011

MDPB034 info consent BM donation FR v2 2011  
MDPB035 info consent PBSC donation FR v2 2011  
MDPB036 info consent lympho donation FR v2 2011  
MDPB037 customs form v2 2011  
MDPB038 MAC request for review v2 2011  
MDPB039 MAC approval v2 2011  
MDPB040 accreditation form transplant center v2 2011  
MDPB041 accreditation form collection center v2 2011  
MDPB043 accreditation form donor center v2 2011  
MDPB044 update request donor SOP and forms v2 2011  
MDPB045 additional invoice donor sample transport v2 2011  
MDPB046 request for unrelated donor to participate in a research study v2 2011  
MDPB047 fee schedule donor v2 2011  
MDPB048 notification of missing status report v2 2011  
MDPB049 incident report v2 2011

## 6. LIST OF DONOR, COLLECTION AND TRANSPLANT CENTERS

### URD DONOR CENTERS

#### ANTWERPEN

Dr. V. Compernelle  
Bloedtransfusiecentrum Antwerpen  
Wilrijkstraat 8  
2650 Edegem  
Contact: Dr. B. Moldenhauer  
Tel: 03/829 00 00  
Fax: 03/829 01 61  
Email: [stamceldonorantwerpen@rodekruis.be](mailto:stamceldonorantwerpen@rodekruis.be)

#### BRUGGE

Dr. M. Hidajat  
A.Z. Sint Jan  
Hematology lab  
Ruddershove,10  
8000 Brugge  
Tel: 050/45 26 10  
Fax: 050/45 26 19  
Contact : Dr. Hidajat  
Email: [melanny.hidajat@azbrugge.be](mailto:melanny.hidajat@azbrugge.be)

#### GENT

Dr. C. Matthys  
Bloedtransfusiecentrum Oost-Vlaanderen  
Ottergemse steenweg 413  
9000 Gent  
Email: [Conny.matthys@rodekruis.be](mailto:Conny.matthys@rodekruis.be)  
Tel : 09/ 244 56 61 or 56  
Fax : 09/ 244 56 64  
Administrative contact person: Nathalie Turpin  
Tel : 09/244 56 65 or 56  
Fax: 09/244 56 64  
Email: [stamceldonorgent@rodekruis.be](mailto:stamceldonorgent@rodekruis.be)

## **LEUVEN (Sofhea)**

Prof. G. Verhoef  
Medical contact: Prof. T. Devos  
Contact: Carla Collijs / Diane Reggers  
U.Z. Leuven Campus Gasthuisberg  
Herestraat,49  
3000 Leuven  
Tel: 016/346 882  
Fax: 016/346 883  
Email: [gregor.verhoef@uzleuven.be](mailto:gregor.verhoef@uzleuven.be)  
[Timothy.devos@uzleuven.be](mailto:Timothy.devos@uzleuven.be)  
[Carla.collijs@uzleuven.be](mailto:Carla.collijs@uzleuven.be)  
[Diane.Reggers@uzleuven.be](mailto:Diane.Reggers@uzleuven.be)  
[Marie-paule.emonds@rodekruis.be](mailto:Marie-paule.emonds@rodekruis.be)

## **MONT – GODINNE**

Dr. JC. Osselaer  
Etablissement de Transfusion Sanguine de Mont-Godinne  
rue G. Thérasse,1  
5530 Yvoir  
Contact : M-C. Vandendaele  
Tel: 081/42 32 18  
Fax: 081/42 32 39  
Email: [marie-claire.vandendaele@uclouvain.be](mailto:marie-claire.vandendaele@uclouvain.be)

## **SFS (LIE-UCL-ULB)**

Pr Deneys – Dr Lambermont  
Service Francophone du Sang  
Rue des Dames Blanches 34  
5000 Namur  
Contact : Pascale Van Muylder, Nadine Wanten  
Tel : 02 / 764 68 98 04/ 366 75 45  
Email : [v.deneys@redcross-transfusion.be](mailto:v.deneys@redcross-transfusion.be)  
[m.lambermont@redcross-transfusion.be](mailto:m.lambermont@redcross-transfusion.be)  
[donneurs.csh@redcross-transfusion.be](mailto:donneurs.csh@redcross-transfusion.be)

