

**Registre France Greffe de Moelle**

**Agence de la biomédecine**



**OPERATION MANUAL**

**version 03/2009**

# SUMMARY

## CHAPTER 1

### INTRODUCTION

## CHAPTER 2

### ACCREDITATION CRITERIA

- 2.1. Donor Centre
- 2.2. Peripheral Donor Centre
- 2.3. Receiving Centre
- 2.4. Transplant Centre
- 2.5. Collection Centre
- 2.6. Cytapheresis Centre
- 2.7. Cord Blood Bank

## CHAPTER 3

### REGISTRATION OF DONORS

- 3.1. Channels of information
- 3.2. Age criteria
- 3.3. Required aptitudes
- 3.4. Protection of donors
- 3.5. Information given to donors

## CHAPTER 4

### HLA TYPING

- 4.1. HLA typing of a new donor/CBU to be registered
- 4.2. Allelic typing of a donor/CBU at the time of a request for complementary tests
- 4.3. Allelic typing of a donor or CBU/patient pair at the time of work up
- 4.4. Archival storage of results
- 4.5. Minimum criteria of donor/recipient HLA compatibility
- 4.6. Minimum criteria of CBU/recipient HLA compatibility

## CHAPTER 5

### INFECTIOUS DISEASE MARKERS

- 5.1. Unrelated HSC donors
- 5.2. Unrelated cord blood units



## **CHAPTER 12**

### **POST-DONATION FOLLOW-UP**

- 12.1. Immediate post-donation follow-up of donors
- 12.2. Long term follow up of HSC donors
- 12.3. National donors solicited for a second/subsequent donation
- 12.4. Evolution of patients

## **CHAPTER 13**

### **DONOR INSURANCE AND EXPENSES REIMBURSEMENT**

- 13.1. Insuring donors
- 13.2. Insuring donors recruited for an HSC donation
- 13.3. Donor expenses reimbursement

## **CHAPTER 14**

### **CONFIDENTIALITY / ANONYMITY**

- 14.1. Generalities
- 14.2. Respect of donor anonymity while exchanging information between Donor Centres and Receiving/Transplant Centres
- 14.3. Respect of donor anonymity while collecting hematopoietic cells
- 14.4. Respect of donor anonymity during her/his hospitalization for bone marrow harvest
- 14.5. Respect of confidentiality clauses

## **CHAPTER 15**

### **CRYOPRESERVATION OF HEMATOPOIETIC STEM CELLS**

**CHAPTER 1**  
**INTRODUCTION**

## ACRONYMS

AFSSAPS	Agence Française de Sécurité Sanitaire des Produits de Santé / <i>French Bureau of Health Care Products Safety</i>
ASHI	American Society of Histocompatibility and Immunogenetics
BMDW	Bone Marrow Donors Worldwide
CMV	Cytomegalovirus
HSC	Hematopoietic Stem Cells
PBSC	Peripheral Blood Stem Cells
EBV	Epstein Barr Virus
EDS	European Donor Secretariat
EfG	Etablissement français des Greffes / <i>French Transplantation Establishment</i>
EFI	European Foundation of Immunogenetics
EFS	Etablissement Français du Sang / <i>French Blood Establishment</i>
EMDIS	European Marrow Donor Information System
FGM	France Greffe de Moelle / <i>French Registry of Unrelated Stem Cell Donors</i>
GBEA	Guide de Bonne Exécution des Analyses de biologie médicale <i>Guidelines for proper execution of medical biology analysis</i>
RFSP	Réseau Français de Sang Placentaire / <i>French Cord Blood Network</i> <i>(France Cord)</i>
SFGM-TC	Société Française de Greffe de Moelle et de Thérapie cellulaire <i>French Society of Bone Marrow Transplant and Cellular Therapy</i>
TGI	Tribunal de Grande Instance / <i>Magistrate's Court</i>
WMDA	World Marrow Donor Association

France Greffe de Moelle (FGM), **French National Registry of hematopoïetic stem cell donors**, was created in 1986 by Professor Jean Dausset and Professor Jean Bernard for patients awaiting an hematopoïetic stem cell transplant and lacking a donor in their family.

The **legal status** of FGM was until December 31st 2005 that of an association ruled by the French law known as “Loi de 1901”. The Bioethic law of August, 6<sup>th</sup> 2004 has defined the missions of the Biomedicine Agency, including in particular the mission “to manage a file of unrelated hematopoietic and mononuclear cells donors, for patients awaiting a transplantation and lacking a donor in their family”.

Since January 1<sup>st</sup> 2006, the FGM Registry has become one of the direction of the Biomedicine Agency. It keeps complying with international rules, in way of staying the privileged interlocutor for all international Registries and consequently participating in and benefiting from the international exchanges.

Inside the Biomedicine Agency, the Registry has created a **steering committee** composed of expert members representing transplant physicians, donor centers, cord blood banks, receiving centers and also one international Registry. The role of this committee is to study and analyze the processes of the Registry, to propose new directions and objectives and to implement the development strategy defined by the “strategy” group of the medical and scientific department, validated by the administration board, of the Biomedicine Agency.

In order to optimize the implementation of the WMDA quality standards (World Marrow Donor Association), the FGM Registry has created internal committees :

- “WMDA/donor centres”: group surveying and implementing the WMDA standards in donor centers and their peripheral centers
- “WMDA/receiving centres”: group which mission is to define, according to the transplant physicians needs, procedures for searching national and international HSC donors and CBUs
- to come: “WMDA/cord blood banks”: group responsible for surveying and implementing the new WMDA standards in the cord blood banks of the France Cord (RFSP) network.

Different **competences** contribute to the good working of the FGM Registry : physicians supervise the staff responsible of the management and coordination of the patients files,

biostatisticians are in charge of scientific surveys and statistical analysis. Financial and administrative personal, as well as personal in charge of the information system are dedicated to the Registry activities.

FGM receives, for **services rendered**, a payment from the transplant hospitals each time national patients are registered on the National Registry, the International Registries and the Cord Blood Banks. Likewise, services rendered for international patients are paid through the Registries.

FGM is granted the assistance of a **Medical experts Committee** composed of 12 transplant physicians, who are members of the Société Française de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC) and hematologists (= external committee), and 2 physicians from FGM (= internal committee). The committee was created in 2000 when PBSC donation has been first proposed to national unrelated donors. His organization and functioning has been simplified since 2006.

All unrelated HSC donation requests, as well as mononuclear cells, must be validated by the Registry physicians at reception. From now on, the external Medical Committee will only be called upon when the age or diseases of the patient doesn't comply with the EBMT and SFGM-TC recommendations.

Only in this case, the file containing the formal recruitment specifying not only the type and amount of cells requested, but also the precise diagnostic and the exact disease stage, must be accompanied with a detailed letter from the transplant physician explaining her/his therapeutic choice. This file allows the committee members to make a benefit/ risk analysis for the patient/unrelated donor pair.

When the external medical committee is activated, the advice is given by a group composed of 3 experts, successively called upon by e-mail or fax, independent from the concerned donor centre. The maximum delay to return an advice is 48 hours. It is transmitted in an anonymous way by the Registry to the national or international transplant physician who can appeal if need be.

Inside of the Biomedicine Agency, and more precisely in the administrative and financial department, the FGM Registry is the **intermediate as far as administrative and financial** matters are concerned, between French transplant hospitals and International Registries (see chapter 7).

FGM has developed and manages its own **information system** called SYRENAD (SYstème de REcherche National de DONneurs). Integrated to the Biomedicine Agency information system, this system is connected, in real time, to all :

- Donor centres,
- Cord blood banks,
- Receiving centres, privileged interlocutors of the transplant physicians.

The FGM Registry receives, via the Receiving centres, all registration requests for national patients. The registration form is validated and signed by the transplant physician and by the head of the histocompatibility laboratory which has performed the HLA typing of the patient. Administrative departments of transplant hospitals, which cover fees for registration and for complementary testings possibly leading up to transplant, issue at that time an order form number which represent the commitment of the hospitals to pay for the search process correlated costs.

- Administrative departments of national transplant hospitals

and to International Registries via EMDIS.

The **international communication network is called EMDIS** (European Marrow Donor Information System). It was developed in 1990, on the initiative of the FGM Registry, in collaboration with the German, English and Dutch Registries, thanks to a grant from the European Community CE DG XIII AIM 2006.

This decentralized network allows all participating Registries to exchange information, from the patient's registration up to the organization of the stem cell collection. The software is regularly updated in order to take into consideration the new needs expressed by the users.

The Réseau Français de Sang Placentaire (RFSP) called "France Cord" is co-managed by the Biomedicine Agency and the Etablissement Français du Sang (EFS). The FGM Registry is involved in the permanent update and management of the **cord blood units data base**, the management of patients' searches on both national and international cord blood banks, on behalf of the transplant physician, and in the organization of CBU shipment and delivery.

In the name of the Biomedicine Agency, the head of the Registry submits to the AFSSAPS **advices relative to the importation of unrelated hematopoietic cells** for therapeutic use (PBSC, mononuclear cells (DLI) and CBU). These advices are submitted before the formal import authorizations are issued by the AFSSAPS to the cell processing units, correspondent of the transplant centres and responsible for requesting the import permit on a case to case basis.

**CHAPTER 2**  
**ACCREDITATION CRITERIA**

## **2.1 Donor Centre**

### **2.1.1 Definition**

A Donor Centre (DC) is established within either a Blood Transfusion Centre belonging to the “Etablissement Français du Sang” (EFS) or within a hospital.

The Donor Centre works under the responsibility of either the Director of the Blood Transfusion Centre or the Director of the hospital.

The Donor Centre follows the rules of the World Marrow Donor Association (WMDA) and is integrated in the accreditation process of the Donor Centres by the National Registry. It may manage peripheral donor centres.

### **2.1.2 Missions**

- 2.1.2.1** The responsible of the Donor Centre receives delegation of authority from the Director of the establishment.
- 2.1.2.2** The Donor Centre is responsible for the registration, selection and recruitment of potential donors.
- 2.1.2.3** The Donor Centre uses SYRENAD (the software provided by the Registry), to enter the following donors items : civil status, addresses, blood group and HLA typing as well as infectious disease markers.
- 2.1.2.4** The Donor Centre connects daily to the FGM database and works in real time.
- 2.1.2.5** The Donor Centre contacts potential donors in order to carry out any complementary examinations requested by national or international transplant physicians.
- 2.1.2.6** The Donor Centre must keep the data base updated each time a donor’s related information changes, such as civil status or clinical/biological characteristics.
- 2.1.2.7** The Donor Centre can have its own histocompatibility laboratory, ASHI or EFI accredited or has established a contract with ASHI or EFI accredited laboratory.

### **2.1.3 Responsibilities**

To any potential new donors willing to be registered, the Donor Centre must send at first a self-evaluation medical questionnaire to this person, in order to evaluate his/her health in general and to avoid unnecessary trip to the Donor Centre in case of a medical contra-indication would exist.

The Donor Centre is responsible for :

### **2.1.3.1 Informing volunteer donors**

#### **2.1.3.1.1 Peripheral blood and bone marrow stem cell donors**

The person who has expressed the intention to be registered as a stem cell donor can send a registration form either to the Registry, to an Association or to the closest Donor Centre directly.

At the Donor Centre, the potential donor is clearly informed on peripheral blood and bone marrow stem cells donation, by a physician experienced in receiving and selecting donors.

**Each person willing to join the Registry must have first agree to become a bone marrow donor.** Additional commitment to donate peripheral blood stem cells is possible.

Written information is given to the donor during the preliminary medical interview. This information specifies the basic principles of this type of donation : free consent, anonymity, and right to withdraw at any time (Bioethic law of August 8<sup>th</sup> 2004).

A medical assessment is mandatory for the selection and registration of a potential donor in order to detect, at this stage, any contra-indication to stem cell donation. A medical health questionnaire is completed and constitutes the first element of the potential donor's file (questionnaire available on SYRENAD).

A list of formal medical contra-indications to stem cell donation is available on SYRENAD. This list is regularly updated.

The donor is precisely informed of any risks linked to the procedures, in particular those related to the anesthesia, those potentially associated to the growth factor administration, and the constraints of the various collection procedures.

The donor is also informed of his blood testing results and can get a copy of these results.

The donor is additionally informed of the necessity to be easily reachable whenever requested for complementary tests or final recruitment.

The donor agrees on the principle of the conservation and use of collected biological material for complementary analyses.

The donor is informed that a second bone marrow or peripheral blood stem cells donation may be necessary later.

The donor is asked to inform his/her Donor Centre of any changes in his/her address; donor should be aware that this is also necessary in case of a second donation request.

The donor must be able to express if she/he agrees on the principle of donating a second time if needed for the same patient. The transplant physician must be immediately informed in case of refusal.

The donor should be informed that in case of peripheral stem cells harvest procedure failure, a bone marrow harvest will have to be carried out.

The initial consent form is co-signed by the donor and the physician having validated him/her as a stem cell donor and is kept in her/his file (form available on SYRENAD).

#### **2.1.3.1.2 Donation of HLA compatible platelets**

The potential donor is also informed that he/she has the possibility to be registered as donor of HLA compatible platelets.

#### **2.1.3.2 Registration of donor**

The initial donor's file contains :

- the medical health questionnaire used at the time of registration, completed by a physician;
- the initial consent form co-signed by the donor and the physician;
- the registration request form, signed by the donor;
- the result of the HLA class I and II typing (ABCw DRB1)

A biological check-up, including infectious disease markers, according to the current legislation, and the determination of ABO/Rhesus blood group are only available in the donor's file if the donor has previously donated blood in an EFS-blood centre.

Infectious disease markers screening at the time of registration is not longer mandatory for stem cell donors (except in case of blood donation). However the medical interview and checkup are required to verify the donor's motivation and the existence of any medical contraindication.

### **2.1.3.3 HLA typing of the donor**

At the time of registration of a potential donor the HLA typing Class I and II is performed: it should be performed by molecular biology techniques, according to the typing strategy defined by the Biomedicine Agency. Extracting DNA and keeping such a sample as biological reserve is recommended.

### **2.1.3.4 Registration of a donor into the local data-base**

#### **2.1.3.4.1 Data entry**

To enter the information related to a donor, the Donor Centre uses the SYRENAD software. The use of SYRENAD is exclusively reserved to the person correspondent to FGM, who has delivered him/her an access via a personal password. This information includes :

- name, first name, maiden name, sex,
- date of birth,
- Mail address, completed by a second address (parents, friends), stipulating name, first name, complete address, telephone number, and eventually an e-mail address,
- telephone number of residence and of workplace, mobile phone number,
- email address,
- HLA-A, B, Cw, DRB1\*,
- blood group, ABO/Rhesus blood group and viral markers, if known,
- Donor acceptance for the kind of donation (bone marrow and PBSC or bone marrow only),
- Weight / height and BMI,
- For female donors: number of pregnancies,
- Number of blood transfusions.

These data are entered into the SYRENAD database. The FGM Registry proceeds daily to backups.

#### **2.1.3.4.2 Updating of donors' particulars**

The Donor Centre is responsible for updating donors' files, such as cancelation and/or transfer of a donor from a Donor Centre to another because of a change of address. The donor who has moved receives a new ID code from the new Donor Centre. Notices of a change of address are sent to the Donor Centre directly by SYRENAD.

The Donor Centre is responsible for transferring the file of the donor who has changed address to the new Donor Center, that is to say: the medical health questionnaire, the infectious disease markers and the blood group if known, the initial consent form and the HLA typing results.

#### **2.1.3.4.3 Updating of biological data**

The Donor Centre is responsible for :

- 2.1.3.4.3.1** printing after each communication with FGM the results of the matching “patients file”, “donors file”, if necessary
- 2.1.3.4.3.2** either calling in, as soon as possible, the donor if a complementary typing is requested. It is recommended to comply with the delay of 8 days without exceeding 15 days (see WMDA standards),
- 2.1.3.4.3.3** or carrying out the HLA complementary typing requested, using preserved DNA samples, but after having checked the constance of the donor’s commitment by mail or by telephone,
- 2.1.3.4.3.4** ascertaining by questioning the donor that she/he still has no medical contra-indications to stem cell donation and completing a medical health questionnaire added to the donor dossier,
- 2.1.3.4.3.5** updating the data base within the 2 days following the validation of the HLA typing by the biologist responsible of the histocompatibility laboratory,

#### **2.1.3.4.4 Transmission of a donor file from one Donor Centre to another**

The transferred donor file must include :

- a copy of the HLA typing and eventually the viral serology results or even the blood group if performed,
- a copy of the medical health questionnaire and the initial consent.

#### **2.1.3.4.5 Transmission of a donor file when the donor moves to another country**

The donor file must be :

- locally archived if the donor moves to a country that doesn’t have an HSC donor Registry
- transferred to the FGM donor secretariat if donor moves to a country having a HSC Registry. With the donor consent, the secretary will transmit her/his dossier to the concerned international Registry.