## **VUB**

Dr. C. Demanet  
HLA Laboratory UZ Brussel  
Laarbeeklaan,105  
1090 Brussel  
Contact person : Dr. C. Demanet  
Tel: 02/477 67 09 Secret: 02/477 67 04  
Fax: 02/477 67 28  
Email: [christian.demanet@uzbrussel.be](mailto:christian.demanet@uzbrussel.be)

## COLLECTION CENTERS

### **ANTWERPEN: "UZA"**

Prof. Z. Berneman  
Universitair Ziekenhuis Antwerpen  
Wilrijkstraat, 10  
2650 Edegem  
Contact: Prof. Berneman  
Administrative contact: Karin Bal / Pascale De Graef  
Tel: 03/ 821 32 32  
Fax: 03/ 821 42 86  
Email : [datacenter.hematologie@uza.be](mailto:datacenter.hematologie@uza.be)

### **BRUGGE: "SJB"**

Dr. J. Billiet  
A.Z. Sint Jan  
Ruddershove, 10  
8000 Brugge  
Contact: Dr. J. Billiet  
Tel: 050/45 26 10  
Fax: 050/ 45 26 19  
Email: [joan.billiet@azbrugge.be](mailto:joan.billiet@azbrugge.be)

### **BRUSSEL - VUB: "VUB"**

Prof. Dr. Rik Schots  
UZ Brussel  
Laarbeeklaan, 101  
1090 Brussel  
Tel: 02/ 477 51 71  
Fax: 02/ 477 80 10  
Email: [rik.schots@uzbrussel.be](mailto:rik.schots@uzbrussel.be)

### **BRUXELLES - UCL: " UCL "**

Dr Catherine Lambert  
Cliniques Universitaires St Luc  
av. Hippocrate,10  
1200 Bruxelles  
Medical contact person : Prof Ferrant  
Administrative contact person : Pascale Van Muylder  
Tel: 02/ 764 17 40  
Fax: 02/ 764 69 38  
Email: [catherine.lambert@uclouvain.be](mailto:catherine.lambert@uclouvain.be)  
[csH-saintluc@uclouvain.be](mailto:csH-saintluc@uclouvain.be)

**BRUXELLES - BORDET: "ULB"**

Prof. D. Bron  
Institut Jules Bordet  
Rue Héger Bordet, 1  
1000 Bruxelles  
Medical contact : Prof. Bron  
Administrative contact: Ms. Leroy  
Tel: 02/541 32 32  
Fax: 02/ 544 02 57  
Email: [dbron@ulb.ac.be](mailto:dbron@ulb.ac.be)

**GENT: "UZG"**

Prof. L. Noens  
U.Z. Gent  
De Pintelaan, 185  
9000 Gent  
Tel: 09/ 332 21 31  
Fax: 09/ 332 27 37  
Email: [lucien.noens@ugent.be](mailto:lucien.noens@ugent.be)

**LEUVEN GASTHUISBERG: "KUL"**

Prof. G. Verhoef  
Medical contact: Dr. D. Dierickx  
U.Z. Leuven Campus Gasthuisberg  
Herestraat, 49  
3000 Leuven  
Contact: Carla Collijs / Diane Reggers  
Tel: 016/ 34 68 82  
Fax: 016/ 34 68 83  
Email: [gregor.verhoef@uzleuven.be](mailto:gregor.verhoef@uzleuven.be)  
[daan.dierickx@uzleuven.be](mailto:daan.dierickx@uzleuven.be)  
[carla.collijs@uzleuven.be](mailto:carla.collijs@uzleuven.be)  
[diane.reggers@uzleuven.be](mailto:diane.reggers@uzleuven.be)

**LIEGE CHU: "LIE"**

Prof. Y. Beguin  
CHU Sart Tilman  
4000 Liege  
Tel : 04/366 72 01  
Fax : 04/366 88 55  
Email: [yes.bequin@chu.ulg.ac.be](mailto:yes.bequin@chu.ulg.ac.be)  
Medical Contact: Dr. E. Baudoux  
Laboratoire de Thérapie Cellulaire  
Dept of Haematology  
Tel: 04/366 83 94  
Fax: 04/ 366 83 91  
Email : [e.baudoux@chu.ulg.ac.be](mailto:e.baudoux@chu.ulg.ac.be)  
Administrative contact : Nadine Wanten  
Tel: 04/366.84 56  
Fax: 04/366.75.47  
Email: [n.wanten@redcross-transfusion.be](mailto:n.wanten@redcross-transfusion.be)

**MONT GODINNE: “GOD”**

Head: Dr. JC. Osselaer  
Etablissement de Transfusion Sanguine de Mont-Godinne  
rue G. Thérasse,1  
5530 Yvoir  
Tel : 081/42 32 42  
Fax : 081/42 32 39  
Email: [jean-claude.osselaer@uclouvain.be](mailto:jean-claude.osselaer@uclouvain.be)

<b>URD TRANSPLANTATION CENTERS</b>
------------------------------------

**ANTWERPEN: “UZA”**

Prof. Z. Berneman  
Universitair Ziekenhuis Antwerpen  
Wilrijkstraat, 10  
2650 Edegem  
Contact: Prof. Berneman  
Administrative contact : Karin Bal / Pascale De Graef  
Tel: 03 /821 32 32  
Fax: 03 /821 42 86  
Email : [datacenter.hematologie@uza.be](mailto:datacenter.hematologie@uza.be)

**ANTWERPEN: “ANS”**

Prof. P. Zachée  
ZNA  
Campus Stuivenberg  
Lange Beeldekensstraat 267  
2060 Antwerpen  
Tel : 03/217 71 11  
Fax: 03/217 72 32  
Email: [pierre.zachee@skynet.be](mailto:pierre.zachee@skynet.be)

**BRUGGE: “SJB”**

Dr. D. Selleslag  
A.Z. Sint Jan  
Department of Hematology  
Ruddershove,10  
8000 Brugge  
Contact: Dr. D. Selleslag  
Tel: 050/ 45 30 60  
Fax: 050/ 45 25 93  
Email: [dominik.selleslag@azbrugge.be](mailto:dominik.selleslag@azbrugge.be)

**BRUSSEL - UZB: “VUB”**

Prof. Dr. R. Schots  
U.Z. Brussel  
Laarbeeklaan,101

1090 Brussel  
Tel: 02 477 51 71  
Fax: 02 477 80 10  
Email: [rik.schots@uzbrussel.be](mailto:rik.schots@uzbrussel.be)

**BRUXELLES - UCL: "UCL"**

Dr. C. Lambert  
Prof. Vermynen (for children)  
Cliniques Universitaires St Luc  
av. Hippocrate,10  
1200 Bruxelles  
Prof Ferrant :  
Tel : 02/764 18 00  
Fax : 02/764 89 59  
Prof Vermynen :  
Tel : 02/764 25 50  
Fax : 02/764 89 16  
Administrative contact : Pascale Van Muylder  
Tel : 02/764 17 40  
Fax : 02/764 69 38  
Email: [catherine.lambert@uclouvain.be](mailto:catherine.lambert@uclouvain.be)  
[christiane.vermylen@uclouvain.be](mailto:christiane.vermylen@uclouvain.be)  
[csh-saintluc@uclouvain.be](mailto:csh-saintluc@uclouvain.be)

**BRUXELLES - BORDET: "ULB"**

Prof. D. Bron  
Institut Jules Bordet  
Rue Heger Bordet,1  
1000 Bruxelles  
Children : Dr Ferster  
Reine Fabiola  
Contact: Prof. D. Bron  
Dr. Ferster:  
Tel : 02/477 32 83  
Fax: 02/477 26 78  
Administrative contact: Sabine Ackermans  
Sandra Michiels  
Tel:02/ 541 32 32 or 02/541 37 28  
Fax: 02/ 544 02 57  
Email: [dbron@ulb.ac.be](mailto:dbron@ulb.ac.be)  
[sabine.ackermans@bordet.be](mailto:sabine.ackermans@bordet.be)  
[sandra.michiels@bordet.be](mailto:sandra.michiels@bordet.be)