### **2.1.3.5 Dispatching of blood samples**

The Donor Centre's responsibility is :

- 2.1.3.5.1** to call in the donor if a blood sample has been requested either by a national transplant physician or by an International Registry. It is recommended to observe a delay of 8 days, with a maximum of 15 days (see WMDA standards),
- 2.1.3.5.2** to ensure that the donor has still no medical contra-indications to stem cell donation, to complete a medical health questionnaire, to verify that she/he is still committed and the type of stem cell donation she/he would consent (bone marrow and PBSC or bone marrow only) and if necessary, to update the file of female donors in terms of number of pregnancies.
- 2.1.3.5.3** to have the donor's blood drawn carried out under the responsibility of a qualified physician belonging either to the Blood Transfusion Establishment or to the Hospital Services, according to the prescription of the transplant physician or of the International Registry,
- 2.1.3.5.4** to have, for the purpose of validating the aptitude of the donor and according to current legislation, the following infectious disease markers carried out :
  - HBs antigen,
  - Anti-HBc antibodies,
  - Anti-HCV antibodies,
  - Anti-HIV1,V2 antibodies,
  - Anti- HTLV1,V2 antibodies,
  - Syphilis screening,
  - CMV antibodies (if unknown or previously negative),
- 2.1.3.5.5** to proceed with ABO/Rh blood group testing if unknown
- 2.1.3.5.6** to have the blood sample sent to the address indicated by FGM either via SYRENAD/EMDIS or via fax (for Registries not connected to EMDIS)
- 2.1.3.5.7** to inform the courier company "May Courier International" with which FGM has signed an agreement and defined transport specifications according to a decree dated April 24<sup>th</sup> 2002, relative to good practice for transporting products and samples collected from human blood,
- 2.1.3.5.8** to inform the Transplant Center or the International Registry of the sample dispatch date, either through SYRENAD/EMDIS or by sending a fax to FGM who will forward the information to non-connected Registries,

**2.1.3.5.9** to prepare, according to current legislation, the parcel which will be picked up by the courier company authorized by FGM. Packaging must comply with IATA requirements,

**2.1.3.5.10** to send, via FGM, as soon as received, the infectious disease markers results to the Transplant Centre or to the International Registry, using either the suitable FGM form or after having entered them on SYRENAD/EMDIS.

#### **2.1.3.6 Capture of HLA typing results**

When the confirmatory typing has been carried out by the HLA laboratory correspondent of the Receiving Centre or the International Registry, the Donor Center captures the results using SYRENAD/EMDIS to update the patient dossier.

The Donor Centre's responsibility is :

**2.1.3.6.1** to capture the results of the HLA typing and the code of the Histocompatibility Laboratory corresponding to the national or international physician having carried out the typing,

**2.1.3.6.2** to inform the donor either of her/his possible selection or of her/his incompatibility with the patient, immediately after reception of the results from the requesting entity.

**2.1.3.6.3** to contact FGM if no result has been transmitted within 6 weeks (45 days) after dispatching blood samples with the purpose of informing the concerned donor.

#### **2.1.3.7 Pre-selection of a donor**

When a donor is pre-selected for donation, either by a national transplant physician or by an International Registry, the Donor Center has the responsibility :

**2.1.3.7.1** to contact the donor and to verify her/his donation commitment, and his/her fitness for donation,

**2.1.3.7.2** to propose and explain to the donor the harvest procedure selected by the transplant physician according to the benefit expected for the patient (bone marrow or PBSC),

**2.1.3.7.3** to propose to the donor the harvesting dates suggested in accordance with the patient's needs,

- 2.1.3.7.4** to verify that the harvesting dates proposed by the transplant physician are accepted by the donor and the Harvesting Centre and to communicate this acceptance to FGM, together with the current weight of the donor (cf : calculation of the estimated quantity of marrow to be harvested),
- 2.1.3.7.5** to inform the donor of the exact location of the harvest and explain step by step the chronology of the harvest
- 2.1.3.7.6** to organize or have the harvesting physician or a local coordinator organize the medical and pre-anesthetic examinations, in accordance with current legislation.

### **2.1.3.8 Donor's aptitude and final clearance**

The final clearance of the donor comes under the responsibility of the harvesting physician or of the physician responsible of performing the cytopheresis.

The Donor Centre has the responsibility :

- 2.1.3.8.1** in the case of a bone marrow donation, to organize or assist the local harvesting physician to organize the pre-anesthetic visit of the donor and the registration of the formal final consent to be signed by the donor at the appropriate Magistrate's Court. It is strongly recommended to address each PBSC donor to the Magistrate's Court, in case the PBSC collection would be insufficient and an emergency bone marrow collection should be organized.
- 2.1.3.8.2** to send to FGM a copy of the donor's final consent, collected from the Magistrate's Court close to her/his area of residence, in accordance with current legislation,
- 2.1.3.8.3** to send to FGM the request for life insurance, which is contracted by FGM for all harvested donors (FGM form 022),
- 2.1.3.8.4** to send to FGM the results of the infectious disease markers carried out in accordance with current legislation, using the FGM form CF 014 (decree N°97-928 dated October 9<sup>th</sup> 1997 relative to sanitary rules, and recommendations of the AFSSAPS, April 2004)
- 2.1.3.8.5** to send to the donor all relevant information concerning the date and place of her/his harvest and the identity of the person in charge of her/his reception and welcome at the Collection Center,
- 2.1.3.8.6** to send to the Cell Processing Unit correspondent to the transplant physician, the medical health questionnaire showing clearance for HSC donation (AFSSAPS recommendation) and the disease markers results,

- 2.1.3.8.7** to have got an agreement with the Administration Department of the Harvesting Centre to cover all expenses related to the harvesting, in way that the donor should be reimbursed in the shortest delays, according to current legislation,
- 2.1.3.8.8** to facilitate the organization of the donor's trip to the Harvesting Center.
- 2.1.3.8.9** to provide the donor with a phone number that he/she will call in case of an emergency occurring the days around the scheduled harvest.

### **2.1.3.9 Harvesting of the recruited donor**

The person in charge of the Donor Centre :

- 2.1.3.9.1** makes sure that the donor has presented her/himself for the harvesting, in compliance with her/his convocation,
- 2.1.3.9.2** gives or has given to the donor the forms allowing her/him to relate her/his experience on the day of harvest and within one month following the harvest,
- 2.1.3.9.3** makes sure that a physician has visited the donor after the harvest and before her/his leaving of the Harvesting Centre,
- 2.1.3.9.4** telephones the donor, eight days after the harvest, in order to collect any suggestions, comments or problems,
- 2.1.3.9.5** reminds the donor that a second marrow donation and even a donation of peripheral blood cells may be needed if the graft is rejected or if the patient relapses and the transplant physician decides to take this therapeutic option.  
The donor must reserve her/himself for a second donation request for the same patient and must be cancelled after donation from the FGM donors file.  
She/he is advised to signal any change of address to the Donor Centre.

## **2.2 Peripheral Donor Centre**

### **2.2.1 Definition**

The Peripheral Donor Centre is a corresponding center to which the Donor Centre delegates the responsibility to welcome the donor for the purpose of registering her/him, or call her/him in for a blood drawn for confirmatory typing.

It adheres to the rules of the WMDA and is integrated, via the Donor Centre, in the process of Donor Centres accreditation performed by the national Registry.

## **2.3 Receiving Centre**

### **2.3.1 Definition**

A Receiving Centre is an entity located either in a Blood Transfusion Establishment belonging to the EFS or in a Hospital unit. It is the privileged interface between FGM and the transplant physicians. It adheres to the rules and standards of the WMDA.

### **2.3.2 Missions**

- 2.3.2.1** The person responsible for the Receiving Centre has received a delegation of authority either from the Head of the Blood Transfusion Establishment or from the Health Establishment.
- 2.3.2.2** It is the correspondent of the transplant physician with whom it jointly manages the files of patients to be registered or already registered on the FGM Registry.
- 2.3.2.3** It validates the HLA typing provided on the patient's registration form which has been sent by the transplant physician.
- 2.3.2.4** It adheres to the WMDA accreditation standards.
- 2.3.2.5** It manages, using SYRENAD software provided by the FGM Registry, the local patient's data base, on behalf of the transplant physician.
- 2.3.2.6** It get connected daily to the FGM Registry database with which it works in real time.
- 2.3.2.7** It controls and validates the HLA typing of the donor/receiver pair.
- 2.3.2.8** It sends the results of the confirmatory HLA typing of the selected donor to the corresponding Donor Centre, via the FGM Registry, each time the Donor Centre sends either a blood sample or DNA samples
- 2.3.2.9** It is equipped with an Histocompatibility Laboratory, ASHI or EFI accredited.

### **2.3.3 Responsibilities**

The Receiving Centre has the following responsibilities :

- 2.3.3.1** to carry out the HLA-A, B, C, DRB1\*, DQB1\*, typing of the patient at the allelic level (4 digits), together with the definition of the parental haplotypes, with the help of a family study. HLA-DPB1\* typing is recommended.
- 2.3.3.2** to validate the registration form (FGM form 001) sent to the national Registry, after verification of the absence of a family donor.

- 2.3.3.3** To send to FGM, within 21 days, in case the form 001 was incomplete (particularly if the allelic typing has not been carried out right away) the complementary data, necessary for the final registration of the patient,
- 2.3.3.4** to perform the final validation of the registration of the patient, performed by the FGM coordinators, using SYRENAD.
- 2.3.3.5** to communicate to the transplant physician any information coming from FGM concerning the management of searches, whether they come from the National Registry or International Registries.
- 2.3.3.6** to send to FGM the messages concerning requests for HLA complementary typing and for blood samples, made by transplant physicians, on behalf of their patients.
- 2.3.3.7** to request complementary exams.  
Requests for HLA-DRB1\*, DQB1\* generic or allelic typing and for HLA Class I allelic typing are made, either via SYRENAD/EMDIS for national donors and International Registries connected to the FGM Registry or via faxed FGM forms for non-connected Registries.
- 2.3.3.8** to request the shipment of blood samples from preselected donors and to carry out the control of the HLA typing initially perform by the Donor Centres.  
Blood samples requests are made either via SYRENAD/EMDIS for national donors and International Registries connected to the FGM Registry or via faxed FGM forms for non-connected Registries.
- 2.3.3.9** to manage search results received from FGM  
Upon receipt of results sent by FGM, the Receiving Centre informs the transplant physician for decision-making. It keeps FGM informed of the physician's decision: pre-selection or non-selection of the donor. He has a maximum delay of 6 weeks (45 days) to make his decision. Decision must be immediately transmitted to the potential donor.
- 2.3.3.10** to verify the HLA typing of the pre-selected donors
- 2.3.3.10.1** Generic typing  
The Histocompatibility Laboratory of the Receiving Centre, ASHI or EFI accredited, carries out the HLA Class I and Class II typing by molecular biology techniques for the purpose of obtaining a non-ambiguous generic result, according to the current WHO nomenclature.

#### **2.3.3.10.2 Allelic typing**

The Histocompatibility Laboratory of the Receiving Centre, ASHI or EFI accredited, carries out the HLA Class I and Class II typing, by molecular biology techniques, for the purpose of obtaining a non-ambiguous allelic result, according to the current WHO nomenclature.

In the case of HLA-A, B, C, DRB1\*, DQB1\* allelic typing requests, a laboratory which cannot deliver a non-ambiguous result, must send the donor DNA sample to an accredited laboratory which can do so, using sequencing techniques.

#### **2.3.3.11 to send the HLA typing results**

The Receiving Center enters in the SYRENAD/EMDIS database the HLA typing results, so the Donor Centre (whether national or international) which has sent the blood samples is kept informed (FGM form 011).

#### **2.3.3.12 to select the donor**

- The final choice of the donor is under the responsibility of the Receiving Centre, in accordance with the transplant physician who requires the HSC collection.
- The final validation of the donor is under the responsibility of the Harvesting Centre.

## **2.4 Transplant Centre**

### **2.4.1 Definition**

A Transplant Centre is an entity located in a Health Establishment. Under the authority of the Head of the Establishment, the transplant physician belongs to a Hematology unit habilitated and authorized to carry out not only autologous transplants but also alloHSC transplants, both related and unrelated.

### **2.4.2 Responsibilities**

The Transplant Centre is responsible for :

#### **2.4.2.1 the registration of the patient on the FGM Registry.**

The transplant physician requests an order form number from the administrative services of his hospital. This number is used for managing the patient's file and invoicing the hospital for all searches performed, including registration and requests for complementary tests, either on the national Registry or on the International Registries.

The transplant physician completes the FGM registration form 001, which becomes a medical prescription. The physician notes the civil status of the patient and completes all items useful to the registration of the patient on the national Registry and International Registries.

The physician chooses which International Registries and/or Cord Blood Banks should be searched.

**2.4.2.2** Prescription for national and international searches

It defines the complementary exams to be requested from the national Registry and International Registries, and/or Cord Blood Banks.

**2.4.2.3** Validation of the list of infectious disease markers of the recruited donor

Upon receipt of the infectious disease markers results of the selected donor, the Receiving/Transplant Centre validates the list which must be conformed to the current legislation (FGM form 014).

If some markers have not been carried out by an International Donor Centre, the Receiving/Transplant Centre is responsible for requesting, via FGM, a blood sample of the donor, drawn in a tube without anti-coagulant, in order to perform the complementary tests.

**2.4.2.4** Sending the donor pre-selection form

The Receiving/Transplant Centre may send to FGM the donor pre-selection form containing all necessary information for the organization of the harvest. FGM is responsible to send this form to the corresponding Donor Centre (FGM form 015).

**2.4.2.5** Sending the HSC prescription form

The Receiving/Transplant Centre may send the FGM form 017 “marrow prescription” or “PBSC prescription” to FGM by fax.

The form contains all necessary information for pre-collection blood samples shipment prior to and on the day of collection and specifies the number of hematopoietic stem cells to be collected. The form also specifies the patient’s conditioning duration and the proposed dates for the harvest.

This form must be signed by the transplant physician then must be validated by the physician in charge of the collection.

The quantity of bone marrow to be collected is calculated in accordance with the weight of the patient and validated in accordance with the weight of the donor.

#### **2.4.2.6** Receiving the donor final clearance form

The FGM form 014 is sent to FGM by the Donor Centre before the transplant date and in any case before the beginning of the patient's conditioning. It is then sent by FGM to the Receiving Centre for the purpose of informing the transplant physician of the final clearance of the donor. Virology tests must be carried out on a blood sample collected in the month preceding the stem cell collection.

**2.4.2.7** Sending to FGM, 8 days at least before the collection, the FGM form 019 reporting all information relative to the organization of the transportation of the hematopoietic stem cells.

**2.4.2.8** Sending to FGM the document attesting the reception of the graft by the Transplant Centre (FGM form 023).

**2.4.2.9** Performing the patient's cancellation on SYRENAD/EMDIS

**2.4.2.10** Sending to FGM the form 021 specifying the transplant date in the exceptional case of previously approved cryopreservation of the HSC,.

**2.4.2.11** In case of importation of PBSC or blood cells (lymphocytes), sending to FGM the copy of the product import permit delivered by the AFSSAPS upon request of the Cell Therapy Laboratory of the Transplant Centre.

Sending to FGM, if the clinical status of the patient requires it, the form 029 requesting a second donation of marrow, PBSC, or lymphocytes.

## **2.5 Harvesting Centre**

### **2.5.1 Definition**

An Harvesting Centre is an entity located in a habilitated Health Establishment. Under the responsibility of the Head of the Establishment, the harvesting physician belongs to a habilitated Hematology unit authorized to carry out either autologous transplants or alloHSC transplants. It is also habilitated to carry out bone marrow harvests.

### **2.5.2 Responsibilities**

The Harvesting Centre is responsible for :

**2.5.2.1** validating the aptitude of the hematopoietic cells donor at the time of the final selection (final consent form available on SYRENAD),

**2.5.2.2** sending to the Donor Centre the report of the pre-anesthetic check-up of the selected donor.

- 2.5.2.3 obtaining if needed and after approval of such a request by the FGM Registry, an anonymous consent from a bone marrow donor to participate in a particular research protocol (form available on SYRENAD or to be requested to FGM), ,
- 2.5.2.4 appointing one or more persons habilitated to carry out marrow harvests.
- 2.5.2.5 harvesting, if possible, the quantity of nucleated cells expected by the transplant physician and collecting the blood samples requested by the prescribing physician.
- 2.5.2.6 sticking on the marrow bags the labels provided by FGM to identify and trace the graft.
- 2.5.2.7 making sure that the courier, designated by the prescribing transplant physician, is present and able to take the responsibility of the graft as soon as the harvesting is finished.
- 2.5.2.8 delivering the collected marrow and the blood samples, if any, in person to the courier according to the name designated by the Transplant Centre (guide of good practices). The graft can also be delivered by the cell processing unit correspondent to the Collection Centre.
- 2.5.2.9 handing over to the courier the FGM form 023 giving the characteristics of the marrow, as well as the airport and customs documents provided by FGM (see chapter 11).