**GENT: “UZG-UGP”**

Prof. L. Noens (for adults) UZG  
Prof. Y. Benoit (for children) UGP  
U.Z. Gent  
De Pintelaan, 185  
9000 Gent  
Contact:  
Prof. L. Noens (adults)  
Tel : 09/ 332 21 25 (office)  
Fax: 09/ 332 27 37  
Email: [lucien.noens@ugent.be](mailto:lucien.noens@ugent.be)  
[yves.benoit@ugent.be](mailto:yves.benoit@ugent.be)  
[HILA.MUD@rodekruis.be](mailto:HILA.MUD@rodekruis.be)

**LEUVEN Gasthuisberg: “KUL”**

Prof. G. Verhoef  
U.Z. Leuven Campus Gasthuisberg  
Herestraat, 49  
3000 Leuven  
Medical contact: Prof. J. Maertens  
Tel : 016/34 68 80  
Fax: 016/34 68 81  
Administrative contact: Carla Collijs / Diane Reggers  
Tel : 016/34 68 82  
Fax: 016/34 68 83  
Email: [gregor.verhoef@uzleuven.be](mailto:gregor.verhoef@uzleuven.be)  
[johan.maertens@uzleuven.be](mailto:johan.maertens@uzleuven.be)  
[carla.collijs@uzleuven.be](mailto:carla.collijs@uzleuven.be)  
[diane.reggers@uzleuven.be](mailto:diane.reggers@uzleuven.be)

**LIEGE CHU: “LIE”**

Prof. Y. Beguin  
CHU Sart Tilman  
4000 Liege  
Tel : 04/366 72 01  
Fax: 04/366 88 55  
Email: [yves.beguin@chu.ulg.ac.be](mailto:yves.beguin@chu.ulg.ac.be)  
Medical Contact: Dr. E. Baudoux  
Laboratoire de Thérapie Cellulaire  
Dept of Haematology  
Tel : 04/366 83 94  
Fax: 04/366 83 91  
Email : [e.baudoux@chu.ulg.ac.be](mailto:e.baudoux@chu.ulg.ac.be)  
Administrative contact : Nadine Wanten  
Tel : 04/366 84 56  
Fax: 04/366 75 47  
Email: [n.wanten@redcross-transfusion.be](mailto:n.wanten@redcross-transfusion.be)

## **7. TASKS/RESPONSABILITIES OF EACH CENTER AND THE MDPB-R AND MDPB- VZW/ASBL SCIENTIFIC COMMITTEE**

### **7.1. MDPB-R**

#### **7.1.1. CRITERIA**

MDPB-R must be a legal entity that guarantees administrative and financial operation with a fixed physical location.

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 must maintain a database of volunteer 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 the transmission must be organized that unauthorized access is prevented –confidentiality is guaranteed.

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

Changes to the status of a of the Registry that may effect WMDA accreditation must be brought to the attention of the WMDA in a timely fashion.

MDPB-R must be a WMDA organizational member. The Registry must complete the WMDA Annual Report Questionnaire.

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

#### **7.1.2. TASKS**

Administrative and financial management of the Belgian donor program.

7.1.2.1. Management of the BM/PBSC donor database. The Coordinator and Board of the Registry define which equipment to be used in line with the International procedures. The coordinator acts as the Belgian representative at International meetings of the registries.

7.1.2.2. Searches for patients from Belgium and abroad: consultation of the database of the MDPB-R (incl. Belgian cord blood bank) and all registries connected into the BMDW through EMDIS (modem), BMDW (Internet) or by fax and of the Netcord network of cord blood banks.

7.1.2.3. 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

7.1.2.4. 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

7.1.2.5. Once a donor has been selected by the Transplant Center, the Registry is coordinating the work-up 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, Marrow by courier
- transmission of the HPC, Marrow prescription form
- notification of the insurance company
- notification of customs at the airport

7.1.2.6. After delivery of the cells to the Transplant Center, the Registry will

- check if the Transplant Center completed the HPC, Marrow delivery report and forward the document to the Collection Center
- send regular follow-up forms for patients abroad

7.1.2.7. a. Invoices for international patients are made by the Registry and sent to the requesting center for

- Typing requests
- Bone marrow or PBSC or lymphocyte collections
- Cord blood delivery requests
- Workup Cancellations of Belgian donors.

Prices are defined by the Board of the Registry. Changes in the fee schedule must be provided to the interested parties 30 days prior to implementation. Billing should occur within 60 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 Center; Donor Centers, HLA labs and cord blood banks.

(The Registry will send order forms to the involved centers for all services rendered). The Registry is not responsible if invoices are not paid.

b. Invoices for national patients are made by the Registry and sent to the requesting center for (until 31/03/2011):

- Additional typing requests
- Verification (confirmatory) typing results on Belgian samples and international blood samples.

Payments by the Transplant Center are made to the Registry who will then distribute a fee as agreed between the different parties involved, after a receiving an invoice. (procedure see a).

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

- 7.1.2.8. Invoices from registries/centers abroad are re-invoiced to the Transplant Centers that initiated the request. Payment to the MDPB-R should be made in the foreign currency to the Registry for the full amount invoice, free of bank charges within 30 days. The Registry regularly sends statements of account and request to pay outstanding invoices. The Registry settles the international invoices in due course.
- 7.1.2.9. The Registry is responsible for the financial management of the donor recruitment cfr agreement RIZIV/INAMI for the period 1/9/2008 – 31/08/2013. The Registry sends quarterly global invoices for the new donor registrations to the RIZIV/INAMI. The Registry will send quarterly order forms to the labs for the typing of the new donor registrations and to the Donor Centers for the registration of the administration costs.
- 7.1.2.10. Statistics: the Registry collects monthly updates on the activities of the Registry.
- 7.1.2.11. Primary contact with the insurance company concerning the policy/contract for the Belgian donors and requests for reimbursement in case of complications post donation.
- 7.1.2.12. Maintain an updated list of participating transplant/donor/collection/HLA typing centers. Printing and distribution of SOPs, forms, brochures and leaflets to all centers as defined during the board meetings or upon request.
- 7.1.2.13. Day to day contact with the Belgian and foreign centers in accordance to the national SOPs, guidelines defined by the Board and the International guidelines. Consults with the vzw. for any medical/scientific question for which no procedures have been defined during previous board meetings to obtain a consensus.
- 7.1.2.14. 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.

## 7.2. Donor Centers

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

- 7.2.1. Each Donor Center is connected with MDPB-R, which is in charge of centralizing data and searching for patients.
- 7.2.2. Each Donor Center is responsible for updating information on its donors and for transmitting consequently all available information to MDPB-R.
- 7.2.3. The Donor Center is responsible for adequate typing of their donors in an accredited HLA typing center.

- 7.2.4. 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 CT sample drawing
  - checking availability (delete donor from Registry database if unavailable)
  - arranging infectious disease marker testing (repeat if > 30 days since last screening)
  - arranging medical exam prior to bone marrow/PBSC/lymphocyte collection
  - informing the Registry for arranging insurance coverage
  - collaborating with the Collection Center
  - ensuring that the required forms for BM/PBSC/lymphocyte collection are completed and forwarded to the Registry
  - informing the Registry and Collection Centers if complications occur post-donation
  - ensuring the donor receives no invoices post-donation
- 7.2.5. Invoices for shipment of blood sample are sent to the requesting center directly (no pass through the Registry).

### 7.3. Collection Centers

Collection of BM/PBSC/lymphocytes in accordance with the national SOPs

- 7.3.1. The Collection Center is fully responsible for
- ensuring the donor is capable of donating either Bone marrow or PBSC or lymphocytes
  - ensuring that an adequate number of autologous blood unit has been stored prior to bone marrow collection if indicated
  - agreeing with the Transplant Center on how to collect the cells (Bone marrow or PBSC or lymphocytes, number of cells, anticoagulant, medium, etc)
  - correct labeling of the bags
  - completing the cell delivery forms
  - ensuring that the patients' 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
- 7.3.2. The hospital is requested to invoice the Registry for the BM/PBSC/lymphocyte collection. This invoice should include all costs.
- 7.3.3. 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.

- 7.3.4. The Collection Center is fully responsible for ensuring the quality of the cell collections in accordance with the SOP. This includes providing their bone marrow or PBSC/lymphocyte collection reports and the donor follow-up report forms in a timely fashion.
- 7.3.5. The Collection Center is responsible for the administrative follow-up of the donor post-donation.