## **2.6 Cytapheresis Centre**

### **2.6.1 Definition**

The Cytapheresis Centre is an entity located in an habilitated Establishment belonging to either the EFS or to an hospital.

### **2.6.2 Responsibilities**

The Cytapheresis Centre is responsible for :

- 2.6.2.1 validating the selected PBSC donor in close cooperation with the hematologist who has medically examined the donor and prescribed the growth factors.
- 2.6.2.2 validating, if it is the case, the lymphocytes donor.
- 2.6.2.3 explaining to the donor, if it is the case, that he is requested to sign an anonymous consent to participate in a particular research protocol (form available on SYRENAD or upon request to FGM).
- 2.6.2.4 appointing one or more persons habilitated to carry out the collections.

- 2.6.2.5** collecting, as precisely as possible, the quantity of CD34+ cells required and the blood samples requested by the transplant physician.
- 2.6.2.6** sticking on the bags the labels provided by FGM to identify and trace the PBSC graft (or the collected lymphocytes, in case of DLI).
- 2.6.2.7** making sure that the courier designated by the prescribing transplant physician is present and able to take the responsibility of the product as soon as the collection is finished.
- 2.6.2.8** handing over to the courier the form providing the characteristics of the PBSC product or lymphocytes as well as the airport and customs forms provided by FGM (see chapter 11).
- 2.6.2.9** sending to FGM, in the case of exportation of the PBSC or lymphocytes collected from a national donor, the copy of the export permit delivered by the AFSSAPS upon request from the Cell Therapy Laboratory of the Collection Centre.

## **2.7 Cord Blood Bank belonging to the RFSP network**

### **2.7.1 Definition**

The Cord Blood Bank is an entity established within a health institution belonging either to the “Etablissement Français du Sang” (EFS) or a hospital department (cell processing unit).

As a member of the RFSP (France Cord), the Cord Blood Bank adheres to quality standards defined by this network and to those of the FACT/Netcord accreditation system.

Moreover the Cord Blood Bank must adhere to the WMDA standards too, as the cord blood units are all registered in the FGM database and the Registry FGM is in charge of their management.

### **2.7.2 Responsibilities**

The Cord Blood Bank is responsible for :

- 2.7.2.1** sending to FGM the characteristics of new cord blood units (CBU) validated according to the common protocol defined by both RFSP and FGM.
- 2.7.2.2** performing via an EFI or ASHI accredited laboratory, the HLA typing of the units at a low or high resolution level following the request made by the transplant physician.
- 2.7.2.3** sending only in the case of final selection and formal recruitment of the CBU.

- a DNA sample extracted from cord blood cells to the laboratory designated by the transplant physician, upon her/his request,
- a maternal blood serum sample or any other biological product that may allow additional disease markers screening,

**2.7.2.4** organizing, together with the Bank in charge of the units and FGM, the shipment of the CBU to the location designated by the transplant physician.

## **2.8 Storage Facility for the whole CBU in Annemasse**

### **2.8.1 Definition**

The Storage Facility of Annemasse is an entity belonging to the “Etablissement Français du Sang” (EFS). As a member of the RFSP, it adheres to quality standards defined by this network and to those of the FACT/Netcord accreditation system.

Moreover the Cord Blood Bank must adhere to the WMDA standards too, as the cord blood units are registered in the FGM database and the Registry is in charge of their management.

### **2.8.2 Responsibilities**

The Storage Facility of Annemasse is responsible:

- 2.8.2.1** to receive, register and cryo-serve in liquid nitrogen tanks, under required conditions, the CBU sent by the Cord Blood Banks, members of the RFSP,
- 2.8.2.2** to correspond with the FGM Registry each time a CBU is recruited by a Transplant Centre, whether national or international,
- 2.8.2.3** to control the tightness of the bag(s), for each CBU pre-selected by any Transplant Centre,
- 2.8.2.4** to permanently conserve a ready dry-shipper in order to be able to face an urgent CBU shipment,
- 2.8.2.5** to prepare and package the bags containing the recruited cryopreserved CBU, according to current legislation, in order to ensure optimal and secured transport conditions,
- 2.8.2.6** to take photographs of the bags in order to certify they were intact at the time of shipment,
- 2.8.2.7** to equip each dry-shipper with a temperature probe (FACT standard),
- 2.8.2.8** to place in the intended envelope all the documents necessary for the CBU transport including the AFSSAPS export permit if needed,

- 2.8.2.9** to seal or lock up the dry-shipper before shipping, in way to ensure the strict respect of the cold chain : in this case, the combination of the locker must be transmitted in a secured way to the receiving laboratory,
- 2.8.2.10** to stick on the dry-shipper all stickers and labels useful to sensitize the courier companies to the content (human graft), and ensure, as much as can do, the conditions of manipulation of the dry-shipper during the transport,
- 2.8.2.11** to deliver the dry-shipper containing the CBU to the person designated by the courier company with which the Biomedicine Agency signed an agreement.

## **2.9 Cell Therapy Laboratory**

- 2.9.1** The Cell Therapy Laboratory (or cell processing laboratory) is located either within an EFS or an Hospital and works under the responsibility of the one or the other. It has an authorization delivered by the AFSSAPS and works under define rules of good practices pertaining to the transformation, including the cryo-preservation of human hematopoïetic stem cells and of mononucleated blood cells used for therapeutic purposes
- 2.9.2** The person responsible for the laboratory or her/his deputy receives the peripheral blood stem cells or the mononucleated cells, or even the medullar stem cells, harvested from a national or an international donor, as well as national and international CBUs, with the purpose of quality control, final validation and delivery of the product for the use of the patient .
- 2.9.3** The Cell Therapy Laboratory affiliated with the Transplant Center is responsible for requesting, from the relevant department of the AFSSAPS, the authorization to import cells for therapeutic use, harvested from international donors and destined for national patients treated by this Transplant Centre (PBSC, lymphocytes or CBU). A copy of this request must be sent together with the infectious disease markers results to FGM, which is responsible to advice the AFSSAPS, in name of the Biomedicine Agency, before the issuing of the permit .
- 2.9.4** The Cell Therapy Laboratory affiliated to the Harvesting Centre is responsible for asking, from the relevant department of the AFSSAPS, the authorization to export cells for therapeutic use, harvested from national donors and destined for international patients (PBSC, lymphocytes or CBU). A copy of this request must be sent with the disease markers results to the FGM Registry

**CHAPTER 3**  
**REGISTRATION OF DONORS**

### 3.1 Channels of information

Potential HSC donors in the general population are nowadays informed via several different channels :

#### **Etablissement Français du Sang (EFS) and Biomedicine Agency networks**

Information on unrelated bone marrow donations is circulated either by physicians responsible for welcoming and informing blood donors or through conventional means (such as bulletins, pamphlets etc...) available in waiting rooms and distributed by the Biomedicine Agency.

#### **Hospital network**

Information is given either by the physicians of the peripheral donor centres, by the clinicians of the pediatric and adult hematology wards or through information bulletins placed in the units, at the disposal of the relatives of hospitalized patients.

#### **Associations network**

Departmental associations like ADOT as well as numerous other associations of patients' relatives work actively to increase the general public awareness about HSC donation.

#### **The Media network**

Edition of articles in the local or national newspapers, radio or television broadcasts, generated by national or regional information campaigns or by patients awaiting an HSC transplant, keep the general public informed and interested in this type of donation.

The general public can also find information on the Biomedicine Agency website : <http://www.agence-biomedecine.fr/> or even on the dedicated website : <http://www.dondemoelleosseuse.fr/> , and can upload a registration request on the bone marrow donor registry.

Persons interested may contact :

- **the National Registry “France Greffe de Moelle” (FGM)** which sends them a complete documentation about bone marrow and stem cell donation and an initial consent form to be signed and returned to FGM or directly to the Donor Centre located close to their place of residence,
- **the Donor Centre**, closest to their place of residence, able to enroll them after having checked their commitment, their understanding of the process and their medical clearance.

## **3.2 Age criteria**

Potential bone marrow donors must be over 18 and under 51 years of age to be registered on the National Registry.

Once registered, they remain on the Registry until their 61 years of age if they so wish and if their medical status allows.

## **3.3 Required aptitudes**

These persons must be in **perfect physical and psychological health** and must have perfectly understood the importance of a long term commitment, without any guarantee to donate their bone marrow and/or their peripheral blood stem cells (PBSC).

They commit themselves to signal any change of name or address, as often as necessary, in order to remain joinable.

They accept the principles of a strict anonymity and a free donation such as described in the bioethical law of 29 July 1994, and its most recent version dated 6 august 2004.

They know they have the right to withdraw at any time.

### **3.3.1 Medical counter-indications for bone marrow donation**

**3.3.1.1** The list of counter-indications for bone marrow donation is defined and validated by the Steering Committee of FGM and made available on SYRENAD.

**3.3.1.2** The medical question session with any potential donor is precise and thorough in order to identify any antecedent or any pathology likely to exclude the person before registration on the National Registry. It is carried out via an initial self-evaluation questionnaire completed by the donor in person (pre-convocation questionnaire) and by the physician interviewing the donor (medical questionnaire used at the time of registration signed and dated by the physician, thus validating the aptitude of the donor).

**3.3.1.3** The clinical examination, carried out in a room which allows the confidentiality of the interview, permits the identification of a possible counter-indication.

**3.3.1.4** Any new donor having stayed for 1 cumulative year in England between 1980 and 1996 cannot be enrolled on the Registry.

**3.3.1.5** Donors already on the Registry, having stayed in England during the years mentioned above, remain on the Registry, as do positive anti-HBc and -HBs

donors. This information is passed on to the transplant physician, if such a donor is pre-selected.

### **3.3.2 Other counter-indication for bone marrow donation**

- 3.3.2.1** Pregnancy is a temporary counter-indication for registration and more generally for bone marrow donation.
- 3.3.2.2** Any woman enrolled on the National Registry who informs her Donor Centre of a current pregnancy must immediately be listed as temporarily unavailable for the duration of her pregnancy and for six months following her delivery.
- 3.3.2.3** Within 7 days before any bone marrow donation from a female donor and anyway before the beginning of the conditioning of the patient, , a pregnancy test must be carried out if the woman is of child-bearing age, to make sure that she is not pregnant.

### **3.3.3 Medical counter-indications for PBSC donation**

- 3.3.3.1** The list of counter-indications for injection of growth factors and therefore for PBSC donation is defined and validated by the medical committee of FGM and available on SYRENAD.
- 3.3.3.2** The medical question session with any potential PBSC donor is precise and thorough in order to identify any antecedent or any pathology likely to exclude any person before registration on the national Registry.
- 3.3.3.3** The clinical examination permits the identification of a possible counter-indication.
- 3.3.3.4** Any new donor having stayed for 1 cumulative year in England between 1980 and 1996 cannot be enrolled on the Registry.
- 3.3.3.5** Donors already on the Registry, having stayed in England within the years mentioned above, remain on the Registry, as do positive anti-HBc and -HBs donors. This information is passed on to the transplant physician, if such a donor is pre-selected.

### **3.3.4 Other counter-indication for PBSC donation**

- 3.3.4.1** Pregnancy is a counter-indication for registration and more generally for PBSC donation.

- 3.3.4.2** Any woman enrolled on the National Registry who informs her Donor Centre of a current pregnancy must immediately be listed as temporarily unavailable for the duration of her pregnancy and for six months following her delivery.
- 3.3.4.3** Within 7 days preceding a PBSC donation from a female donor, and in any case before any injection of growth factors and conditioning of the patient, a pregnancy test must be carried out, if the woman is of child-bearing age, to make sure that she is not pregnant.
- 3.3.4.4** A donor over 51 years of age cannot be injected with growth factors.
- 3.3.4.5** A donor who has shown an allergic reaction can't donate HSC via cytopheresis.

### **3.4 Protection of donors**

- 3.4.1** A donor may, at any time during her/his enrolment, change her/his mind and request to be withdrawn from the Registry (bioethical law of 29/07/1994 and 6/08/2004).
- 3.4.2** The anonymity of the donor must be respected. She/he is enrolled on the National Registry under an anonymous code which is automatically given by the FGM software. Only this code will be transmitted within the network of compatibility searches subsequently carried out.
- 3.4.3** The guarantee of the security of the donor is essential at all times. Any risk, foreseen during the validation process of any donor, susceptible to harm the donor's security and health, must temporarily or permanently exclude the donor from the donation process,
- 3.4.4** The quantity of HSC collected from the selected donor (marrow or PBSC) must not exceed the theoretical maximum quantity calculated in accordance with her/his own body weight (Bone Marrow) or the previously established standards (PBSC).
- 3.4.5** No information of a personal nature concerning the donor is given to the Transplant Centre, except if this information can put the patient at risk. In this case the information is given via the Registry only after the donor has been informed.
- 3.4.6** The outcome of the patients, if known by the FGM Registry, is transmitted anonymously to donors via the Donor Centre only if the donors request it expressly, but consideration must be given to the type of information to be transmitted, the psychological profile of the donor and her/his eventual emotional link with the patient.
- 3.4.7** After their donation, all donors must benefit from an immediate follow-up, then yearly without any maximum duration length established yet.

## **Registration of donors initially related to a patient**

**3.4.8** Registration of persons otherwise related to a patient already transplanted or awaiting a transplant, is carried out with insistence on the obligation of an anonymous donation, for the benefit of all national and international patients.

**3.4.9** Patients' relatives are exhaustively informed about stem cell donation.

**3.4.10** These donor files must mention the family link with the patient and the type of pathology presented by the patient.

## **3.5 Information given to donors**

From the time of her/his initial registration up until her/his eventual HSC donation, the donor receives clear, precise and objective information concerning the commitment which she/he has undertaken.

### **3.5.1 At the time of registration**

The donor identity is controlled through his/her identity papers by the physician who signs the initial consent form.

The potential donor is informed, both orally and in written, about all the issues to be accepted and respected before agreeing to become a bone marrow donor :

- voluntary and unpaid donation,
- anonymity to be respected,
- commitment to advise of any address and civil status changes,
- reimbursement of all expenses generated by the stem cell collection organization,
- insurance coverage contracted by FGM,
- authorization given for storage of her/his own biological material which could be used for search and research purposes linked only to the potential stem cell donation,
- pre-acceptance of general anesthesia and intra-bone harvest in the case of bone marrow donation,
- pre-acceptance of an injection of growth factors and a cytopheresis collection in case of a PBSC donation,
- pre-acceptance of a possible second donation of bone marrow, peripheral blood stem cells or lymphocytes (DLI), **for the benefit of the same patient.**
- Potential risks associated to harvest procedures must be clearly explained by the physician responsible to deliver the information.

All questions that the donor is likely to ask must be answered clearly and precisely and any points not understood must be clarified.

A written document, named “initial voluntary commitment to donate bone marrow”, setting out essential key points to know and to accept, is read and co-signed by the donor and the physician who informed her/him, at the time of her/his actual registration.

### **3.5.2 At the time of a request for complementary tests**

**3.5.2.1** Each time the donor is called for complementary compatibility tests, the Donor Centre checks her/his aptitude to remain on the national Registry, the quality of her/his commitment and makes sure that she/he possesses all necessary information.

**3.5.2.2** The donor is kept informed of the results of all complementary tests performed within 6 weeks after testing (WMDA standard). If this information has not been spontaneously transmitted by the requesting Receiving Centre which carried out the tests, it will be claimed by the Donor Centre, via FGM, and given to the donor.

**3.5.2.3** The donor regularly receives a national information bulletin, yearly circulated to all registered French stem cell donors by FGM. This bulletin helps her/him :

- to remember her/his commitment to the national Registry of bone marrow donors, particularly when she/he has not been called for HLA complementary tests,
- to be updated on the Registry statistics and activity
- to better understand the evolution of HSC transplants,
- to inform of any changes of address or civil status, using a reply coupon.
- To ask any question that seems important to her/him or suggest any improvement.

### **3.5.3 At the time of recruitment of a donor for a bone marrow or PBSC donation**

**3.5.3.1** All information necessary to obtain the final acceptance and clearance of the donor to proceed to a bone marrow or a PBSC donation is given to the donor (see chapter 3.6.1).

**3.5.3.2** The donor receives a detailed information brochure edited by FGM reminding him/her of the various and chronological stages of HSC donation.