#### 7.4. Transplant Centers

- 7.4.1. 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.
- 7.4.2. 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 work-up of the donor), BM/PBSC/lymphocyte prescription form, details on the courier, etc.
- 7.4.3. The Transplant Center has to provide a courier for the transportation of the bone marrow or PBSC. It is responsible for ensuring the transport of cells from the Collection Center to the Transplant Center.
- 7.4.4. The Transplant Center must provide MDPB-R patient follow-up report forms in a timely fashion. The Transplant Center is also responsible for sending patient follow-up forms requested by foreign registries.

#### 7.5. MDPB-VZW/ASBL- Scientific committee

- 7.5.1. The MDPB-vzw/asbl is responsible for general medical/scientific supervision of the SOP. The MDPB-vzw/asbl consist of a general assembly, a board and a number of committees.
- 7.5.2. The MDPB-vzw/asbl provides medical/scientific support to its members.
- 7.5.3. The MDPB-vzw/asbl is responsible for the SOPs: design, regularly reviews and amendments (distribution by the Registry). The board may incorporate urgent amendments into the SOP but all changes must be approved by the general assembly.
- 7.5.4. The MDPB-vzw/asbl 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.
- 7.5.5. The general assembly of the MDPB-vzw/asbl elects the board of the MDPB-vzw/asbl every 4 years.
- 7.5.6. The general assembly of the MDPB-vzw/asbl. designates the members of the medical advisory committee (MAC) for a term of 4 years. The MAC must be consulted for any medical question /

procedure not covered by the SOP and this committee will take the final decision.

- 7.5.7. The general assembly of the MDPB-vzw/asbl. designates the members of the quality assurance committee (QAC) for a term of 4 years. The QAC is responsible for the annual review of all patient follow-up report forms, donor follow-up report forms, and bone marrow or PBSC/lymphocyte collection report forms. The annual report of the QAC shall be reviewed by the board of the MDPB-vzw/asbl and then submitted for final approval by the General Assembly of the MDPB-vzw/asbl.
- 7.5.8. Upon proposal by the board of the MDPB-vzw/asbl, the general assembly of the vzw/asbl decides on the list of centers that will be accepted as Donor - Collection and Transplant Center.
- 7.5.9. The board of the MDPB vzw/asbl takes all necessary steps to ensure compliance of participating centers with the SOP. This may include temporary suspension of accreditation that must be confirmed by the next General Assembly of vzw. The General Assembly of the MDPB-vzw/asbl may decide to remove the accreditation of that center.
- 7.5.10. The MDPB-vzw/asbl 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.

#### 7.6. 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 and financial responsibilities.

This agreement will be signed by the General directors of Rode Kruis Vlaanderen and Croix Rouge de Belgique, and the president of the MDPB-vzw/asbl by the one hand and by the Medical director and the Financial director of the hospital or other institution as appropriate on the other hand.

## **8. INFORMATION TECHNOLOGY AND INFORMATION MANAGEMENT**

### 8.1. General information management

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

- 8.1.1. The Registry must maintain records of its activities and must maintain a database of cord blood information.
- 8.1.2. All patient and donor communications and records must be stored to ensure confidentiality and to allow for traceability of the donors and steps of the donation process.
  - 8.1.2.1 The Registry must assign a unique and anonymous identifier to each cord blood unit. This identifier must be used to track cord blood unit with their associated data and biological material and their participation in the donation process long term.
  - 8.1.2.2 The registry's documentation must describe the rules for handling information pertaining to patients, donors and search processes.
  - 8.1.2.3. The system of quality management shall include an assessment of all electronic functions to ensure that errors and problems are reported and resolved.
  - 8.1.2.4 The access to donor and patient data information in the registry as well as the transmission of this information to and from the registry must be organized in a way that accidental or unauthorized access, destruction or modification is prevented and confidentiality is guaranteed.
  - 8.1.2.5 Records must be maintained for an appropriate period of time, at least as dictated by national laws or standards. Key documents related to cord traceability must be maintained at a minimum for thirty (30) years following donation. Data storage may be on paper or in electronic form.