- 3.5.3.3** The vital issue that the 15 days prior to the bone marrow or PBSC harvest represent for the patient must be clearly explained to the donor. The donor is informed that she/he may take back her/his consent at any time but is given the possibility to assess the risks for the patient, particularly during patient conditioning before the transplant (bioethical law of 29 July 1994 and 6 August 2004).
- 3.5.3.4** The donor may contact the Donor Centre at any time to obtain an answer to any question she/he may have.
- 3.5.3.5** The duration required by the collection(s) as well as all stages preceding the marrow or PBSC donation are clarified to the donor and their organization is facilitated by the Donor Centre :
- medical check-up,
  - complete biological and infectious check-up,
- in the case of a bone marrow donation :**
- pre-anesthetic check-up,
  - blood drawn for final tests
  - blood drawn for auto-transfusion, if need be,
  - donor's final consent at the local Magistrate's Court,
  - organization of her/his hospital stay, and information about the location of the harvest
- in the case of a PBSC donation :**
- detailed procedure for the growth factors injections,
  - organization of the cytopheresis collection(s), and information about the location of the harvest
- 3.5.3.6** In case of professional or holidays travel within the 15 days preceding donation, the donor must previously transmit a phone number to the donor centre (preferably mobile phone number). In the same way, the donor centre must communicate a phone number that the donor can call at any time in case of any emergency.
- 3.5.3.7** A nominative complementary insurance coverage is contracted by the FGM Registry for each harvested donor. The contract clauses are available to donors upon request.

### **3.5.4 At the time of a second donation request**

**3.5.4.1** Any donor having donated bone marrow or PBSC is immediately deleted from the local and national donor file by the Donor Centre concerned. She/he cannot be recruited again for another patient.

The donor having donated HSC remains “in reserve” for the patient, if necessary. The donor is precisely informed of the possibility of having to eventually donate again for the same patient and must clarify her/his position on this eventuality, as precisely as possible. There again, it is important that the donor can be easily tracked. She/he is asked to signal any future changes of address.

If the donor declares at this stage that he refuses any subsequent donation, the transplant physician must be immediately informed.

**CHAPTER 4**  
**HLA TYPING**

HLA typings are performed by the Histocompatibility Laboratories of the Donor and Receiving Centres, as well as those of Cord Blood Banks, which have been EFI or ASHI accredited and comply with the GBEA.

Any Histocompatibility Laboratory which is not EFI or ASHI accredited must send their donors and recipients' DNAs to a laboratory which is EFI or ASHI accredited.

The nomenclature used is the one defined by the International Nomenclature Committee. Nomenclature updates are published annually in the review "Tissue Antigens" and are regularly made available on the website of various organizations.

#### **4.1 HLA typing of a new donor/CBU to be registered**

**4.1.1** Any new donor/CBU to be registered will be **HLA-A, B, C, DRB1\***, typed.

**4.1.2** The HLA-A, B, C typing of a new donor/CBU, to be registered on the local and national files, is carried out either by serology techniques using commercial reagents, the marketing of which has been authorized by AFSSAPS, or by molecular biology techniques using authorized commercial reagents. The definition level is communicated by the Registry.

In the case of an ambiguous serological antigen, molecular biology techniques are used. The list of antigens to be defined is the one published by the HLA Nomenclature Committee of the WHO. A serological typing is recommended in way to insure the antigenic expression of HLA molecules.

**4.1.3** The HLA-DRB1\* typing of a new donor/CBU to be registered on the donors/CBUs file is carried out by molecular biology techniques. The list of alleles to be defined is sent by FGM to all Histocompatibility Laboratories.

**4.1.4** The storage of a quantity of 100µg of DNA is recommended.

#### **4.2 Allelic typing of a donor/CBU at the time of a request for complementary tests**

The request for allelic typing is sent by FGM upon receipt of a request coming from the transplant physicians or International Registries.

The laboratory carries out the HLA Class I A\*, B\*, C\* and/or the HLA Class II DRB1\*, DQB1\*, DPB1\* typing, according to the request and the definition level expected by the transplant physician.

The result must be transcribed **without ambiguity**. The use of all techniques published up to the day of the request is recommended in order to remove any ambiguities.

If the HLA laboratory of the donor centre or the cord blood bank cannot perform the HLA typing at the resolution level expected by the transplant centre, a donor/CBU DNA sample must be sent to a skilled laboratory able to perform the typing.

An ambiguous allelic typing result cannot be invoiced to International Registries.

#### **4.3 Allelic typing of a donor or CBU/patient pair at the time of work up of a donor**

This typing is carried out by the Histocompatibility Laboratory correspondent to the transplant physician.

The laboratory carries out, on a new sample from both donor/ patient or CBU/patient, the HLA Class I A\*, B\*, C\* and the HLA Class II DRB1\*, DQB1\*, DPB1\* typing.

The result is entered in the SYRENAD database, without any ambiguity. The use of all techniques published up to the day of the request is recommended in order to remove any ambiguity.

#### **4.4 Archival storage of results**

**4.4.1** The result of the HLA typing can be sent to the donor's physician or to the donor him/her-self, upon demand.

**4.4.2** The result of the HLA typing is filed in the initial dossier of the donor. This dossier includes: the medical questionnaire, the infectious disease markers results, an the ABO/Rh blood group, the initial consent form completed by the donor at the time of her/his registration. In case of a CBU, the documents stored in the file are those relative to the mother.

**4.4.3** The dossier of the harvested donor must be kept for 30 years.

#### **4.5 Minimum criteria of donor/recipient HLA compatibility**

The minimum HLA compatibility criteria requested to allow the formal national donor work up concern the AB and DRB1 HLA antigens :

- generic, or allelic (strongly recommended), AB HLA identity and allelic DRB1 (4 digits)

A national donor recruitment can nevertheless be authorized, if there is a major mismatch concerning one of the class I antigens (A or B), provided that the DRB1 HLA identity can be preserved at an allelic level (4 digits).

Any recruitment that doesn't fulfil these conditions will be examined and submitted to the validation of the internal expert committee, after having taken advice from the HLA referent dedicated to the Registry.

#### **4.6 Minimum criteria of CBU/recipient HLA compatibility**

The minimum HLA compatibility criteria requested to allow the formal recruitment of a national CBU concerns the AB and DRB1 HLA antigens :

AB at generic level (2 digits), or at allelic level(4 digits/strongly recommended) HLA identity and DRB1 at allelic level(4 digits)

The recruitment of a national CBU can nevertheless be authorized, in the case of 1 or 2 major mismatches existing preferably on one or the two class I antigens (A or B). An allelic identity at DRB1 locus (4 digits) should as far as possible be preserved and maintained.

**CHAPTER 5**  
**INFECTIOUS DISEASE MARKERS**

All French laboratories performing biomedical analysis must comply with the GBEA (good practice guidelines for biomedical analysis, order from 26 November 1999, modified 26 April 2002).

## **5.1 Unrelated HSC donors**

### **5.1.1 Validation of a donor's initial aptitude at the time of registration**

Since 1<sup>st</sup> January 2008 infectious markers disease markers screening is no more mandatory at the time of initial registration.

If the potential donor is a recent blood donor (current year), the results of the screening performed to validate the blood donor can be entered into SYRENAD, as well as the ABO/Rh blood group if known.

### **5.1.2 Validation of a donor's aptitude at the time of despatch of a blood sample**

Before any despatch of donor blood samples to National or International Transplant Centres, the testing of the following infectious disease markers, by the laboratory of the Donor Centre, is mandatory:

- Syphilis screening
- HBs antigen
- Anti-HBc antibodies,
- Anti-HCV antibodies,
- Anti-HIV1-V2 antibodies,
- Anti-HTLV1-V2 antibodies,
- Anti-CMV antibodies (if unknown or previously negative).

**The ABO/Rh blood group test must be performed, if unknown.**

The results of these tests are transmitted, as soon as obtained, to the Transplant Centre. Any positive markers (except CMV) must be immediately mentioned to the requesting Transplant Centre. At this stage of the search process, any infectious disease marker (except CMV) found initially positive and retested as positive, leads to the deferral of the donor and her/his deletion from the national Registry file.

The type of tubes into which the blood samples are drawn must conform to the Transplant Centre's request.

The blood samples drawn must be labeled in full respect of the **donor's anonymity**. Only the code of the donor may appear on the tube. The drawn date must also be noted on the tubes.

The samples must be packed in a secure box (provided by FGM), in conformity with the Ministerial Order of 24 April 2002 re “homologation of rules pertaining to the good practices for the transportation of harvests, products and samples originating from human blood”.

### **5.1.3 Final validation of the aptitude to donate HSC**

Carrying out the following infectious disease markers, which contribute to the detection of transmissible diseases, is imperatively required to validate a donor’s final aptitude to donate HSC, **within 1 month of the collection**

In accordance with decree n° 97-928 of 9 October 1997, the following markers are required, in France, at the present time, to validate a graft of HSC :

- Syphilis screening
- HBs antigen
- Anti-HBc antibodies
- Anti-HBs antibodies (AFSSAPS recommendation)
- Anti-HCV antibodies
- Anti-HIV1, V2 antibodies (2 serological techniques)
- HIV p24 antigen or HIV PCR
- Anti HTLV1, V2 antibodies
- Toxoplasmosis (IgM and IgG)
- Anti-EBV antibodies (IgM and IgG or total)
- Anti-CMV antibodies (IgM and IgG or total)
- Malaria, if necessary.

The name of techniques, and/or kits, used to test these markers, are mentioned in writing on the document which recapitulates the results (FGM form 014).

It must be noted that :

- anti-HIV1-V2 tests must be done twice, using either two different techniques or two different reagents. This information is mandatory when exporting or importing cellular products for therapeutic uses (peripheral stem cells or lymphocytes) which need approval from the relevant services of the AFSSAPS.
- P24 detection can be replaced by a HIV PCR (DNA)

Any positive result is immediately communicated, via FGM, to the transplant physician who is the only person habilitated to make the decision to accept or release the donor (decree n° 97-928 of 9 October 1997). Moreover, in the frame of the decree upon exceptional transplant (December 2005), a positive tested donor for B and C hepatitis can be harvested relying on the patient benefit/risk analysis.

In accordance with this same decree, the results of these markers must be transmitted, in all cases and in their entirety, to the Transplant Centre **BEFORE** the day chosen for the beginning of the patient's conditioning.

According to potential exposure to specific infectious agents (Chagas disease, West Nile Virus, malaria, Chikungunya...), complementary testing must be performed, and the transplant physician consequently informed.

The donor must be validated **during the month** preceding her/his HSC donation (medical and serological aptitudes - Good Practices – Ministerial Order of 16 December 1998).

A serum sample of the donor must be drawn **on the day** of the HSC collection and kept in a serum repository by the Transplant Centre ( for any retrospective study if needed ).

In the case of an international donor, if all the required infectious disease markers cannot be performed by the International Donor Centre laboratory, a blood sample from the donor must be requested by the French Transplant Centre for completion of the tests required. Thus, the list of mandatory markers will be completed, allowing a full validation of the future graft.

#### **5.1.4 Follow-up of the donor**

If an infectious disease marker is positive, the physician in charge of the Donor Centre will inform the donor's and, if the donor wishes, the donor's own physician.

If the transplant physician selects a donor presenting a positive marker, the donor follow up must be organized in the way described in the decree related to derogate transplants (December 2005).

## 5.2 Unrelated cord blood units

### 5.2.1 Validation of a CBU at registration

Infectious disease markers requested to validate a CBU at the time of its registration on the Registry are tested on a maternal serum sample:

- at time of delivery (day 0)
- at day + 60 or even later after delivery (quarantine period)

Infectious disease markers, tested according to current national legislation, are the same as those tested for HSC unrelated donors, and are as follows :

- Syphilis screening
- HBs antigen
- Anti-HBc antibodies
- Anti-HBs antibodies (AFSSAPS recommendation)
- Anti-HCV antibodies
- Anti-HIV1, V2 antibodies (2 serological techniques)
- HIV p24 antigen or HIV PCR
- Anti HTLV1, V2 antibodies
- Toxoplasmosis (IgM and IgG)
- Anti-EBV antibodies (IgM and IgG or total)
- Anti-CMV antibodies (IgM and IgG or total)
- Malaria, if necessary.

These infectious disease marker testing results must remain negative after the quarantine period in order to allow the registration of the CBU. Only positive IgG for EBV, CMV and toxoplasmosis can be accepted .

Maternal serum from day 0 to day  $\geq 60$  for each CBU must be preserved in a way to allow the completion of any complementary serological test, if needed by the importing country or in case of a modification in the national legislation.

The ABO/Rh blood groups are also tested before the CBU cryo-preservation. In any case, the results of testings performed on the maternal serum are transmitted to the mother. The mother must be precisely informed in case of a positive result.

**CHAPTER 6**  
**SEARCH PROCESS FOR UNRELATED DONORS**  
**(Hematopoietic Stem Cells Donors**  
**and Cord Blood Units)**

Once a national or international transplant physician has decided to initiate a search, this will be carried out by FGM on both the National and the International Registries of hematopoietic stem cells donors and/or on the National and the International Cord Blood Banks.

## 6.1 National Patients

### 6.1.1 Registration of a patient

**6.1.1.1** The searches are performed, according to the transplant physician's prescription, after the mandatory registration of the patient has been made on the national FGM Registry.

The patient's registration form request (FGM form 001) must be received by FGM by fax or e-mail. It contains all necessary information required for a successful registration.

**6.1.1.2** This form is validated and signed by the transplant physician for its clinical part, by the administrative services of the Transplant Hospital for the financial part (order number) and by the person in charge of the HLA Laboratory, correspondent for the transplant physician for the HLA typing of the patient.

**6.1.1.3** The diagnosis must conform to the current list of indications established by the EBMT and validated by the SFGM-TC (*French Society of Marrow Transplant and Cellular Therapy*). If this is not the case, the dossier is sent, before registration, to the FGM Medical expert Committee whose role is to decide on the pertinence of the indication.

**6.1.1.4** The age of the patient must not, in principle, exceed 55 years, **except** if the patient is a candidate for an allo-transplant of unrelated PBSC, **with reduced intensity conditioning regimen**. In this case the transplant physician must sign the page 2 of the form CF001, stating that she/he recognizes the following restrictive clauses associated with this type of registration :

- any subsequent request made to formally recruit an unrelated donor in view of a PBSC donation will be linked to the approval of the FGM expert Committee,
- any French unrelated donor, aged over 51 years, will not be authorized to donate PBSC (Ministerial Order of 16 December 1998 – good practices),
- any donor requested for a PBSC donation is free to either accept or refuse this type of collection.

- 6.1.1.5** Capture of information contained in the form CF001 is carried out, within 24 hours following the receipt of the document, by the FGM national coordinator in charge, who will make all necessary controls.
- 6.1.1.6** If any mandatory information is missing, the national coordinator sends a request for complementary information to the Receiving Centre. The same process applies in the case of partial information but, here, the patient's registration is, nevertheless, made by the national coordinator who then requests the complementary information from the Receiving Centre.
- 6.1.1.7** The patient's registration receipt is sent via SYRENAD to the Receiving Centre which must then validate the data captured by FGM, to make the registration effective.

## **6.1.2 Search methods**

### **6.1.2.1 Searches for national donors**

The following searches may be carried out on the national Registry :

- HLA class I matched donors,
- HLA class I and II matched donors (DRB1),
- HLA class I and II matched donors (DRB1 and DQB1),
- HLA Class I (A or B) major or minor mismatched donors.

The results of the searches are available to the requesting Receiving Centre as soon as captured via the SYRENAD software.

### **6.1.2.2 Searches for national cord blood units**

The searches for national cord blood units belonging to the Cord Blood Banks network RFSP (*French Cord Blood Network = France Cord*) are made via SYRENAD and are managed by FGM.

The SYRENAD-Cord software searches in the cord blood database and lists the existing cord blood units, according to the number of nucleated and CD34+ cells collected and their degree of HLA compatibility.

### **6.1.2.3 Searches for national donors and cord blood units (CBU) are daily repeated. All new data concerning new located donor/CBU or donor/CBU already selected for a patient are daily transmitted to Donor and Receiving Centre.**

### **6.1.3 Searches for HSC international donors**

FGM carries out all the searches, upon request of the transplant physician. International searches are carried out either via the EMDIS communication system or by fax for non-connected Registries.

More than 69 Registries and 43 cord blood banks can now be searched.

Registries are searched either systematically or selectively, following consultation of the BMDW database, listing the phenotypes of worldwide unrelated donors and CBUs.

The BMDW database may be consulted on Internet by the transplant physicians and the receiving centres, using an access code provided by FGM or using SYRENAD.

Through the EMDIS communication system, searches are repeated automatically and search reports are transmitted.

For non connected Registries, searches are repeated by fax when they are requested by the transplant physicians.

### **6.1.4 Searches for international cord blood units**

Following consultation of the BMDW database or SYRENAD-Cord, the listed cord blood units can be located and the searches organized.

Searches are managed by the FGM national coordinators who are responsible for carrying out the searches and organizing the transfer of units from the cord blood Bank to the requesting Transplant Centre.

Searches can be repeated upon request by the transplant physician.

### **6.1.5 Requests for complementary tests**

The requests for complementary tests (HLA typing, virology etc.) are made by the transplant physicians, through their Receiving Centres, using SYRENAD or by faxing FGM the forms edited by non connected Banks or Registries.

The donor identity must be verified by the donor centre, each time she/he is requested for complementary tests.

At the stage of a blood sample request, per national regulation, a national donor cannot be reserved for a patient. The donor centre has to inform the FGM Registry when a donor, who has provided a blood sample less than 6 weeks ago, is requested again for another patient. The transplant centre responsible for the initial patient must then clearly specify if he has plans to formally work up this donor or not.

A donor can only be reserved for a patient if a transplant date has been clearly planned.

## **6.2 International Patients**

Searches are carried out, upon request coming from an International Registry or transplant physician, following the formal registration of the patient.

If the age of the patient exceeds 60 years old, the registration request must be reviewed by the Medical expert Committee of the Registry.

There are, again, two communication systems :

- EMDIS,
- Fax (non-connected Registries).

Searches are managed by an FGM international coordinator.

For patients registered through the EMDIS system, any new data concerning national donors are transmitted automatically to the connected Registries. For non connected Registries, the search report is edited and transmitted within 24 hours following the patient registration. Searches are either, automatically, monthly repeated or repeated upon specific request. Only HLA class I and II identical donor data are transmitted to the transplant centers.

**CHAPTER 7**  
**ADMINISTRATION AND ACCOUNTANCY**

FGM Registry assumes its mission within the Biomedicine Agency, administrative public institution, legally subject to separation between organizer and the state treasurer. The specificity of this type of public institutions is aimed at separating treatment of financial operations from administrative ones.

On one hand the handling of budget and fees, the orders, the verification of supplier invoices, the payroll management and the issuing of client invoices which are the organizer responsibility, i.e. FGM Registry at Biomedicine Agency.

On the other hand the suppliers invoices and salary payments, the client invoices addressing, the payment collection as well as marking of the ledger of the different flows which are part of the state treasurer department perimeter of responsibility (structure depending from public accountancy).

For the organizer part, the whole of the administrative and accounts operations are processed within the administrative and financial direction at the Biomedicine Agency.

For the state treasurer part, requests for payments and payment collections are processed within the allotted time set by law under the personal financial responsibility of a state treasurer.

The costs invoiced by the Biomedicine Agency for the FGM Registry services are published annually in the Bulletin Officiel.

The Biomedicine Agency uses a recognised software in order to process in a secured manner the financial operations and to respect the accountancy rules. Interfaces were developed between the FGM database software Syrenad and the Biomedicine Agency financial software.

### **Imperative point**

The name of the donor should never appear on the invoices in order to guarantee his anonymity. Only his identification code is shown as per available in Syrenad database.

## **7.1 Services for national patients**

### **7.1.1 National patient / national CBU or donor**

The administrative services of the transplant hospital give their financial agreement to the request for registration on the National Registry by issuing an order form number that will follow the patient among all the service requests.

The order form number is written by the transplant physician on the FGM registration form CF001. This document will then be transmitted to the FGM coordination that will proceed with the patient registration on the SYRENAD database.

Through the interface with the financial software, a registration invoice is automatically issued to the financial service of the transplant hospital.

### **7.1.2 Requests for complementary tests**

Important comment : the billing for exams and harvests listed on SYRENAD and performed on national donors is always made **at price cost and directly** (without intermediary of the Biomedicine Agency) by the establishment performing the service in the transplant hospital. Only the blood sample transport is paid by the Biomedicine Agency, and then billed to the transplant hospital at price cost.

#### **7.1.2.1 HLA generic or allelic typing, despatching of blood samples**

The requests are made upon a prescription from the transplant physician in charge of the patient.

The requests and the order form number must appear on any invoices issued by the providing establishment.

#### **7.1.2.2 Infectious disease markers**

At the time of pre-selection of a donor the legally mandatory infectious disease markers, expected by the transplant physician, are invoiced by the financial services of the providing establishment which also gives the patient's order form number.

#### **7.1.2.3 Pre-anesthesia check-up, autologous blood draw and marrow or PBSC harvest of the selected donor**

Same administrative procedure as 7.1.2.2. above.

#### **7.1.2.4 Donor expenses :**

The donor expenses are reimbursed by the establishment performing the harvest and then re-billed to the transplant establishment.

### **7.1.3 Cord blood units release**

In opposition to services involving HSC donors, the release of CBU are directly billed to the Biomedicine Agency by the cord blood banks members of the RFSP network. The banks then re-bill to the transplant establishment. The transport cost is added to this price.

### **7.1.4 National patient / international CBU or donor**

**7.1.4.1** The procedure follows the one described in paragraph 7.1.1. Besides the transplant physician indicates his wish to interrogate the international registries by ticking off the box provided for this purpose on CF001 form.

In accordance with WMDA accreditation standards FGM Registry is through the Agence de la biomedecine the financial intermediary at cost price of all service requested by a national transplant physician from international registries.

**7.1.4.2** All of transplant physicians orders are referenced in Syrenad and interfaced with the invoicing software

**7.1.4.3** The applicable fees are the ones transmitted by the international registries or cord blood banks. They are publicised twice a year to the transplant hospitals (physicians and administrative services) depending on updated information received from international correspondents.

**7.1.4.4** All of invoices issued by the international registries to the attention of transplant centres financial services are transmitted through FGM Registry.

**7.1.4.5** Invoices are validated by FGM Registry once patient ID, service provided and invoice addressee have been verified.

**7.1.4.6** The patient ID provided by the transplant centre financial department covers the registration of the patient and complementary exams requests: HLA typing, blood samples shipments, SC collections and CBU shipments.

**7.1.4.7** The organizer department, after verification of the international registries invoices, issues payment requests for the service provided.

**7.1.4.8** In case of disagreement with the invoices, credit notes are requested from the international registries.

**7.1.4.9** The state treasurer of the Biomedicine Agency pays the international registries invoices within the allotted time and by modalities in conformity with the requirements of the WMDA accreditation standards.

**7.1.4.10** FGM Registry, via the orders interface, edit the client invoices to the attention of the national transplant centres based on the services invoiced by the international registries and to which are added the Registry administrative fees. The payment of services invoiced in foreign currency is based on the exchange rate of the day the supplier invoice is issued.

## **7.2 Services for international patients**

### **7.2.1 Patient registration**

International patients registration on FGM Registry is not billed. The patients are directly registered on Syrenad by their national registry if it is connected to EMDIS. For non connected registries, the registration is processed by fax through a specific form CI 001. These international patients are registered on Syrenad by FGM Registry coordinators.

### **7.2.2 Requests for complementary exams**

Requests made by international physicians are processed by an order identified in Syrenad by the patient ID. These requests also embedded the requested donor code. They are automatically transmitted to donor centres that will process them for FGM Registry.

When results are received in Syrenad, by interface with the invoicing software, an invoice to the attention of the international client is issued in Euros, based on the fee published in the Bulletin Officiel.

The order is linked to the invoice at its time of reception and control. The supplier invoices are verified on the basis of the fee decided by FGM Registry. If the invoice is correct, a request for payment is transmitted by the organizer to the state treasurer. In case of error, a credit note is requested by telephone or by email.

### **7.2.3 Blood sample shipment**

The procedure for blood / CT samples request by transplant physicians, via their national registry, follows the same process as per the complementary HLA exams one.

Blood / CT samples shipments are invoiced per patient to the international client after reception of the courier company invoice and blood collection fees are separated from transport costs.

The supplier invoices from donor centres are verified on the basis of the fee decided by FGM Registry and the transport cost on the basis of the public contract signed with the transport company appointed.

#### **7.2.4 Availability of HSC grafts**

International client's invoices are issued monthly following the summary list provided by the Registry management. One invoice is issued per patient. In the case of cord blood units, it is necessary to await reception of the courier company invoice to issue the client invoice. The price billed tallies with the contractual rate specified in the Registry's price list published at the Bulletin Officiel and to which is added the transport cost if necessary.

Supplier invoices delivered from donor centres or cord blood banks are verified on the basis of the fee decided by FGM Registry and the courier company invoices on the basis of the public contract signed.

Donor expenses are refunded by the institution that proceeds with the collection and then invoiced back to the transplant centre.

### **7.3 Increase size and optimisation of the unrelated stem cell donors file**

**7.3.1** A part of the FGM Registry annual budget is dedicated to the increase and improvement of the bone marrow donors registry. These financial costs are not included in calculation of services provided by FGM Registry but are funded by the Biomedicine Agency general budget.

#### **7.3.2 New bone marrow donors registration**

An annual quota is transmitted to each donor centre with a supplier order. This quota indicates the number of donors the centres are likely to register depending on the strategic aim set for the growth of the bone marrow donors registry.

Services requested from donor centres are the purpose of a several years lasting public contract indicating their term and prices as well as the terms and conditions for their review.

A donor's list is transmitted by FGM Registry on the basis of the data shown in Syrenad to the Accounts department who issues / edits a payment request to the benefit of the donor centres. At the end of the year, FGM Registry proceeds with a detailed account per donor centres including possible adjustments.

**CHAPTER 8**  
**RECRUITMENT OF HEMATOPOIETIC STEM CELLS**  
**DONORS**

## **8.1 Recruitment of a bone marrow donor**

### **8.1.1 Recruitment of a national donor for a national patient**

**8.1.1.1** The recruitment of a national donor for a national patient is made via the SYRENAD software, provided by FGM to all French Receiving Centres, but also via the FGM recruitment forms (forms 016 and 017) made available to the transplant and receiving centers on SYRENAD. The entire data, necessary for the donor recruitment, is transmitted to the Donor Centre :

- identification of the patient and the Transplant Centre,
- code of the recruited donor,
- complete HLA typing of the donor/patient pair,
- diagnosis and phase of the patient's disease,
- duration of patient conditioning,
- bone marrow prescription,
- additional blood tubes required,
- suggested harvesting dates.

The stem cell prescription must be signed by the transplant physician.

**8.1.1.2** The donor must receive the most clear, objective and precise information about the procedure, its advantages and inconveniences, eventual secondary effects. She/he must benefit from a delay to make and give a decision.

**8.1.1.3** The donor receives a document called "Bone marrow donation" that explains the different steps of the marrow harvest organization.

**8.1.1.4** The Donor Centre will organize, together with the donor and the harvesting team, the procedure for recruitment and validation :

- verification of the donor identity at each step of the validation (identity papers required),
- validation of the donor's actual commitment "Final Consent form" available on SYRENAD,
- settlement of a definitive date for the marrow collection,
- medical, biological and pre-anesthetic aptitude check-up, including the final medical clearance questionnaire
- Validation of the bone marrow prescription according to the calculation linked to the donor's weight :

Theoretical calculation :

$$\begin{aligned} & \text{Donor weight in kg} \times 20\text{mL} \\ & = \text{Maximum collected volume} \\ & \quad \times 0,22 \\ & = \text{Theoretical quantity of CNT to be collected} \end{aligned}$$

- blood drawn for auto-transfusion, if needed (not mandatory: according to the hemoglobin level of the donor; applicable if level less or around 11g/l)
- virology and serology tests (according to current legislation, see chapter 5),
- attendance of the donor at the local Magistrate's Court for signature of the formal final donation consent (Cf. Bioethic law from July 1994 and august 2004),
- complementary insurance coverage (insurance company with which FGM has signed a contract)
- organization of the donor's hospitalization.

The medical clearance must always be validated by a physician who is not a member of the transplant team.

**8.1.1.5** FGM coordinates the work-up with the Donor and Receiving/Transplant Centres. All the documents necessary for the medical and biological validation of the donor are controlled and validated by the Registry physicians, and sent to the Receiving/Transplant Centre.

**8.1.1.6** Follow up questionnaires are given to the donor at the time of donation : a questionnaire to be completed immediately after donation, another 1 month after donation, and a long term follow up questionnaire. It is necessary for the donor centre to follow up the donor yearly with a questionnaire to be completed during a phone conversation with the donor (forms available on SYRENAD) The content of the questionnaires can be entered directly on SYRENAD in the concerned donor file.

## **8.1.2 Recruitment of an international donor for a national patient**

**8.1.2.1** The procedure for recruiting an international donor varies according to the Registry responsible for that donor.

Depending on the Registry, the recruitment may be carried out :

- either via the EMDIS network,

- or by fax (for non-connected Registries) using specific forms (standardized WMDA forms available on SYRENAD).

**8.1.2.2** FGM coordinates the organization of the work-up with the concerned Registry and the Receiving/Transplant Centre.

**8.1.2.3** The chronology of the recruitment's organization is the same as for a national donor (see paragraph 8.1.1.).

**8.1.2.4** FGM communicates to the concerned Registry the list of infectious disease markers which are mandatory for the donor's validation. If one or more of these markers cannot be carried out by the International Donor Centre, a blood sample of the donor is then requested, and has to be sent to the IDM laboratory of the Transplant Centre which will carry out the missing tests allowing the complete validation of the international donor. It is strongly recommended, as far as possible, to perform a complete validation of the infectious disease markers before the conditioning of the patient begins, particularly when the delay between the recruitment and the beginning of the conditioning is short.

### **8.1.3 Recruitment of a national donor for an international patient**

**8.1.3.1** Depending on the Registry of the international patient, the recruitment of a national donor is carried out :

- either via the EMDIS network,
- or by fax using specific FGM forms ( FGM form 016 and 017).

**8.1.3.2** FGM coordinates the organization of the work-up with the concerned international Registry and the national Donor Centre, in charge of the recruited donor.

**8.1.3.3** The chronology of the recruitment organization is the same as for a national patient (see paragraph 8.1.1.).

**8.1.3.4** Follow up questionnaires are given to the donor at the time of donation : a questionnaire to be completed immediately after donation, another 1 month after donation, and a long term follow up questionnaire. It is necessary for the donor centre to follow up the donor yearly with a questionnaire to be complete via a phone conversation with the donor (forms available on SYRENAD) The content of the questionnaires can be entered directly on SYRENAD, in the concerned donor file.

## **8.2 Recruitment of a cord blood unit**

### **8.2.1 Recruitment of a national cord blood unit for a national patient**

- 8.2.1.1** FGM coordinates the organization of the recruitment of a national cord blood unit in close cooperation with the concerned Bank and the requesting Receiving/Transplant Centre.
- 8.2.1.2** Validated national cord blood units are stored either by the Cord Blood Bank itself (reduced volume units) or by the National CBU Storage Centre located in Annemasse, for all other units.
- 8.2.1.3** All information needed for the CBU recruitment are transmitted to the Bank of origin of the cord blood unit and/or to the National CBU Storage Centre :
- identification of the patient and the Transplant Centre,
  - ID code of the requested cord blood unit,
  - HLA typing of both patient and cord blood unit,
  - suggested date of shipment,
  - planned date of conditioning and transplant.
- 8.2.1.4** The storage centre or the bank verifies the availability and the integrity of the CBU, as well as the adequacy between the announced ID code and the one written on the CBU bag(s).
- 8.2.1.5** When the Bank has received this information, the shipment of the cord blood unit to the Transplant Centre can be organized by FGM.

### **8.2.2 Recruitment of an international cord blood unit for a national patient**

- 8.2.2.1** FGM coordinates the organization of the recruitment of international cord blood units and facilitates the exchanges of information between the Banks of origin and the national Receiving/Transplant Centres.
- 8.2.2.2** The recruitment of an international cord blood unit follows the procedure applied by each Bank. This procedure varies from one Bank to another.
- 8.2.2.3** FGM and the Transplant Centre make sure that the infectious disease markers, tested by the Bank of origin to validate the unit, are in conformity with the current French legislation. If one or more markers are missing, it is then necessary :
- either and preferably to request, before the shipment of the cord blood unit, a sample of maternal serum so that these markers can be tested in France,
  - or, alternatively, to ask the Bank of origin itself to test these missing markers and to send the results before shipping the unit.

**8.2.2.4** When all the results are received, the shipment of the cord blood unit can be organized by FGM.

The FGM Registry insures that a DNA sample of the selected unit has been sent to the HLA laboratory correspondent to the transplant center for final confirmatory typing.

**8.2.2.5** The Cell Therapy Laboratory of the Transplant Centre requests an import permit to the AFSSAPS (French Agency of Health Products Safety), in accordance with the decree n° 2000-156 of 23 February 2002 and informs the FGM Registry of this request.

**8.2.2.6** The FGM Director, in name of the Biomedicine Agency and after verifying all the infectious diseases markers results, submits an advice to the AFSSAPS which if positive, allow the delivery of an import permit to the transplant centre.

**8.2.2.7** No cord blood unit may be imported without an authorization from the AFSSAPS. It is only upon reception of this authorization that the importation of the unit may take place.

### **8.2.3 Recruitment of a national cord blood unit for an international patient**

**8.2.3.1** FGM coordinates the organization of the recruitment of national cord blood units and facilitates the exchanges of information between the National Cord Blood Bank and the International Transplant Centre.