### 8.2. System administration

- 8.2.1. The key components of a Registry's hardware, software and network architecture and external connections must be adequately documented.
- 8.2.2. Electronic connection and communication with the outside world must be organized and performed with greatest possible care minimizing vulnerabilities and exploitation risks.
- 8.2.3. Redundant or fault tolerant software and hardware architecture should be used as much as technically and economically feasible to reduce the probability of failure or data loss and the possible length of a down time.
- 8.2.4. Backup of all systems and data must be performed regularly at reasonable intervals. Backups must be validated by data restoration tests. These activities must be documented.
- 8.2.5. The overall documentation system must provide all information necessary for trained and skilled staff to keep the IT systems operational.
- 8.2.6. A procedure for the definition, specification, implementation, validation and authorization of relevant systems (software, hardware, network) must be

established and documented. Each such process itself must be appropriately documented on a continuous basis.

- 8.2.7. Any such system installed must be accompanied with adequate documentation for its maintenance (in particular detail if developed in house), administration and operation.
- 8.2.8. Any modifications to such systems must be performed in a way fulfilling 5.03.1 and 5.03.2.
- 8.2.9. Reliance on any one individual should be minimized and critical technical components should be redundant wherever possible.
- 8.2.10. Any function described in 5.01, 5.02 and 5.03 may be performed by or with the help of third parties (e. g. a company or a university). If so, the registry must make sure that the qualification of the respective partner and the quality of the service provided fulfills all requirements specified here. Responsibilities of both parties must be described in writing.

### 8.3. Essential Functionality of IT Systems

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

### 8.4. Software application Syrenad

The software application SYRENAD facilitates the search process for unrelated donors and Cord blood units for the benefit of patients in need of a stem cell transplantation. SYRENAD provides a link with international registries (connected to the EMDIS network) and operates in accordance with international procedures and in compliance with the SOP'S. (Collaboration agreement between the participating parties).

### 8.5. Collaboration cooperative centers – MDPB-R

The CBB and MDPB-R work in close collaboration on future projects to be implemented in new EMDIS releases.

## 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
BM	Bone Marrow
BMDW	Bone Marrow Donors Worldwide
CB	Cord Blood
DLI	Donor Lymphocyte Infusion
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
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
TC	Therapeutic cells
HPC, A	HPC, Apheresis
HPC, M	HPC, Marrow
HPC, CB	HPC, Cord Blood
TC, A	TC, Apheresis
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
NAT	Nucleic Acid Testing
NC	Nucleated cells
NMDP	National Marrow Donor Program
PBSC	Peripheral Blood Stem cells
QAC	Quality Assurance Committee
SEAR	Serious events and adverse events
SOP	Standard Operating Procedures
SPEAR	Serious product events and adverse effects Registry
SYRENAD	Software application used by MDPB-R, developed by French Registry (FGM)
TC	Therapeutic Cells
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)".

## 10. REFERENCE DOCUMENTS

SEAR	Sear Manual Version 1.4 September 2010
SPEAR	Spear Manual Version 1.2 September 2010
Minutes Clinical Working Group	WMDA congress, Minneapolis October 2010

## 11. STANDARDS

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

<b>EFI STANDARDS</b>	European Federation of Immunogenetics standards, Version 5.6, effective from 1ste May 2009
<b>BELGIAN STANDARDS</b>	HGR/CSS standards Nr 8271 (Hoge Gezondheidsraad / Conseil supérieur de la Santé) (2 July 2008) <a href="http://www.portal.health.fgov.be/portal">www.portal.health.fgov.be/portal</a>
<b>SEATTLE CRITERIA</b>	BLOOD, 15 December 2007, Vol 110, number 13
<b>EUROPEAN DIRECTIVES</b>	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 2006 (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. <a href="http://ec.europa.eu/health/ph_threats/human_substance/legal_tissues_cells_en.htm">http://ec.europa.eu/health/ph_threats/human_substance/legal_tissues_cells_en.htm</a>
<b>JACIE</b>	International standards for cellular therapy product collection, processing and administration. (Fourth edition, October 2008) <a href="http://www.jacie.org">www.jacie.org</a>
<b>WMDA standards</b>	World Marrow Donor Association International standards for unrelated hematopoietic stem cell donor registries. Version January 1, 2011. <a href="http://www.worldmarrow.org">www.worldmarrow.org</a>
<b>EBMT</b>	European Group for Blood and Marrow Transplantation Operational Manual (2004 Revised Edition) EBMT Transplant guidelines and accreditation Indications for unrelated HSCT transplantation :

	<p>“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.” <a href="http://www.ebmt.org">www.ebmt.org</a></p>
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