**8.2.3.2** The recruitment of a national cord blood unit is carried out according to current FGM procedures.

A cord blood unit may only be shipped out if its HLA typing has been confirmed :

- either by the Bank itself (FACT standard), 48 hours prior to the shipment of the CBU, from an attached segment.
- or by the requesting Transplant Centre (following reception of a DNA sample sent at the time of the CBU formal recruitment).

**8.2.3.3** The Cell Therapy Laboratory of the Bank of origin must, before shipment, obtain from the AFSSAPS an export permit for the recruited unit, in accordance with the decree N° 2000-156 of 23 February 2000.

### **8.3 Recruitment of a national PBSC donor**

- 8.3.1** A recruitment request for this type of donation must be first reviewed by FGM as far as, age of donor (under 51 years), indications (type and stage of the disease), benefits versus risks analysis, are concerned.
- 8.3.2** The donor centre is officially informed of the request and has to explain it to the donor.
- 8.3.3** The donor must be informed, as clearly, objectively and precisely as possible, of the whole procedure, its advantages and disadvantages, and must be granted time to formally give a reply.
- 8.3.4** The donor receives a document named “PBSC donation” for reading. It explains the different steps of organization of this type of donation.
- 8.3.5** A document entitled “Notice of information and written consent of a PBSC donor” is given to the donor, to be read and signed. This document, equivalent to an “Informed consent”, is co-signed by the donor and by the physician who has explained the procedure, if the donor accepts to receive growth factors and, therefore, to donate this type of stem cells.
- 8.3.6** It is recommended (but not mandatory) that the donor goes to the local Magistrate’s Court in the case of an urgent need of bone marrow harvest (which may occur within 24-48h in the absence of PBSC mobilization).
- 8.3.7** The PBSC collection is scheduled on a date which suits the transplant physician, the donor, the Donor Centre and the Collection Centre.
- 8.3.8** A complete medical, biological and serological check-up, together with a control of the peripheral venous access, is carried out and the results are communicated to the transplant physician, before the beginning of the patient’s conditioning.
- 8.3.9** A medical questionnaire showing the final aptitude of the donor, must be signed by the physician who performed the interview, and sent to the transplant physician.
- 8.3.10** The growth factors must be provided to the donor by the Hospital Central Pharmacy, from a medical prescription made by the hematologist of the hospital or the Collection Centre, who has performed the medical examination of the donor. In no case the donor should buy them in an urban pharmacy.
- 8.3.11** The infectious disease markers to be tested are the same as those tested for a bone marrow donation (chapter 5.1).

- 8.3.12** The injections of growth factors may be done at the donor's home, following the protocol decided by the prescribing physician. A prescription of 10µg/kg/day performed in 2 subcutaneous injections of 5 µg/kg, morning and evening during 5 days is recommended, as well as controlling the blood cell count at day +3 of the injections.
- 8.3.13** The donor must be given a phone number to call in case of any emergency or questions, for the duration of the injections.
- 8.3.14** The PBSC collection may be performed in one or two sessions (maximum), with a one-day interval, depending on the number of CD34+ cells to be collected.
- 8.3.15** The donor will be followed up after the donation, by the hematology unit of the hospital. A blood cell count must be performed at day +8.
- 8.3.16** A person designated by the transplant team will come to collect the graft at the Collection Centre.
- 8.3.17** An export permit must have been previously obtained from the AFSSAPS, if the patient is of international origin.
- 8.3.18** Follow-up questionnaires are given to the donor when preparing her/his donation : one to be completed at the time of growth factor injections, another immediately after the donation, one to be completed within the month following the donation and a long-term questionnaire which the donor may complete annually. It is necessary for the donor centre to follow up the donor yearly with a questionnaire to be completed by phoning the donor (forms available on SYRENAD) The content can be entered directly on SYRENAD in the donor file, by the donor centre.

#### **8.4 Recruitment of an HSC donor for a second donation**

Some donors, after having donated their stem cells may, within a time-frame varying from one month to several years, be requested for a second donation, for the benefit of the same patient. That is why each donor solicited for a 1<sup>st</sup> donation must systematically be informed of the eventuality of a second donation. In case of denial, the transplant physician must be immediately informed

This second donation can concern :

- bone marrow,
- PBSC (**only considered if the 1<sup>st</sup> donation was bone marrow**),
- peripheral lymphocytes (DLI).

## 8.4.1 Recruitment of a national donor

In the case of a national donor, the request for a second donation is sent to the FGM internal expert Committee, whose role it is to review and validate the pertinence of the request in term of patient's benefits/donor's risks..

The Donor Centre and the donor are formally informed of this request only if validated by the experts Committee. The chronology of the recruitment organization is the same as that for a first donation (paragraphs 8.1 and 8.3).

Any donor having donated PBSC as a first donation must not be solicited for a second donation of PBSC but may be solicited only for a bone marrow donation.

### 8.4.1.1 Recruitment of a national donor for a second donation of peripheral lymphocytes (DLI)

**8.4.1.1.1** When a donor has been informed of the transplant physician request and has accepted the principle of a lymphocyte collection, the collection (cytapheresis) is then organized by the Donor Centre.

**8.4.1.1.2** The donor does not have to go to the local Magistrate's Court, but the apheresis centre carrying out the lymphapheresis, must have her/him sign a local Informed Consent form which specifies the nature of the procedure and its eventual risks.

**8.4.1.1.3** The validation of the donor consists of :

- peripheral venous access examination,
- mandatory infectious disease markers tests performance (chapter 5.3).

**8.4.1.1.4** The cytapheresis session is scheduled according to the urgency of the request and the availability of both the donor and the donor center. Any request specified as urgent must be explained and justified.

**8.4.1.1.5** **Only one session of lymphapheresis** can be organized. If needed, a second apheresis may be carried out after at least one month period, upon explicit request of the transplant physician and after the donor has been informed and agreed.

**8.4.1.1.6** The cytapheresis product may be sent to the Cell Therapy laboratory of the Transplant Centre by :

- either a Transport Company habilitated and approved by the EFS of the cytapheresis site, if the donation is dedicated to a national patient,
- or a person designated by the Transplant Centre, if the donation is dedicated to an international patient.

**8.4.1.1.7** An export permit must be obtained from the AFSSAPS if the donation is dedicated to an international patient.

**8.4.1.1.8** An acknowledgement of receipt of the cellular product is faxed to FGM by the Transplant Centre upon reception of the product.

**8.4.1.2 Recruitment of a national donor for a second bone marrow donation**

The recruitment procedure is the same as that for a first bone marrow donation (paragraphs 8.1.1 and 8.1.3).

**8.4.1.3 Recruitment of a national donor for a second donation of PBSC**

The recruitment procedure is the same as that for a first donation of PBSC (paragraph 8.3).

CAUTION : a donor having given PBSC as a first donation cannot be solicited for a second PBSC donation, only a bone marrow harvest is possible.

**Recruitment of an international donor**

8.4.2.1 In the case of an international donor, each Registry, through its own Medical expert Committee, will consider and decide upon any second donation request made for a national patient.

8.4.2.2 All mandatory infectious disease markers (decree n° 97-928 of 9 October 1997 and decree N° 2003-1153 of 28 November 2003) must have been tested either by the International Donor Centre concerned and/or by the Transplant Centre laboratory, before the cell product transfusion may be given to the patient (paragraph 8.1.2).

8.4.2.3 In the case of a donation of PBSC or lymphocytes (DLI) an import permit must be obtained from the AFSSAPS. The Cell Therapy Laboratory of the transplant centre must, before shipment, must obtain from the AFSSAPS an import permit, with respect to the decree N° 2000-156 of 23 February 2000, and must inform FGM consequently.

8.4.2.4 The FGM Director, in the name of the Biomedicine Agency and after having verify the infectious diseases markers results, submits an advice to the AFSSAPS which, if positive, allows the delivery of the import permit.

8.4.2.5 No PBSC may be imported without an authorization from AFSSAPS. It is only upon receipt of this authorization that the shipment of the graft may take place.

**CHAPTER 9**  
**PRESERVATION OF BIOLOGICAL MATERIAL FROM**  
**UNRELATED DONOR AND PATIENT PAIRS**

## 9.1 Purpose

The purpose of the preservation of biological material from potential donors and from donor/patient pairs is to enable their use for future search or research.

**9.1.1** The preserved samples consist of frozen lymphocytes, extracted DNA and serum. Transformed EBV lines are recommended.

**9.1.2** The initial consent form advises the donor of the preservation of biological material which could be used, after the donation, for complementary HLA typing or even for research purposes linked to the transplant performed. The donor signs this form at the time of her/his registration on the National Registry.

**9.1.3** A sample of the donor' serum, dated day 0 from the collection, may be kept for the purpose of performing retrospectively infectious disease markers testing, if needed.

## 9.2 Site of preservation

### 9.2.1 Donor Centre laboratory

The extracted DNA is used to carry out additional HLA typings, after having verified the acceptance of the concerned donor to proceed.

### 9.2.2 Receiving Centre laboratory

**9.2.3.1** The biological material necessary to extract DNA and to constitute cell lines of the **donor**, is collected either during the weeks preceding the HSC collection or on the day of the collection itself, for both national and international donors. The request is made on the HSC collection prescription form.

**9.2.3.2** The biological material necessary to extract DNA and to constitute cell lines of the **patient**, is collected outside the periods of relapse and conditioning.

**9.2.3.3** A quantity of at least 2 cryo tubes, each containing  $5 \times 10^6$  viable cells for both donor and patient is preserved according to the current procedure,

**9.2.3.4** The biological material of the donor/patient pair is preserved according to the recommendations published in various protocol studies (e.g. Histocompatibility Workshop).

**9.2.3.5** A blood sample of the donor/patient pair is preserved according to current legislation.

**CHAPTER 10**  
**ORGANIZATION OF HEMATOPOIETIC**  
**STEM CELLS COLLECTIONS**

## **10.1 Organization of bone marrow harvests**

The Harvesting Centres are habilitated hospitals authorized by competent authorities to carry out bone marrow harvests (decree n° 97-306 of 1<sup>st</sup> April 1997). They have the qualified personnel and the technical equipment necessary for this organization.

Each Donor Centre is geographically linked to an Harvesting Centre with which it organizes bone marrow harvests from recruited donors.

The Harvesting Centre's responsibility is to take in charge the hospitalization of the donor, the bone marrow harvest, as well as the immediate and short-term follow-up of the donor (during hospitalization and the first year thereafter).

### **10.1.1 Evaluation and pre-donation check-up of bone marrow donors**

Bone marrow donors, having accepted the principle of a bone marrow donation, undergo a clinical and biological check-up, leading to validation or invalidation of their aptitude to donate bone marrow.

**10.1.1.1** A complete clinical evaluation is carried out additionally to the anesthetic consultation during the month prior to the scheduled bone marrow harvest. This check-up is carried out by a physician who is not a member of the transplant team, in order to avoid any conflict of interest.

Donors presenting counter-indications to bone marrow donation are deferred (list of counter-indications available on SYRENAD).

**10.1.1.2** During this consultation, biological blood tests are carried out, including at least :

- blood group (ABO/Rh),
- blood cell count/hemogram,
- coagulation tests,
- Pregnancy test for every female donor of child bearing age performed 7 days prior to the beginning of the patient's conditioning (paragraph B6.6, standards JACIE, 3<sup>rd</sup> version)
- mandatory infectious disease markers (form 014).

**10.1.1.3** One or two whole blood collections for auto-transfusion purposes are made, only if necessary (hemoglobin level equal or less than 11g/l), for further infusion during the marrow harvest,. These blood collections can be made 2 or 3 weeks before the bone marrow donation.

**10.1.1.4** The President of the Magistrate's Court of the donor's locality of residence has the responsibility (cf. Bioethics laws of July 1994 and August 2004) to

get the donor's final consent, to validate her/his understanding of the process, her/his willingness to respect the anonymity of the donation and to verify the absence of any moral pressure.

The quantity of bone marrow requested by the transplant physician is validated by the harvesting physician, according to the body weight of the donor (see paragraph 8.1.1.4)

The theoretical quantity of bone marrow to be harvested must not endanger the health of the donor. It is communicated, as an estimation, to the transplant physician, for his information, before the beginning of the patient's conditioning (form 017/ Validation of bone marrow prescription). If there is a discrepancy between the quantity expected by the transplant physician and the quantity likely to be harvested by the harvesting physician (lower quantity), the transplant physician decides :

- either to accept the lower quantity suggested,
- to choose another source of HSC (PBSC), if the donor agrees
- or to release this donor and select another compatible donor, if any.

**10.1.1.5** Upon request from the Transplant Centre, a blood sample from the donor may be despatched during the month prior to donation, to carry out complementary tests.

**10.1.1.6** Upon request from the Donor Centre, FGM insures the donor against all pre-, per- and post-risks which may be related to the marrow harvest. This insurance policy remains valid for 3 years post-harvest (form 022).

## **10.1.2 Bone marrow harvests**

### **10.1.2.1 Hospitalization of the donor**

**10.1.2.1.1** The donor is hospitalized the day before the harvest, in a surgical or medical unit, for a total period of 48 hours.

**10.1.2.1.2** No expenses related to the organization of the marrow harvest will remain at the charge of the donor (decree n° 2000-409 of 11 May 2000).

**10.1.2.1.3** The donor will be attributed, if possible, a single room with telephone and television.

**10.1.2.1.4** The donor is monitored by the staff of the unit which will prepare her/him for the marrow harvest. She/he must not be considered as a patient.

### **10.1.2.2 Harvest of the donor**

**10.1.2.2.1** The marrow harvest is carried out in an operating theatre.

**10.1.2.2.2** Except for special cases (clearly explained to the donor before the harvest), the harvesting is performed on the **posterior** left and right iliac crests. Harvesting on anterior iliac crests may only be carried out in case of absolute necessity and only if the donor has been made aware and has agreed upon this principle prior to the collection.

Harvesting bone marrow at the sternum level is strictly **forbidden** (practical modalities of rules of Good Practices pertaining to bone marrow donation/ transplantation from an unrelated volunteer donor // EfG/SFGM-TC, 21 March 2000).

**10.1.2.2.3** The marrow harvest takes into consideration the quantity of marrow requested by the transplant physician and approved by the harvesting physician, and the eventual constraints related to the quality of the donor's marrow (rich or poor cell count).

**10.1.2.2.4** The harvesting physician must specify if the harvested marrow has been filtered or not, in the operating theatre (form 023).

**10.1.2.2.5** Upon written explicit request from the transplant physician, blood samples from the donor can be drawn, for complementary tests, immediately after the bone marrow harvest. They will be included for despatch with the marrow bags.

It is however recommended, even if no request has been made, to systematically send 5 ml of donor blood, collected without anticoagulant, in the perspective of an eventual retrospective serological survey (blood sample at day 0 of the HSC harvest).

**10.1.2.2.6** If blood for auto-transfusion has been previously collected from the donor, it will be transfused back to her/him during the marrow harvest.

**10.1.2.2.7** The bone marrow harvest is carried out under general anesthesia (exceptionally under epidural anesthesia).

**10.1.2.2.8** The marrow is harvested using the anti-coagulant and medium specified by the transplant physician. If the type of anti-coagulant to be used has not been specified, ACD is automatically used (specific bags).

**10.1.2.2.9** Neither manipulation of the marrow, nor cryopreservation, must be carried out at the harvesting site, (except in case of specific and explicit request

made by the transplant physician, validated by FGM and approved by the collection centre's cell therapy laboratory).

### **10.1.2.3 Packaging of the harvested marrow**

**10.1.2.3.1** The harvested marrow is put into appropriate bags of 600 ml each. The total volume of marrow and anti-coagulant must not exceed 500ml. Bags must not be inflated.

**10.1.2.3.2** These bags are immediately and individually labeled, with stickers directly provided by FGM, in accordance with the decree n° 2000-156 dated 26 February 2000.

The following details are mandatory mentioned on the stickers :

- type of human product (Bone Marrow)
- complete address of the Harvesting Centre,
- donor's ID code,
- temperature to be respected during transportation (for bone marrow = room temperature, ie between 18°C and 24°C or in accordance with the specific request of the transplant physician, if any),
- patient's name,
- date and time of harvest,
- complete address of the Transplant Centre.

**10.1.2.3.3** The following documents must travel with the marrow bags :

- a copy of the infectious disease markers/Donor Final Clearance form. This form is dated and signed by the physician responsible for the donor's final validation,
- FGM form 023, duly completed by the harvesting physician and mentioning the following :
  - total number of nucleated cells harvested and anti-coagulant used,
  - marrow filtered, or not,
  - number of blood tubes provided, if any,
  - remarks concerning the quality of the marrow (rich or poor) or particular circumstances which may have occurred during the harvest.

**10.1.2.3.4** The bags are wrapped in protective device (surgical gauze or quilted paper). Each bag is packaged individually in a closed plastic bag. Blood tubes are placed in a specific package to avoid contact of glass with the bags in case of broken glass.

**10.1.2.3.5** Bags are subsequently placed, with the blood tubes, if any, in a special isotherm container, brought by the courier him/her-self which must ensure optimal conditions during transportation (see chapter 11), at room temperature (between 18°C and 24°C) or in accordance with the specific request of the transplant physician),

**10.1.2.3.6** The donor's anonymity must be completely respected. In no case the first and last names of the donor must appear on the marrow bags or on the blood tubes. Only the donor's ID code must be used.

### **10.1.3 Immediate follow-up of the donor**

**10.1.3.1** The donor remains in the hospital for the next 24 hours after the donation.

**10.1.3.2** Questionnaires are given to the donor to collect her/his feelings and comments about her/his experience before, during and after her/his marrow donation. These documents, to be completed immediately as well as one month after the donation, are meant as a satisfaction survey and are analyzed as such by FGM (forms available on SYRENAD). If necessary, corrective and preventive measures can be taken.

**10.1.3.3** The harvesting physician or a member of the harvesting team will visit the donor after the donation, in order to reply to any question she/he may have.

**10.1.3.4** A member of the Donor Centre will visit the donor before her/his release from hospital, to make sure that the harvesting and its immediate follow-up have been satisfactory.

**10.1.3.5** The donor must be informed of the eventuality of donating again cells to the same patient in a variable time frame. In case of refusal, this information is immediately transmitted to the concerned transplant center by the FGM Registry.

**10.1.3.6** A sick leave is usually prescribed to the donor (Circular letter DSS/DH/DGS/2000 N° 357 of 30 June 2000). Its duration varies with the donor's job and the speed of her/his recovery. It normally covers an average period of one week.

**10.1.3.7** The donor is informed that he must call the donor centre in case of any health issues, occurring even a long time after donation.

**10.1.3.8** A letter must be sent to the donor's physician by the donor centre or the harvesting physician in order to inform her/him of the donation and the follow up to be performed.

## **10.2 Organization of peripheral blood stem cells collections**

The Collection Centres are Blood Transfusion Centres or habilitated hospitals authorized to carry out PBSC collections. They have the qualified personnel and the technical equipment necessary for this organization.

Each Donor Centre is geographically linked to a Collection Centre with which it organizes PBSC collections for recruited donors.

The Collection Centre's responsibility is to take in charge the organization of the collection, as well as the immediate follow-up of the donor.

### **10.2.1 Evaluation and pre-donation check-up of PBSC donors**

**10.2.1.1** PBSC donors **must be under 51 years of age** (Ministerial Order relative to Good Practices for collection, dated 16 December 1998).

Donors must not present any counter-indications to the injection of growth factors (list of counter-indications available on SYRENAD).

**10.2.1.2** An evaluation of peripheral veinous access is carried out by the cytapheresis physician.

**10.2.1.3** A complete and detailed explanation of the preparative procedure for PBSC collection is given to the donor, who is also given time to think about the donation before taking her/his final decision. A document called "PBSC donation" is also provided to the donor.

**10.2.1.4** The donor remains free to accept or refuse at any time this type of donation.

**10.2.1.5** A medical check-up performed by an hematologist is scheduled the month prior to the PBSC collection. Donors presenting counter-indications to the injection of growth factors are deferred.

At this time :

- the hematologist writes a medical prescription for the growth factors (recommended dose : 10 µg/day/Kg of donor's body weight divided in 2 sub-cutaneous injections/day (morning and evening), for a recommended

duration period of 5 days. Injections can be made at the donor's home by a registered nurse,

- the hematologist writes additionally a prescription for a blood cell count to be performed at day+3 after the beginning of the growth factor injections.
- the donor signs her/his formal final consent to a PBSC donation. This document is co-signed by the physician (form available on SYRENAD).
- A document attesting of the donor medical clearance is sent by the hematologist to the donor centre (form available on SYRENAD).

**10.2.1.6** The donor's consent does not have to be registered at the local Magistrate's Court. However, this procedure is strongly recommended in case of the possible organization, on an urgent basis, of a bone marrow harvest if

- the donor has not mobilized properly and sufficiently,
- there is a peripheral venous access problem during the cytopheresis
- there are signs of serious thrombocytopenia occurring during the collection.

**10.2.1.7** The donor must consequently be informed of the possibility of having to make a bone marrow donation in emergency if the PBSC collection procedure fails.

**10.2.1.8** A biological and serological blood check-up is carried out, including at least :

- blood group (ABO/Rh),
- blood cell count/hemogram,
- mandatory infectious disease markers,
- coagulation tests (decision of the physician prescribing the growth factors).

**10.2.1.9** One or two sessions (maximum) of cytopheresis, with a one-day interval, are scheduled depending on the total number of CD34<sup>+</sup> cells requested by the transplant physician.

**10.2.1.10** The quantity of PBSC requested by the transplant physician is validated beforehand by the physician who will carry out the cytopheresis. The quantity of PBSC (and so the number of cytopheresis) is evaluated and communicated to the transplant physician, **before** the beginning of the patient's conditioning.

**10.2.1.11** Upon request from the Transplant Centre, a blood sample from the donor may be despatched during the month prior to donation, to carry out complementary tests.

**10.2.1.12** FGM contracts for the donor a specific risk insurance related specifically to the PBSC collection. This insurance policy remains valid for a 10 years period post-collection. The transplant centre must inform the FGM physicians and/or the donor center of any health issue leading to postponing or canceling the transplant, in particular within the 5 days when the donor undergoes growth factor injections.

## **10.2.2 PBSC collection**

### **10.2.2.1. Reception of the donor**

**10.2.2.1.1** The donor has received, over a period of 5 days, subcutaneous injections of growth factors 2 times per day (morning and evening), prescribed by the hematologist. If the blood cell count performed at day + 3 shows a number of white blood cells higher than 70 000/mm<sup>3</sup>, the harvest must be organized earlier, in the morning of day + 4.

The donor receives a questionnaire allowing her/him to daily report and measure secondary effects occurring during the injections period (form available on SYRENAD).

**10.2.2.1.2** The donor is provided with a phone number to call in case of an emergency or any issues. Moreover, the donor centre must have the phone number of the donor (mobile if possible) in order to be able to contact him/her in case of an emergency linked to the patient (health deterioration and harvest cancelled during donor preparation).

**10.2.2.1.3** The donor goes to the Collection Centre on the day of the first session of cytopheresis and is then totally managed by the collection team.

### **10.2.2.2. Collecting the PBSC**

**10.2.2.2.1** The PBSC collection is carried out in a habilitated establishment, staffed by competent personnel, at day + 5 (except if the donor cell count at day +3 justifies an earlier cytopheresis).

**10.2.2.2.2** The installation and the monitoring of the donor, as well as the duration of the cytopheresis, follow the current procedures of the establishment.

- 10.2.2.2.3** If there is a problem occurring during the collection, it is not recommended to install a central line. The transplant physician having been informed, the donor must be made ready to donate bone marrow (see paragraph 10.1.2).
- 10.2.2.2.4** Upon written, explicit request from the transplant physician, blood samples from the donor can be drawn, on the day of the PBSC collection, for complementary tests. They will be included for despatch with the PBSC bags.
- 10.2.2.2.5** The validation of the cytopheresis product, the total cell count and the quality controls are performed on the day of the collection by the cell processing unit corresponding to the harvesting center and are made available to the transplant centre, as soon as obtained.
- 10.2.2.2.6** If the expected quantity of CD34+ cells has not been obtained in one cytopheresis session, a second session is organized the following day.
- 10.2.2.2.7** If it appears evident that 2 cytopheresis sessions will be necessary (high amount of CD34+ cells expected), it is recommended to organize the first session in the afternoon of the first day and the second session in the morning of the second day. This will reduce the delay of conservation of the 1st graft and make the transport of the graft easier.
- 10.2.2.2.8** Neither manipulation nor cryopreservation of the graft is carried out at the collection site (except prearranged and explicit request made by the transplant physician, validated by FGM and approved by the collecting physician's cell therapy laboratory).

### **10.2.2.3. Packaging of the PBSC collection**

- 10.2.2.3.1** The graft is put into appropriate bags.
- 10.2.2.3.2** These bags are immediately and individually labeled, with stickers exclusively provided by FGM, in accordance with the decree N° 2000-156 dated 26 February 2000.

The following details are mentioned on the stickers :

- type of human product (PBSC)
- complete address of the Collection Centre,
- donor's ID code,
- temperature to be respected during transportation (Ministerial Order of 16 December 1998),

- patient's name,
- date and time of collection(s),
- complete address of the Transplant Centre.

**10.2.2.3.3** The following documents are accompanying the graft :

- a copy of the infectious disease markers/Donor Final Clearance form. The form is dated and signed by the physician responsible for the donor,
- FGM form 023, duly completed by the cell processing unit of the collecting physician and mentioning the following :
  - Total number of CD34<sup>+</sup> cells collected and anti-coagulant used,
  - number of blood tubes provided, if any,
  - remarks concerning the quality of the graft (rich, poor...) and any undercurrent event occurred at the time of harvest.

**10.2.2.3.4** The bags are wrapped in protective device (surgical gauze or quilted paper). Each bag is packaged individually in a closed plastic bag. Blood tubes are placed in a specific package to avoid contact of glass with the bags, in case of broken glass.

**10.2.2.3.5** The bags are subsequently placed, with the blood tubes if any, in a special isotherm container which will ensure optimal conditions during transportation (see chapter 11), at the temperature rate expected by the transplant physician.

**10.2.2.3.6** The donor's anonymity must be completely respected. In no cases the first and last names of the donor must appear on the bags or on the blood tubes. Only the ID code of the donor must be used.

### **10.2.1.13 Immediate follow-up of the donor (see chapter 12)**

**10.2.2.4.1** The immediate follow-up of the donor is ensured by the Collection Centre and the Donor Centre who contact the donor at her/his place of residence, one week after the donation, to enquire after her/his well-being. A blood cell count is performed at day + 8. In case of problem, it is controlled 1 month later, and again until normalization.

**10.2.2.4.2** Follow-up questionnaires are given to the donor on the day of the collection, to gather her/his feelings and comments about her/his

experiences before, during and after the PBSC collection (form available on SYRENAD).

The documents to be completed immediately, as well as one month after the donation, are considered as a satisfaction survey and are analyzed as such by FGM. If necessary, corrective and preventive measures will be taken.

**10.2.2.4.3** The donor center is asked to insure an annual follow up to occur by phone at the anniversary of the donation using a pre-established follow up questionnaire (form available on SYRENAD). The warning is automatically sent by SYRENAD at the anniversary date of the collection.

**10.2.2.4.4** A sick leave is sometimes prescribed to the donor. Its duration varies with the donor's job and the speed of her/his recovery.

### **10.3 Organization of lymphocytes collection (DLI)**

A lymphocyte collection can occur a long time after a 1st donation, upon the request of the transplant physician (2nd donation request forms). The emergency level, if any must be motivated.

The Collection Centres are Blood Transfusion Centres or habilitated hospitals authorized to carry out cytapheresis. They have the qualified personnel and the technical equipment necessary for this organization.

Each Donor Centre is geographically linked to a Collection Centre with which it organizes lymphocyte collections from recruited donors.

The Collection Centre's responsibility is to take in charge the organization of the collection as well as the immediate follow-up of the donor.

#### **10.3.1 Evaluation and pre-donation check-up of PBSC donors**

**10.3.1.1** Lymphocyte donors must be under 51 years of age (Ministerial Order relative to Good Practices for collection, dated 16 December 1998). However, in a 2<sup>nd</sup> donation context, as a donor can have exceeded the age limit several years after 1<sup>st</sup> donation, and if a lymphocyte donation seems to be the best therapeutic option for the patient, an exception is allowed by the AFSSAPS upon written request.

**10.3.1.2** Donors must present neither medical nor cytapheresis counter-indications (list of counter-indications available on SYRENAD).

- 10.3.1.3** An evaluation of the peripheral venous access of the donor is carried out by the cytapheresis physician.
- 10.3.1.4** A complete and detailed explanation of the preparative procedure for lymphocyte collection is given to the donor, who is also given time to think about the procedure before taking her/his final decision.
- 10.3.1.5** The donor remains free to accept or refuse at any time this type of donation.
- 10.3.1.6** A medical check-up performed by an hematologist is organized **the month prior to the lymphocyte collection.**
- 10.3.1.7** The donor's consent does not have to be registered at the local Magistrate's Court. The centre performing the cytapheresis will ask the donor to sign the usual consent in place in the establishment.
- 10.3.1.8** A biological and serological blood check-up is carried out, including at least :
- blood group (ABO/Rh),
  - blood cell count/hemogram,
  - mandatory infectious disease markers,
  - pregnancy test for every female donor in child bearing age, performed 7 days prior the beginning of the patients' conditioning (paragraph B6.6, standards JACIE, 3rd version)
  - coagulation tests
- 10.3.1.9** Only one session of lymphapheresis will be scheduled. If needed, a 2<sup>nd</sup> session will be organized, upon formal request of the transplant physician, at least 1 month after the first one, after informing and obtaining a consent from the donor.
- 10.3.1.10** The cytapheresis product must be dispatched to the cell processing unit :
- By an habilitated courier company authorized by the establishment where cytapheresis takes place, in case of a national patient ;
  - By a person designed by the transplant centre, for an international patient.
- 10.3.1.11** An export permit must have been obtained from the AFSSAPS if the patient is international.
- 10.3.1.12** An acknowledgement receipt is sent by fax by the transplant centre to RFGM (form 023) upon reception of the cells.

**CHAPTER 11**  
**TRANSPORTATION OF HEMATOPOIETIC STEM CELLS**

## 11.1 Transportation of bone marrow and PBSC grafts

- 11.1.1** Each graft is transported by a person nominated and delegated by the transplant physician, who must ensure that he/she has received the appropriate training on HSC transportation (WMDA standard).. This person (the courier) is responsible for the transportation of the graft from the Collection Centre to the Transplant Centre.
- 11.1.2** In case of a national collection occurring for a national patient, the courier may, depending on the distance between the Harvesting and Transplant Centres, arrive at the collection site either on the day of the harvest or on the day before, according to arrangements made with the harvesting physician.
- 11.1.3** All measures must be taken to have the graft transported within 12 to 36 hours. The travel time must not exceed 72 hours.
- 11.1.4** Nominated documents are prepared by FGM. The HSC prescription and the donor infectious disease markers results are handed over to the courier in order to facilitate the conveyance of the graft. These documents are to be shown to any person entitled at the airport security check-point to verify the type of product being conveyed.
- 11.1.5** The graft is transported, at the temperature rate prescribed by the transplant physician, in an isotherm container, mandatory labelled in order to ensure the traceability of the product.
- 11.1.6** The labels are affixed to the outside of the container and mention :
- type of product of human origin being transported,
  - name, address and telephone number of the Collection Centre,
  - donor's ID code and patient's name,
  - name, address and telephone number of the Transplant Centre,
  - date of collection(s),
  - emergency phone number to call in case of problem.
- 11.1.7** If the graft is transported by air, it must absolutely not be x-rayed when going through the airport security area. It may be shown to and handled with care by the airport authorities. The isotherm container may be **emptied** to be x-rayed but once the graft has been put back into the container, it must remain at all time with the courier in the aircraft.
- 11.1.8** The courier must :

- have been trained appropriately and clearly informed of her/his mission particularly on the potential risks of deterioration of the graft during transport,
- have a sense of responsibility and a practical mind,
- be in possession of valid travel documents (identity card or passport with visas if necessary),
- be fluent in English (international transport only),
- be in possession of a credit card (international),
- be in possession of a mobile phone (tri or quadri band)
- be in possession of the telephone numbers of the persons to be contacted in case of any emergency or problem,
- mention her/his presence upon arrival in the harvest location,
- present her/himself on arrival at the Collection Centre,
- make sure that the graft does not go through an x-ray machine,
- never allow her/himself to be separated, for any reason, from the container during the entire transport,
- cooperate with all relevant transport authorities,
- strictly respects the donor/patient anonymity (see Bioethics laws of July 1944 and August 2004)
- keep and show, when necessary, the nominative documents attesting of her/his mission,
- hand over the graft personally to an identified member of the transplant team, or an identified member of the cell processing unit if requested,
- attest to FGM that the graft has been delivered to the Transplant Centre (form 023).

**11.1.9** The courier is in possession of the import/export permit form delivered by the AFSSAPS.

**11.1.10** The courier with the graft normally travel by rail or air (according to distances), exceptionally by road. The courier must not transport the graft by car if he/she is the driver of the car.

**11.1.9.1** In case of air transport :

FGM faxes the appropriate documents to the airport authorities, 24 hours in advance, for the following purposes :

- to signal the importation or exportation of a graft of human origin,

- to request all airport personnel to assist the courier if needed, to facilitate her/his journey in case of any unexpected problems (delays, flight cancellations, etc...) particularly when there is a correspondance involved in the travel itinerary.

**11.1.9.2** In the case of rail transport :

FGM notifies the rail authorities only when it concerns an international transport (Eurostar, Thalys, etc...).

## **11.2 Transportation of cord blood units**

### **11.2.1 National cord blood units**

**11.2.1.1** National cord blood units are transported in adequate dry-shippers from the Bank of origin or storage, to the cell processing unit of the requesting Transplant Centre, using the services of an FGM-accredited Transport Company, either May Courier International for the most part of destinations, or World Courier for destination not covered by the first one. Both of them are adequately and specifically insured against any cord blood damages risks .

**11.2.1.2** A dry-shipper can contain 1 but even 2 cord blood units if both of them are dedicated to the same patient (with the formal agreement of the transplant physician).

**11.2.1.3** Cord blood units are transported by road, rail or air by the courier company.

**11.2.1.3.1** Road transport is used for short distances. The dry-shipper containing the cryo-preserved unit is transported door-to-door by the driver, after having been placed in a **strict vertical position** in the car.

**11.2.1.3.2** Rail or air transport involves :

- transportation of the dry-shipper by the Transport Company, from the Bank of origin to the closest railway station or airport,
- reception of the dry-shipper by the dedicated personnel of the Transport Company upon arrival of the train or aircraft at its final destination,
- transportation of the dry-shipper by the dedicated personnel of the Transport Company to the Transplant Centre,
- the dry-shipper must be sealed and locked up, and kept strictly in a vertical position.

## **11.2.2 International cord blood units**

**11.2.1.1** International cord blood units are transported in adequate dry-shippers from the International Bank of origin to the national Transplant Centre, using the services of a transport company chosen by the International Bank or eventually, by the transport company (ies) accredited by FGM.

**11.2.1.2** Import permit for these cord blood units must have been obtained by AFSSAPS before entry on the national territory.

## **11.2.3 Dry-shipper**

**11.2.3.1** The laboratory receiving the CBU must take the unit out of the dry-shipper immediately after reception in way to check its good condition. The emptied dry-shipper must be immediately returned to its bank of origin in its original packaging. If the CBU was maintained in a metallic rack, and if the laboratory doesn't need it to preserve the unit until thawing, it must be sent back together with the dry-shipper.

**11.2.3.2** Alternatively, a dry-shipper may be lent by the Transplant Centre. This must remain an exception. It is then transported empty from the Transplant Centre to the Cord Blood Bank where the unit is located. Upon reception, the dry-shipper is then conditioned, prepared and sent back loaded, with the unit, to the Transplant Centre.

## **11.3 Transportation of lymphocytes**

**11.3.1** The lymphocytes collected for a second donation are transported in an isotherm container at the temperature rate specified by the transplant physician, in accordance in France with the published good practices (Ministerial Order of 16 December 1998).

**11.3.2** When the product is collected from a national donor for a national patient, transportation may be carried out by a dedicated Transport Company, selected and habilitated by the Harvesting Centre, in conformity with the specifications established by the EFS (French Blood Establishment). It represents a door-to-door transportation respectful of the previously agreed conditions and deadlines.

**11.3.3** When the product is collected from a national donor for an international patient, or vice-versa, the transportation of lymphocytes must be handled by a person designated by the Transplant Centre.

An import or export permit must have been obtained from the AFSSAPS.

**11.3.4** The traceability of the transported product must be managed in the same way than that for an HSC graft (see paragraph 11.1).

The date and time of the collection must be noted on the document accompanying the lymphocytes.

A copy of the mononucleated cells or CD3 cells count and the results of the infectious disease markers, must accompany the collected product.

**CHAPTER 12**  
**POST-DONATION FOLLOW-UP**

## **12.1 Immediate post-donation follow-up of donors**

All serious events and adverse effects related to the donor or to the product are reported anonymously to the WMDA SEAR/SPEAR by FGM every 3 months, according to current WMDA procedure.

### **12.1.1 Marrow donors**

**12.1.1.1** The Harvesting Centre is responsible for the care of the donor on the day of the harvest and during the entire length of her/his hospitalization.

**12.1.1.2** After the donor has been released from the hospital, the Donor Centre telephones her/him, approximately one week after the donation, to enquire about her/his health status.

**12.1.1.3** The donor is informed that should she/he have any problem or feel unexpectedly tired, she/he must contact, as soon as possible, the physician in charge at the Donor Centre, who will, if necessary, alert the Harvesting Centre and the FGM Registry.

FGM would then make a declaration to its insurance company, which would consequently open a specific dossier.

A biovigilance declaration to the AFSSAPS must be undertaken by the official biovigilance correspondent of the donor or harvesting centre (with a copy to FGM). If the problem is likely to have an effect on the health of the transplanted patient, FGM will inform immediately the transplant physician or the International Registry concerned. The AFSSAPS is kept informed of the patient's follow up.

**12.1.1.4** Any unrelated french donor having donated bone marrow is immediately deleted from the local and national donor data base. This donor, therefore, cannot be requested for another patient.

**12.1.1.5** Follow up questionnaires are given to the harvested donor to be completed immediately, as well as one month after the donation (forms available on SYRENAD).

### **12.1.2 PBSC donors**

**12.1.2.1** The Collection Centre is responsible for the care of the donor on the day of the harvest and during the entire length of her/his stay at the cytopheresis centre.

- 12.1.2.2** After the donor has left the centre, the Donor Centre must telephone her/him 8 days after the donation, to enquire about her/his health status.
- 12.1.2.3** The donor is informed that should she/he have any problem or feel unexpectedly tired, she/he must immediately contact the physician in charge at the Donor Centre, who will if necessary, alert the collection Centre, the hematologist and the FGM Registry.
- FGM will make a declaration to the insurance company and a dossier will be immediately opened. A biovigilance declaration to the AFSSAPS must be undertaken by the biovigilance correspondent of the donor or collection centre (with a copy to FGM). If the problem is likely to have an effect on the health of the transplanted patient, FGM informs immediately the transplant physician or the International Registry concerned. The AFSSAPS is kept informed of the patient's follow up.
- 12.1.2.4** Any unrelated donor having donated PBSC is immediately deleted from the local and national donor data base. This donor, therefore, cannot be requested for another patient.
- 12.1.2.5** Follow up questionnaires are given to the donor to be completed immediately as well as one month after his/her donation (forms available on SYRENAD).
- 12.1.2.6** The donor centre fills annually, at the birthday date of the donation, a long term follow up questionnaire, completed via a telephone conversation between the physician in charge at the donor centre and the concerned donor (form available on SYRENAD).

## **12.2 Long term follow up of HSC donors**

- 12.2.1** Unrelated stem cell donors must be annually followed up.
- 12.2.2** SYRENAD informs automatically the donor centre of the anniversary of donation by sending a reminding message (bone marrow or PBSC).
- 12.2.3** The physician in charge at the donor centre calls the concerned donor in order to get information about his/her health status since donation. It must be an open and convivial phone call.
- 12.2.4** A questionnaire containing open questions (available on SYRENAD) must be completed at this time by the physician, according to the donor responses. The name of the person who performs this follow up must be clearly mentioned on the questionnaire that must be dated and signed.
- 12.2.5** The completed annual follow up questionnaire is :

- entered on SYRENAD in the donor file
- sent by fax to the FGM physicians for information and action if needed

**12.2.6** In case of a problem likely to be linked to the donation, FGM previously informed by the donor centre, makes a declaration to its insurance company (paragraph 12.1.1.3).

**12.2.7** The donor centre must ensure during this contact with the donor that it still has his/her correct address(es) and phone number(s).

### **12.3 National donors solicited for a second/subsequent donation**

**12.3.1** Second/subsequent donation for the same patient

**12.3.1.1** Requests for three types of second/subsequent donation may arise, within a timeframe varying from one month to several years post-donation :

- request for a bone marrow harvest,
- request for a PBSC collection,
- request for a peripheral lymphocytes collection (DLI).

**12.3.1.2** A donor who already donated PBSC as first donation cannot be approached for a second / subsequent PBSC donation. Only bone marrow harvest or lymphocytes donation may be possible.

**12.3.1.3** The request coming from the Transplant Centre is immediately reviewed by the FGM's internal expert Committee.

**12.3.1.4** In case of a positive decision, the request is forwarded to the Donor Centre concerned, who will then contact the donor in order to obtain her/his answer.

**12.3.1.5** The validation check-up of the donor is the same as that carried out for a first donation.

**12.3.1.6** Marrow or PBSC grafts must be transported under the responsibility of a person selected and nominated by the transplant physician.

**12.3.1.7** If the transport only occurs in France, lymphocytes (DLI) may be transported, unaccompanied, by an habilitated Transport Company. The decision remains with the transplant physician.

## **12.4 Evolution of patients**

**12.4.1** The patients' follow-up is monitored by FGM only in the case of international patients who have received a graft from national donors (bone marrow, PBSC or cord blood unit).

A synthetic follow-up form (cf WMDA recommendations) is sent to the Transplant Centre for completion and return to FGM who will subsequently forward it to the Donor Centre or the cord blood bank for their information.

**12.4.2** The follow-up of national patients transplanted with national donors is under the responsibility of the SFGM-TC (French Society of Marrow Transplant and Cellular Therapy).

**12.4.3** The follow-up of national patients transplanted from international donors is similar to a transmission of information on the outcome of transplanted patients, made upon request of the International Registry which has facilitated the HSC harvest.

This transmission of information comes within the framework of international cooperation defined by the WMDA.

**12.4.4** The follow-up of national patients transplanted with national or international cord blood units is under the responsibility of EUROCORD

**CHAPTER 13**  
**DONOR INSURANCE AND EXPENSES REIMBURSEMENT**

## **13.1 Insuring donors**

### **13.1.1 Insuring potential donors**

FGM has contracted, with its private insurance company, a policy covering civil liability for unrelated volunteer donors. The contract has been concluded between the Biomedicine Agency and AXA Insurance.

**13.1.2** The donors are insured by the FGM Registry for their trip to and from the Donor Centre, made necessary for the organization of the medical examination, which needs to be performed prior to their registration into the National Registry.

**13.1.3** The donors are also insured against any incidents or accidents linked to both the blood drawn preceding their registration and the complementary medical tests which may be requested by a national transplant physician or an International Registry.

## **13.2 Insuring donors recruited for an HSC donation**

**13.2.1** After the final validation of the donor's aptitude by the physician in charge, a request to insure the donor is sent to FGM by the Donor Centre (form 020)

**13.2.2** The FGM Registry sends to its insurance company a nominative declaration of harvesting for the concerned donor, giving the precise date(s) of the planned collection(s) and the type of cells to be collected.

**13.2.3** The contract stipulates that any incident which may be linked to the donation must be declared within 3 years following the date of a bone marrow harvest and within 10 years following the date of a PBSC collection.

**13.2.4** Any incident must be immediately declared to FGM who will register it and transmit the declaration to its insurance company.

**13.2.5** After an evaluation made by experts nominated by the insurance company, the amount estimated for the damages is paid to the donor, before the precise damages responsibility has been undertaken, only if a relation cause/effect is demonstrated.

**13.2.6** In case of a damages request, the search for the responsible body/entity or bodies/entities is undertaken by the FGM insurance company.

## **13.3 Donor expenses reimbursement**

Current legislation stipulates that travel and hotel expenses as well as losses of salary occurring in the frame of organization of a HSC collection must be reimbursed to

donors (Public Health Code, articles R1211-2 to R1211-10 and circular letter DSS/DH/DGS N° 2000-357 of 30 June 2000).

### **13.3.1 Reimbursing the donor**

The donor is reimbursed by the centre which performed the stem cell collection upon presentation of written proofs, for:

- travel expenses related to:
  - tests performed before and after the harvest,
  - journey undertaken for declaration of consent at the Magistrate's Court.
- losses of salary
- hotel expenses

A document established by the FGM Registry and indicating the terms of the reimbursement procedure is available upon request and is regularly updated according to instructions submitted by the administration.

### **13.3.2 Invoicing the Transplant Centre**

#### 13.3.2.1 Donation for a national patient

The Collection Center then invoices the Transplant Centre for the total amount paid out.

#### 13.3.2.2 Donation for an international patient

The total amount paid out by the Collection Center is then invoiced to the FGM Registry, which is the intermediary in administrative and financial matters between French centers and International Registries.

**CHAPTER 14**  
**CONFIDENTIALITY / ANONYMITY**

## **14.1 Generalities**

In conformity with current legislation, donation of any human products including of course hematopoietic stem cells is in France strictly anonymous. At the time of her/his registration on the national Registry, the donor agrees on the principle of never seeking for the identity of the patient and respecting strictly the principle of anonymity.

In other countries the patient may, after a certain time varying from Registry to Registry, meet her/his donor and some publicity may be made around this meeting.

Nevertheless, the respect of anonymity in France extends to both international patients and donors.

## **14.2 Respect of donor anonymity while exchanging information between Donor Centres and Receiving/Transplant Centres**

**14.2.1** No document, due to be exchanged between a Donor Centre and a Receiving/Transplant Centre, may carry nominative identification of the donor.

The donor must always be mentioned by her/his ID code, automatically attributed by SYRENAD at the time of her/his registration on the Registry.

**14.2.2** No document may carry on the same page both the nominative identity of the patient and the nominative identity of the donor.

**14.2.3** Only the donor insurance request forms, exclusively sent by the Donor Centre to the attention of FGM before any collection of hematopoietic cells, mention the name and first name of the concerned donor (cf: nominative insurance).

**14.2.4** Blood samples exchanged must only carry the ID code of the donor or the code of the patient.

## **14.3 Respect of donor anonymity while collecting hematopoietic cells**

**14.3.1** Grafts are labelled with the ID code of the donor and the name of the patient. The name of the donor must never be mentioned.

**14.3.2** All documents necessary for the transportation of hematopoietic cells are handed over to the person responsible for this transportation.

**14.3.3** Anonymous correspondence may be allowed between a donor and a patient but must transit via FGM who is responsible of ensuring the strict respect of the anonymity (cf: bio-ethics law dated july 1994 and august 2004).

#### **14.4 Respect of donor anonymity during her/his hospitalization for bone marrow harvest (decree n° 2000-409 dated 11 May 2000)**

In order to preserve the anonymity of the donor, her/his hospitalization must not bring about any request whatsoever for financial compensation from the Social Security Centre responsible for this donor.

#### **14.5 Respect of confidentiality clauses**

- 14.5.1** No information of a personal, professional, family or medical nature, concerning an HSC donor or patient may be communicated to a Receiving/Transplant Centre or a Donor Centre.
- 14.5.2** If a donor is deferred at the time of an HSC work-up, the precise reason(s) for this deferral must not be shared.
- 14.5.3** Any positive infectious disease marker result must, after verification, be immediately and confidentially communicated to the donor, and if requested by the donor, to his/her personal physician.
- 14.5.4** The persons responsible for the transportation of hematopoietic cells must strictly obey to the rules of anonymity observance between donor and patient and to the rules of confidentiality observance.

**CHAPTER 15**  
**CRYOPRESERVATION OF HEMATOPOIETIC STEM CELLS**

- 15.1** The cryopreservation of HSC, collected from an unrelated donor, can only be foreseen upon an explicit and well-argued written request from the Transplant Centre, accepted by the FGM Registry (Good Practices of harvest, FGM/EfG March 2000).
- 15.2** No cryopreservation of HSC may be carried out without the concerned donor having been informed of this project and having agreed upon it.
- 15.3** In case of a collection date conflict, linked to a real incompatibility between the availability of the donor and the optimal date of patient's transplant, cryopreservation of HSC can be accepted by the Registry and consequently carried out by the Transplant Centre upon reception of the graft.
- 15.4** The cryopreservation of HSC may be, only upon explicit request from the transplant centre, validated by FGM and the donor centre, carried out in France before departure of the graft from the collection centre.
- 15.5** In all cases, the decision to cryopreserve HSC must be taken consensually between the transplant centre, the donor centre and FGM.
- 15.6** The date (or time-frame) of transplant is given by the transplant physician before the collection and cryopreservation of the HSC.
- 15.7** The transplant physician informs FGM of any postponement of the transplant date and gives the reasons for this delay. A new date, or period, is given. This information is immediately communicated to the donor centre or to the international Registry concerned.
- 15.8** After cryopreservation, when the transplant has finally been carried out, the transplant physician informs FGM in order that the donor centre or the international Registry be advised. The patient's file is then closed.
- 15.9** The Registry must be informed of the cryopreservation of any portion of a graft made for the purpose of performing, if ever needed, an ulterior transplant.
- 15.10** In case of patient health deterioration prior to the initially scheduled transplant date, the transplant physician must immediately inform the FGM physicians (emergency phone numbers available) or even the concerned International Registry if an emergency phone number has been provided.
- 15.11** In this context, the donor preparation must not continue and the harvest process must not take place for cryopreservation purpose, except if the donor centre or the International Registry has precisely agreed.